Scientific Publications Compendium

2017·**2018**·2019

Nestlé HealthScience

Prologue

Dear Reader,

In 2018, Nestlé Health Science contributed to a number of scientific publications covering a broad spectrum of clinical conditions. I am now pleased to share with you this booklet, which summarises these publications as well as those contributed by the worldwide scientific community.

As an innovative health science company, we strongly believe in leveraging and investing in leading-edge science. We strive to forge a new industry, based on inherently safe nutritional therapies, which improve quality of life and provide clinical and health economic value. Our aim is to maximise the role of nutrition in empowering healthier lives.

I also take this opportunity to thank all the experts involved in this work, namely Healthcare Professionals, Institutions and Nestlé Health Science colleagues. Our meaningful scientific partnership will positively impact patients and consumers' lives.

I hope you will enjoy the read.

Best regards,

Moreno Perugini, MBA, MHE
Global Head of Medical Affairs and Market Access
Nestlé Health Science

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Pediatrics

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Summary of study protocol

Protocol for the validation of sensitivity and specificity of the Cow's Milk related Symptom Score (CoMiSS) against open food challenge in a single blinded, prospective, multicentre trial in infants

Vandenplas Y, Mukherjee R, Dupont C, Eigenmann P, Høst A, Kuitunen M, Ribes-Koninkx C, Shah N, Szajewska H, von Berg A, Heine R and Zhao Z, on behalf the Chinese CoMiSS Investigator Team

BMJ Open. 2018 May 17;8(5):e019968

https://www.ncbi.nlm.nih.gov/pubmed/29773698

• Background

The diagnosis of Cow's milk protein allergy (CMPA) in infants can be hampered by non-specific symptoms leading to a misdiagnosis and further delayed diagnosis as a result. Non-IgE-mediated CMPA is diagnosed through a 2-4 week elimination diet followed by an oral food challenge (OFC). Improved methods of identifying CMPA-related symptoms may improve the time to diagnosis, thus reducing clinical impact. The Cow's Milk-related Symptom Score (CoMiSS) aims to increase awareness of CMPA and may be used by primary care practitioners to aid earlier diagnosis. This report describes a study protocol, designed to assess whether CoMISS can be used as a diagnostic tool for CMPA.

• Methods

A prospective study will be carried out in 10 centres in China. Infants aged 0-6 months, exclusively formula-fed, with symptoms indicative of CMPA will be included. A standardised symptom scorecard will be completed at baseline. All infants will be initiated onto a 2-week protocol consisting of an amino acid based formula. No cow's milk protein will be permitted during this phase. Infants will then go through an OFC in a hospital environment, using a standard cow's milk formula, followed by an open home challenge over the following 2 weeks. CoMISS will be determined at study entry and will be repeated at week 2 (before the initial OFC), and either at week 4 (at the end of the 2-week, home OFC phase), or when symptoms of CMPA reappear. Infant weight and length will be monitored at each time point. The accuracy of the CoMISS baseline score in predicting the result of the OFC will be calculated.

Review Summary

Lactose intolerance and gastrointestinal cow's milk allergy in infants and children – common misconceptions revisited

Heine R, AlRefaee F, Bachina P, De Leon J, Geng L, Gong S, Madrazo J, Ngamphaiboon J, Ong C and Rogacion J

World Allergy Organization Journal (2017) 10:41

https://www.ncbi.nlm.nih.gov/pubmed/29270244

The aim of this review paper was to provide an overview of the physiology, diagnosis and treatment of lactose intolerance (LI) in infants, as well as addressing confusion around the diagnosis and treatment approaches for LI and cow's milk allergy (CMA).

Lactose, the predominant carbohydrate in mammalian milk, needs to be hydrolysed by lactase before being absorbed in the gastrointestinal system. Full-term infants can produce enough lactose to digest approximately 1 litre per day of breast milk. Malabsorption of lactose in infants has been linked with beneficial probiotic effects, for example development of a gut microbiota rich in *Bifidobacterium*. In many human populations, production of lactase declines from full-term birth. This lactose non-persistence (LNP) affects approximately 70% of the world's population and is the leading cause of LI. Primary LI often first becomes apparent after the age of 5 and when present in younger children, is commonly as a result of underlying gastrointestinal conditions, for example viral gastroenteritis, giardiasis, cow's milk enteropathy, celiac disease or Crohn's disease. Under this scenario, LI often resolves as the underlying condition improves and may not represent a permanent intolerance.

Misdiagnosis, as a result of confusion between LI and CMA in children and infants, can result in inappropriate dietary management and unnecessary restriction of dairy based foods, with associated impact on nutrition. Treatment of LI in infants should involve reduction of foods containing lactose, but complete elimination should be avoided. By contrast, most infants with suspected CMA, can tolerate lactose, (except when an enteropathy with secondary lactase deficiency is present) and require a different approach, involving a total elimination of cow's milk protein from their diet.

Congress Proceedings Summary

Nutritional modulation: disease management in paediatric Crohn's disease

Ruemmele F, Russell R, de Ridder L, van Limbergen J, Navas López VM and Sigall-Boneh R

Combined Satellite Symposia Proceedings, ESPGHAN, 12th May 2017, Prague | PIBD, 14th September 2017, Barcelona

Appropriate management of nutrition is increasingly recognised as a crucial component in the effective management of Crohn's disease (CD). Exclusive enteral nutrition (EEN) is a widely recommended approach in paediatric patients with CD. The observed short-term clinical benefits include initiation of clinical remission, mucosal and transmural healing as well as longer-term benefits including reduced rates of relapse and long-term avoidance of corticosteroids. More general benefits such as a positive effect on growth and nutritional status, improved bone health and better health-related quality of life have also been reported.

Despite the body of research supporting the use of EEN in CD, little is known about its mode of action. Changes in gut microbiota are known to accompany CD. To evaluate the interconnected roles of gut microbiota and the influence of nutritional therapy, a novel method, nutrinomics, has been proposed. This will involve the evaluation of metagenomics, transcriptomics, and metabolomics in patients with CD treated with EEN. Potential outcomes from this work could include identification of clinical and microbiome markers, leading to tailored management of CD.

Several barriers to the adoption of EEN have been identified. These may be overcome through the adoption of enabling strategies. Examples include improved education of healthcare professionals, highlighting the efficacy of EEN on clinical outcomes, improved communication with patients and their carers and improved patient support services for example home support. These interventions will require a multi-disciplinary approach and should include the advice of a dietician. These measures may improve the rates of uptake of EEN leading to meaningful clinical and humanistic benefits.

Study Summary

Diagnosis and management of cow's milk protein allergy - how big is the gap between ideal and reality? A quality-of-care survey in Europe

Werkstetter K, Chmielewska A, Dolinšek J, Estourgie-van, Burk F, Korponay-Szabó I, Kurppa K, Mišak Z, Papadopoulou A, Popp A, Ribes-Konickx C, Szentes B, Szitányi P, Theisen A, Troncone R, Veres G, West C and Koletzko S

Congress abstract: ESPGHAN, 51st Annual meeting, Geneva, Switzerland, 9-12 May, 2018

https://journals.lww.com/jpgn/Documents/ESPGHAN2018_Abstract%20Book_JPGN_FINAL_2018%2004%2006.pdf

• Background

Guidelines for the diagnosis and management of cow's milk protein allergy (CMPA) were published by ESPGHAN in 2012. The aim of this study was to assess the extent to which these guidelines have been implemented throughout Europe.

• Methods

An anonymous on-line survey, including medical case examples presenting various hypothetical scenarios with multiple choice responses, was sent to paediatricians or general practitioners in 13 European countries between February 2015 to December 2016.

• Results

The survey was completed by 2551 physicians (86.8% paediatricians). When asked how to exclude CMPA in a 10-month old infant with failure to thrive and chronic diarrhoea, 68% of physicians responded that they would adopt an elimination diet and challenge procedure (consistent with the guidelines). Other common responses (not consistent with guidelines) included negative IgE result (19%), skin prick test (8%), or elimination of lactose (5%). When asked which alternative formula would be appropriate for an infant with CMPA refusing extensively hydrolysed formulae (EHF), 63% correctly selected amino acid-based formula and 51% soy-based formulae, but many respondents selected inappropriate formulae (partially hydrolysed, 19%, goat's milk-based, 11% and lactose-free cow's milk based formula, 6%). In a scenario involving a 5-month old, developing swelling of the lips and eyelids after drinking infant formula, following exclusive breast-feeding, only 26% of physicians identified the correct response (resumption of breastfeeding with the usual maternal diet); incorrect responses included resumption of breast-feeding under maternal elimination of dairy products (46% of respondents) switch to EHF (21%) or amino acid-based formula (6%). In terms of complimentary foods for the same child, a higher proportion (53%) of respondents correctly identified that suitable weaning foods should strictly avoid CMP. Other responses included elimination of other allergens until first birthday (15%), offering complementary foods offered from 6-months (25%) and immediate offering of complementary foods with no restrictions (5%). Assuming this child proved negative for specific IgE a variety of responses were recommended including CMP challenge (selected by 46% of physicians), elimination diet up to 12-months (36%), C1-esterase inhibitor deficiency test (6%) and to test IgG against CMP (5%); the remaining 7% thought that CMPA was unlikely in the described scenario.

• Conclusion

Major inconsistencies in the management of CMPA are apparent across Europe including in the testing, implementation of an elimination diet and selection of appropriate infant formulae. Dissemination of education and training is required.

Study Summary

International survey identifies educational needs around the management of infants with cow's milk allergy and lactose intolerance

Madrazo JA, Alrefaee, F, Bachina P, De Leon JC, Geng L, Gong S, Järvi A, Heine RG, Ngamphaiboon J, Ong C and Rogacion JM

Allergy 73 :S105. Congress abstract: European Academy of Allergy and Clinical Immunology Congress, 26–30 May 2018, Munich, Germany

https://onlinelibrary.wiley.com/toc/13989995/2018/73/S105

• Background

Difficulties in differentiating between cow's milk protein allergy (CMPA) and lactose intolerance (LI) can lead to delays in diagnosis or misdiagnosis and appropriate dietary intervention. The aim of this study was to explore the clinical practice and education needs of medical practitioners.

• Methods

A survey was sent to physicians in China, India, Singapore, Thailand, Mexico, Kuwait, United Kingdom, Australia (online) and the Philippines (paper-based). The questionnaire included 12 multiple choice questions, two hypothetical case scenarios and 10 questions on educational needs (Likert scale of 1-5).

• Results

1663 physicians responded, including general practitioners (22%), paediatricians (39.7%) paediatric allergists (6.9%), paediatric gastroenterologists (11.2%) and other specialties (20%). Overall, 62% of participants were confident in their management of CMPA and 61% were confident they could provide a differential diagnosis of CMPA and LI. The questionnaire identified several areas of confusion; although primary LI rarely manifests in infancy, 73.7% of physicians identified it as a significant problem in the first year. Physicians had less knowledge about the management of non-IgE CMA, although management of IgE CMA was relatively well understood. Extensively hydrolysed formula (EHF), the appropriate first-line treatment in infants with CMPA, was correctly identified by 59% of respondents; some confusion relating to the difference between lactose-free and lactose-containing EHF was apparent. Partially-hydrolysed formula was reported by 10.6% of respondents for the management of infants with IgE CMA, which was not consistent with the guidelines. For secondary LI, lactose restriction was accurately recommended as a response to viral gastroenteritis (44% of responses) or cow's milk protein enteropathy (36%). In a case scenario describing CMPA anaphylaxis, only 23.6% of respondents correctly identified the best intervention (amino acid-based formula). 82% of responding physicians were interested in educational support in this area.

• Conclusion

Clinical practice often deviates from gold standard management of CMPA. Targeted medical educational programs may help to promote evidence-based practice.

Study Summary

Extensively hydrolysed formulas for the management of cow's milk protein allergy in infants: is extensive hydrolysis sufficient to guarantee success?

Nutten S, Järvi A, Maynard F, Affolter M, Fryer P and Kuslys M

Allergy 73 :S105. Congress abstract: European Academy of Allergy and Clinical Immunology Congress, Munich, Germany, 26–30 May 2018

https://onlinelibrary.wiley.com/toc/13989995/2018/73/S105

• Background

Most extensively hydrolysed formulae (EHF) are intended for and are expected to be well tolerated for the management of cow's milk protein allergy (CMPA). However, there is currently no aligned definition to characterize EHF and recent studies have reported significant heterogeneity. The aim of this study was to analyse commercially available EHFs in regard to their suitability for CMPA management.

• Methods

Samples of EHF, obtained from 11 countries and representing different manufacturers were assessed. Molecular weight (MW) distribution of hydrolysates and residual proteins and peptide profiling were assessed using SDS-PAGE gels and size exclusion-high-performance liquid chromatography (SE-HPLC). Specific constituents including nitrogen fraction, lactose, total and free amino acids, β-lactoglobulin and casein were quantified.

• Results

Significant variation in peptide MW was observed between samples, with peptides >1.2kDa in size representing between 1 and 36%. MW distribution correlated with β-lactoglobulin. 80% of samples had detectable levels of β-lactoglobulin (i.e. above the limit of quantification of 0.010mg/kg). β-lactoglobulin levels detected in the different samples varied between 0.02mg/kg to 36mg/kg. High levels of residual β-lactoglobulin were evident even in some samples which displayed an otherwise high degree of hydrolysis.

• Conclusion

A wide range of hydrolysis was evident in a variety of commercially available EHF. In some samples, description as 'extensively hydrolysed' may be misleading and the suitability of such formulae in the effective management of CMPA requires further investigation. Although desirable, degree of hydrolysis alone may not be sufficient to define EHF and other quality control measures are needed to ensure the safety and suitablilty of products. Guidelines to better define EHF formulae are required.

Congress Proceedings Summary

Towards Optimised Management of Cow's Milk Protein Allergy

Eigenmann P, Madrazo-de la Garza JA, Nutten S and O'Mahony L

Satellite Symposium proceedings, European Academy of Allergy and Clinical Immunology (EAACI), 28th May 2018
Congress in Munich, Germany
https://secure.viewer.zmags.com/publication/cc49e238#/cc49e238/1

Current management of patients diagnosed with cow's milk protein allergy (CMPA) is suboptimal. Key challenges include the difficulties in obtaining an accurate and timely diagnosis in infants with CMPA who often present with non-specific symptoms. These symptoms can often be consistent with a range of other conditions meaning that CMPA is often misdiagnosed. One of the commonest misdiagnoses is lactose intolerance, which is a rare condition in infants. Improved education of healthcare practitioners is required to aid deeper understanding of the distinctions between CMPA and lactose intolerance and may enable earlier and more accurate diagnosis.

Once diagnosed, management of CMPA requires a dietary intervention through the provision of therapeutic formula such as extensively hydrolysed formulae (eHF). The composition of commercially available formulae has been found to vary considerably and includes large differences in peptide profiles and residual allergenicity. The variability observed, reflects the lack of a definition of eHF composition. Although clinical trials are required to confirm high levels (>90%) of tolerance in infants with CMPA, the composition of the eHF used in the studies is rarely characterised. It is important that these products are subjected to rigorous quality control and are reproducible throughout the product lifecyle, to ensure their safety and suitability. Gradual establishment of a stable gut microbiome is increasingly recognised as an important development over the early years of life. A delay in microbiome maturity can lead to increased risk of developing food allergies. In infants with CMPA, differences in microbiome have been identified. Provision of eHF containing lactose may be an important nutritional strategy to support microbiome establishment in infants with CMPA.

Congress Satellite Symposium Proceedings Summary

Optimising the approach to cow's milk protein allergy: State-of-the-art in food allergy with special focus on cow's milk protein allergy

Järvinen-Seppo K

Nestle Nutrition Institute, Satellite Symposium Summary, ESPGHAN 2018, Geneva, Switzerland

https://www.nestlenutrition-institute.org/docs/default-source/global-dcoument-library/publications/secured/nni-symposium-proceedings-espghan-may-2018---optimising-the-approach-to.pdf?sfvrsn=90ca42ed_0 (free membership required)

The aim of the presentation was to gain a deeper understanding of food allergies, in particular cow's milk protein allergy (CMPA). Between 6-8% of children present with a food allergy and prevalence of CMPA varies from 1-10% depending on the country or region studied, with incidence currently increasing. The principle allergens present in cow's milk include caseins, and whey proteins including β-lactoglobulin and α-lactalbumin. CMPA, can be IgE-mediated, non IgE-mediated, or mixed aetiology, characterised by different symptoms.

IgE-mediated allergy is well characterised and easy to diagnose through a skin prick test. On a molecular level, digested and absorbed allergen proteins are processed by white blood cells, culminating in release of specific IgE antibodies against the specific milk protein, which are then bound on mast cells. Re-exposure to the same allergens, stimulates the release of mediators such as histamine and tryptase, resulting in the allergic symptoms.

Non IgE-mediated CMPA, can cause allergic proctocolitis (in which loose stools appear in infants who are otherwise well) and food protein-induced enterocolitis (FPIES, in which emesis within 4 hours of consumption can occur followed by diahorreal symptoms within 24 hours of ingestion). Mechanisms underlying non-IgE mediated CMPA are less well understood and diagnosis is not based on specific IgE.

Avoidance of cow's milk is the best treatment and alternative nutritional sources may be needed. Prognosis is good and most manifestations of non IgE-mediated CMPA are outgrown during early childhood and in up to 80% of children IgE-mediated CMPA, typically by early adolescence.

Study Summary

Hypoallergenicity of a whey-based, extensively hydrolysed infant formula prepared with non-porcine enzymes

Heine RG, Nowak-Węgrzyn A, Czerkies L, Kuslys M, Nutten S, Simons PJ and Collins B

Congress abstract: FAAM, Copenhagen, Denmark, 18-20 October 2018

NO LINK TO THIS CONGRESS ABSTRACT AVAILABLE

• Background

Extensively hydrolysed formula (EHF) provides important nutritional support in some patients with cow's milk protein allergy (CMPA). The aim of the study was to assess whether a 100% whey-based EHF prepared with non-porcine enzymes could be confirmed as hypoallergenic according to defined criteria.

• Methods

Experimental EHF was produced with a non-porcine enzyme mixture (test formula) and compared with a commercially available EHF produced using porcine enzymes (control). Peptide molecular weight (MW) distribution, residual allergen content and in vitro functional allergenicity were tested. Hypoallergenicity and safety were clinically assessed through double-blind placebo-controlled food challenges (DBPCFC) in children between the ages of 2 months and 8 years with diagnosed CMPA. Following the DBPCFC, patients who had no response to either formula were entered into a one-week challenge with the test formula. Hypoallerginicity was defined as >90% tolerance during this final phase.

• Results

No differences in the MW distribution of the two formulae were observed with no caseins, no intact milk proteins and only trace levels of β-lactoglobulin identified. In vitro tests did not demonstrate any residual allergenicity. In a modified intent-to-treat cohort, 66/67 (98.5%) children with CMPA tolerated the test formula and 67/69 (97.1%) tolerated the control formula. 65 patients continued into the open phase of the clinical study and all 65 patients tolerated the test formula during the 1-week duration.

• Conclusion

A 100% whey-based EHF, produced using non-porcine enzymes, was demonstrated to be hypoallergenic and well tolerated in children with CMPA in Peptide composition and residual allergen content was comparable to commercially available formulae produced using porcine enzymes.

Study Summary

Benefit of oral nutritional supplements for children with acute lymphoblastic leukaemia during remission induction chemotherapy: a quasi-experimental study

Liang R, Chen GY, Fu SX, Zhong J and Ma Y

Asia Pac J Clin Nutr 2018;27(1):144-147

https://www.ncbi.nlm.nih.gov/pubmed/29222892

• Background

Children with acute lymphoblastic leukaemia (ALL) often suffer from malnutrition. This study investigated whether the adoption of oral nutritional supplements (ONS), could improve the nutritional status and be of clinical benefit in children with ALL, undergoing chemotherapy.

• Methods

A prospective single centre study was carried out on 127 paediatric patients diagnosed with ALL undergoing remission-induction chemotherapy. Children were being treated on two wards within the hospital; patients on one ward received ONS (Peptamen®, n=60) while patients on a second ward (control group, n=67) received a low-fat diet with no supplementation.

• Results

Patients in the two groups were equally matched for age and sex and no differences in other clinical parameters were identified between groups at baseline ($p>0.05$). At the end of the study, significantly greater weight-loss was reported in the control group compared with the group who were given ONS ($p<0.05$). Significantly higher serum concentrations of total protein, albumin, and pre-albumin ($p><0.01$) and haemoglobin ($p<0.05$) were observed in the ONS group compared with the control group, suggesting that ONS had improved the patients' nutritional status. Consistent with these finding, the ONS group required fewer interventions such as albumin or blood product infusions. Lower incidence of complications, including hypoalbuminaemia, gastrointestinal complications, and infection were observed in the ONS group ($p<0.05$) and the group receiving ONS, had lower overall hospital costs compared with the control group.

• Conclusion

Provision of ONS may be of benefit to children undergoing remission-induction chemotherapy, through improving nutritional status,helping to avoid complications and reduce the cost of hospitalisation.

Study Summary

Cow's Milk-related Symptom Score as a predictive tool for cow's milk allergy in Indian children aged 0–24 months

Prasad R, Venkata RSA, Ghokale P, Chakravarty P and Anwar F

Asia Pac Allergy. 2018 Oct 17;8(4):e36. doi: 10.5415/apallergy.2018.8.e36
https://www.ncbi.nlm.nih.gov/pubmed/30402403

• Background

Cow's milk protein allergy (CMPA) is a common food allergy among children, which results predominantly in non-specific symptoms potentially leading to delayed or mis-diagnosis. The Cow's Milk-related Symptom Score (CoMiSS) combines information about general, dermatological, gastrointestinal and respiratory symptoms to help identify CMPA and can be used as an awareness tool for use in primary care. The aim of this study was to assess the positive and negative predictive value of CoMiSS in the diagnosis of CMPA in children, in a primary care setting in India.

• Methods

A pilot, multi-centre, randomised study was carried out in India, over a 4-month period. Children between the ages of 0-24 months, who presented with symptoms that could be indicative of CMPA were enrolled. The CoMiSS tool was administered via a pre-determined questionnaire. The presence or absence of CMPA was subsequently confirmed using an oral food challenge, skin prick test or by ImmunoCAP test.

• Results

83 children with symptoms of CMPA were enrolled. The most common symptoms included gastrointestinal (61% of participants), respiratory (41%) and dermatological (33%) complaints. CoMiSS scores >12 were recorded in 72.3% of children of whom 84.3% were confirmed to have CMPA. The CoMiSS tool had a positive predictive value of 93% and a negative predictive value of 33%.

• Conclusion

CoMiSS can be of use to predict CMPA in children below the age of 2 years and may help to hasten diagnosis. Further evaluation of CoMiSS is warranted.

Congress Satellite Symposium Proceedings Summary

Optimising the approach to cow's milk protein allergy: the challenge of correct diagnosis and management of cow's milk protein allergy

Koletzko S

Nestle Nutrition Institute Satellite Symposium Summary, ESPGHAN 2018, Geneva, Switzerland

https://www.nestlenutrition-institute.org/docs/default-source/global-dcoument-library/publications/secured/nni-symposium-proceedings-espghan-may-2018---optimising-the-approach-to.pdf?sfvrsn=90ca42ed_0 (free membership required)

• Background

Reaching a correct and early diagnosis for CMPA is important to ensure appropriate treatment and monitoring but can be challenging due to the wide range of non-specific symptoms with which infants can present. Treatment approaches commonly include avoidance of cow's milk allergens, with nutrition provided from specialised alternative formulae.

• Methods

Guidelines detailing the approach for diagnosis and treatment of CMPA were published by ESPGHAN in 2012. A survey designed to explore the compliance of paediatricians with these guidelines was sent to physicians in 13 European countries and consisted of a number of hypothetical scenarios, with multiple choice answers.

• Results

Over 2500 responses were received. While the main points of treatment for CMPA were understood by the majority of individuals, some aspects of diagnosis and treatment, covered by the guidelines were poorly understood. In infants diagnosed with CMPA who refused extensively hydrolysed formula, appropriate alternatives (soy- or amino acid-based formulae or milk-free baby cereals) were chosen by the majority of respondents but 19% of participants chose partially hydrolysed formula and 11% chose goats milk. These are both inappropriate alternatives since partially hydrolsed formulas are not safe in children with CMPA as they might have an allergic reaction to the whey protein and peptides in these formulas and 90% of children with CMPA also react to goat's milk. In infants being switched from breast milk to standard formula, in whom an allergic response was observed, the recommended approach was to revert to breast-feeding, correctly chosen by 26% of respondents. 46% of respondents agreed with the return to breast-feeding but that the mother should eliminate diary from her own diet, not considered to be necessary by the guidelines.

• Conclusion

The survey demonstrated that certain aspects relating to the treatment and management of CMPA in infants, as outlined in the guidelines, are inconsistently applied.

Congress Satellite Symposium Proceedings Summary

Optimising the approach to cow's milk protein allergy: the gut microbiome in infants with cow's milk protein allergy – implications for treatment

West C

Nestle Nutrition Institute Satellite Symposium Summary, ESPGHAN 2018, Geneva, Switzerland

https://www.nestlenutrition-institute.org/docs/default-source/global-dcoument-library/publications/secured/nni-symposium-proceedings-espghan-may-2018---optimising-the-approach-to.pdf?sfvrsn=90ca42ed_0 (free membership required)

Postnatal exposure of infants, initially mediated via exposure to maternal microbiota during delivery and through breastmilk, promotes oral tolerance to potential food allergens. Early microbiological species that colonise the infant gut include *Bifidobacteria*, with an increasing complexity and diversity of gut microbiota developing throughout early childhood. Low gut biodiversity in infants, along with an over-representation of *Enterobacteriaceae* and under-representation of *Bacteroidaceae* have been associated with subsequent food sensitization. It has been hypothesised that lower proportions of immunomodulatory bacteria (such as *Bacteroidetes* and *Enterobacteriaceae*) may be associated with an exaggerated inflammatory cytokine response and may influence the development of the innate immune response. The microbiome also is understood to influence the development and resolution of CMPA; a difference has been observed in the microbiome of infants in whom CMPA resolved by the age of 6-months, compared with those whose CMPA resolved at a later stage. Early resolution was associated with microbiota enriched with *Clostridia* class, whereas *Bacteroidetes* and *Enterobacter* were seen in subjects whose CMPA did not resolve. This suggests that the developing microbiome can influence both the tolerance to, and persistence of CMPA.

Potential novel approaches to the management of CMPA, include the generation of a tolerogenic environment in the gut through the addition of fibre, pre-, pro-, and synbiotics or lactose to specialty formula. Meta-genomic studies are also needed to provide a more detailed understanding of the functional role of the different species present in both healthy and dysfunctional microbiota.

Study Summary

Experience of using a semi-elemental formula for home enteral nutrition in children: a multicenter cross-sectional study

Leonard M, Caldari D, Mas E, Lambe C, Comte A, Ley D, Peretti N, Borderon C, Marinier E, Coste ME, Lamireau T, Rubio A, Turquet A, Dubern B, Dabadie A, Gautry J, Kyheng M, Guimber D and Gottrand F

Journal of Pediatric Gastroenterology and Nutrition, Publish Ahead of Print; DOI: 10.1097/MPG.0000000000002236

https://www.ncbi.nlm.nih.gov/pubmed/30562309

• Background

The impact of semi-elemental enteral formulas in children is not widely reported. The aim of this study was to describe the tolerance and success rate of the Peptamen Junior® semi elemental formula in children being cared for at home.

• Methods

A retrospective, multicenter survey was carried out on a cohort of 136 patients receiving Peptamen Junior® at home-care settings in 14 tertiary care settings in France. Anthropomorphic characteristics, tolerance and adverse events were recorded at baseline, 3, 6 and 12 months and then at annual intervals. Success of the diet was defined as an increase in body mass index (BMI) z-score during the first 6 months.

• Results

Mean patient age was 9.8 years. Mean BMI z-score was -1.0 and mean height z-score was -1.1 at baseline. The most common indications included digestive (35.3%), neurological (33.1%) and haematological (19.9%) conditions. Semi elemental formula was most commonly initiated because of failure of another diet (51.9%), severe malnutrition (14.1%), cystic fibrosis (8.1%) and switch from parental nutrition (8.1%). Adverse events were recorded in 39.2% of patients, with 8.2% requiring medical attention. The semi elemental formula on average provided 75.6% of the calorific intake of the patients. The success rate of the diet, defined by the proportion of children in whom BMI improved or remained normal, was 88.3%.

• Conclusion

The semi-elemental formula was well tolerated and resulted in improvements in BMI in children managed in a home environment, with a wide range of conditions with malabsorption and/or failing to tolerate a polymeric enteral formula.

Study Summary

Development of a decision aid prototype for parents considering tube feeding for their children

Rivero C, Rodríguez A, Moreno A, Vives I, Layola M, Gabás-Rivera C and Aceituno S

Congress abstract: ISPOR Europe, Barcelona, 10-14 November 2018

https://tools.ispor.org/ScientificPresentationsDatabase/Presentation/86771?pdfid=56260

• Background

It is important for parents to be involved in making decisions regarding their children's medical needs. The aim of this study was to develop and assess a prototype Patient Decision Aid (PDA) to facilitate shared decision making (SDM) with physicians and to support parents considering enteral tube feeding for their children.

• Methods

The approach presented by the International Patient Decision Aids Standards (IPDAS) was adopted during development of the prototype PDA. Firstly, a steering committee was established consisting of 4 paediatric gastroenterologists and 2 parents. Next, a needs and preferences assessment was conducted through reviewing published literature relating to the safety and efficacy of tube feeding as well as discussions in focus groups composed of pediatricians and parents. And finally, the design of the PDA prototype. Prototype PDA design followed an iterative process based on the results of the literature review and input from the focus groups.

• Results

The prototype PDA and its scope included two options, firstly, relating to the initiation of tube feeding and secondly, relating to the option of changing the route of administration (e.g. nasogastric to gastrostomy). The prototype PDA consisted of 3 parts. A section on information included general information on enteral feeding, comparison between different options and frequently asked questions. A section exploring parents' preferences, included a rating system to clarify parental values and concerns. The final section, summarised any current problems with feeding and any particular concerns or gaps, for discussion with the physician.

• Conclusion

A prototype PDA to assist parents in decisions relating to enteral feeding in their children was developed. Following this, there will be 2 other phases of development to verify its acceptance and effectiveness. The developed PDA will be used in clinical practice to encourage stronger SDM while taking into consideration personal values.

Study Summary

The need for developing a decision aid tool about feeding options

López E, Moreno A, Rivero C, Rodríguez A, Vives I, Layola M and Lizán L

Value in Health 20: A762. Congress abstract: ISPOR 20th annual European congress, Glasgow, November 2017

https://www.valueinhealthjournal.com/article/S1098-3015(17)32495-6/pdf

• Background

In this study, we establish the characteristics of feeding options that could potentially steer decisions in changing from oral to enteral tube feeding (ETF) so that it could be incorporated in a Patient Decision Aid (PDA)

• Methods

A systematic search of Medline, the Cochrane library and ISI-WOK was conducted according to the Oxford Centre for Evidence-based medicine levels of evidence. Inclusion criteria included publication between January 1st 2005 and June 6th 2016 in English or Spanish, and studies carried out in Europe or North America.

• Results

742 studies were identified of which 7 were analysed. Thirteen items were identified with potential to influence decisions relating to ETF. Eight of these items had disadvantageous connotations and included loss of food tasting, loss of life normality, loss of independence, loss of social role, feelings of blame, concern about permanently loss of ability to eat, perceived loss of dignity and loss of quality of life. Three items with advantageous connotations included, less time needed for feeding, best caloric control and longer overall survival. The remaining two items had uncertain connotations; potential feeding complications and patient-caregiver relationship during feeding could either be construed as positive or negative depending on the circumstances and the emotional connections between the patient and their caregiver.

• Conclusion

The majority of items that influence the decision of whether to initiate ETF have disadvantageous connotations; this may delay the switch to ETF. A PDA is required to clarify the relative weight of these items and aid decision making.

Review Summary

Assessment of nutritional status and functioning in older adults at risk for mobility disability

Fielding R

Congress abstract: 14th International Congress of the European Geriatric Medicine Society (EuGMS), Berlin, Germany

https://link.springer.com/article/10.1007%2Fs41999-018-0097-4

• Background

Sarcopenia is an age-related condition involving the degenerative loss of muscle mass, resulting in reduced physical ability and increasing need for supportive services. Physiological changes in the ability of muscles to generate force are associated with the condition, in particular changes in the proteins that provide contractile forces, metabolism and neuromuscular activity. Underpinning these changes is an observed increase in turnover of skeletal muscle protein, now a well characterised phenomenon associated with increasing age. Sarcopenia is often associated with inadequate nutritional status; some observational studies have suggested a link between adequate nutritional control, in particular dietary protein and improvements in muscle function. Despite this evidence, efforts are not generally made to assess nutritional status and muscle function in aged individuals with limited mobility.

• Methods

A review of the published literature was conducted to explore the possible mechanisms of how increasing vitamin D and protein in diets may result in improved lean muscle function. Alternative methods of assessing nutritional state and motor skills were also examined.

• Results

Dietary factors, in particular dietary protein, interact with the anabolic metabolic pathways, stimulated by exercise. This anabolic effect is necessary to produce new tissue, including muscle tissue and can also influence body fat distribution.

• Conclusion

Nutritional factors have an important role in the attenuation and minimisation of the effects of age-related sarcopenia.

Study Summary

A comparison of the safety of starch vs. gum based thickening products for patients with post stroke dysphagia

Aldridge CG and Nagaratnam K

Eur Geriatr Med (2018) 9(Suppl 1):1; Congress abstract: 14th International Congress of the European Geriatric Medicine Society, Berlin, Germany, 10-12 October 2018

https://doi.org/10.1007/s41999-018-0097-4

• Background

Dysphagia is a common consequence of stroke, affecting between 50-70% of patients. Management of dysphagia during the acute phase, focusses on compensatory measures, for example modifications to the consistency of food and drink to ease its ingestion. One such measure is the thickening of fluid which can be achieved with thickening agents made either of starch or gum. Several issues with starch-based thickeners, including poor stability, increased viscosity over time and loss of viscosity when in contact with salivary amylase have led to an emerging preference for gum-based thickeners. The aim of this study was to compare compliance of gum-based or starch-based agents to the recommended consistency, following stroke.

• Methods

This study reports an audit carried out on an acute stroke unit. At two separate time periods, either gum-based or starch-based thickening agents were used to thicken patients' drinks, to a recommended consistency according to the recommendation of the SLT. Drinks were placed at the bedside where they were freely available. Fluid consistency of the drinks and its compliance with the recommended fluid consistency, were rated by a qualified SLT.

• Results

22 assessments were completed. Only 11% of drinks thickened with the starch-based agent were found to comply with the specific recommendation provided by the SLT. In comparison, drinks prepared with the gum-based thickening agent were compliant in 92% of cases tested.

• Conclusion

Poor stability of starch-based thickening agents resulted in deviation from the recommended fluid consistency in the majority of cases. Gum-based thickening agents may improve the compliance with fluid consistency.

Study Summary

Effect of vitamin D supplementation on 25(OH)D status in elite athletes with spinal cord injury

Pritchett K, Pritchett R, Stark L, Broad E, and LaCroix M

Int J Sport Nutr Exerc Metab. 2018 Sep 8:1-6
https://www.ncbi.nlm.nih.gov/pubmed/29757043

• Background

A large proportion of athletes with spinal cord injury are believed to have vitamin D deficiency or insufficiency, indicated via low levels of 25(OH)D, a metabolite produced by hydroxylation of vitamin D3. Vitamin D3 deficiency is linked to impaired muscle strength. The aim of the study was to (1) determine if 12 – 16 weeks supplementation of vitamin D3 could moderate the concentration of 25(OH)D and (2) measure if the resulting 25(OH)D status could affect the muscle performance of professional athletes who had sustained spinal cord injury

• Methods

Thirty-four members of the USA and Canadian Paralympic team agreed to participate in the study. Measurement of 25(OH)D concentrations along with a range of performance measures including hand-grip strength and 20m wheelchair sprint, were carried out before and after a vitamin D supplementation protocol. Vitamin D supplements were tailored to initial 25(OH) D concentrations; individuals with vitamin D deficiency (<50nmol/L of 25(OH)D) received vitamin D supplementation at a dose of 50,000IU/week for 8 weeks and individuals with vitamin D insufficiency (50-75nmol/L 25(OH)D) received 35,000IU/week for 4 weeks. Thereafter, all participants, including those with sufficient vitamin D at baseline, received 15,000 IU/week (maintenance dose).

• Results

A significant increase in 25(OH)D concentration was measured following supplementation (66.3 ± 24.3 nmol/L before; 111.3 ± 30.8 nmol/L following supplementation, $p<0.001$) and the proportion of participants with sufficient vitamin concentration increased from 26% pre-supplementation to 91% post-supplementation. An improvement in hand-grip strength was observed in 62% of participants following supplementation. No change in the 20m wheelchair sprint was observed.

• Conclusion

The supplementation protocols used in the study reduced the incidence of vitamin D deficiency and insufficiency in elite athletes with spinal cord injury.

Study Summary

Effects of a systemic enzyme therapy in healthy active adults after exhaustive eccentric exercise: a randomised, two stage, double-blinded, placebo controlled trial

Marzin T, Lorkowski G, Reule C, Rau S Pabst E, Vester J and Pabst H

BMJ Open Sport Exerc Med 2017;2:e000191
https://www.ncbi.nlm.nih.gov/pubmed/28879033

• Background

Exhaustive exercise can reduce the muscle strength during a 48-hour recovery window. Systemic enzyme therapy (SET) may minimize these effects through its anti-inflammatory properties. The aim of this study was to investigate whether administration of SET could improve recovery following exhaustive eccentric exercise.

• Methods

A randomised, placebo-controlled two stage study was conducted; stage 1 consisted of a crossover design (n=28) and stage 2 consisted of a parallel design study (n=44). Participants were given either daily placebo or SET (Wobenzyn) from 72 hours prior, to 72 hours following the isokinetic loading of the quadriceps (an exhaustive eccentric exercise). As a surrogate for the wide-ranging nature of muscle damage brought on by exercise, the main outcome measured was muscle strength of the quadriceps. Biomarkers of muscle metabolism and damage, inflammatory and immune response, and redox status were explored.

• Results

Patients treated with SET in the crossover study (stage 1) retained more muscle strength and recovered faster compared with patients given placebo (p=0.0332). No statistically significant differences were observed in the stage 2 (parallel) study. Improved biomarker profiles were observed in patients treated with SET compared with placebo in a pooled analysis.

• Conclusion

SET applied before and after an exhaustive eccentric exercise event may have a protective effect against temporary, exercise-induced loss of muscle strength. It was also demonstrated to induce greater maximal concentric strength in volunteers from the less strength trained group. SET also has a beneficial effect on the expression of biomarkers relating to inflammation and metabolism. Further investigation is required to fully appreciate the application of these results.

Study Summary

Supplementation with high-dose docosahexaenoic acid increases the Omega-3 index more than high-dose eicosapentaenoic acid

Allaire J, Harrisb W, Vorsa C, Charesta A, Marina J, Harris Jackson K, Tchernof A, Couture P, Lamarche B

Prostaglandins Leukot Essent Fatty Acids. 2017 May;120:8-14
https://www.ncbi.nlm.nih.gov/pubmed/28515020

• Background

The Omega-3 index (O3I), the ratio of eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids on red blood cell (RBC) membranes is known to be inversely correlated with coronary heart disease and coronary mortality. EPA and DHA supplementation, to increase the O3I may therefore reduce cardiovascular risk factors. The aim of this study was to investigate the effect of EPA and DHA supplementation on the O3I in an obese population with subclinical inflammation.

• Methods

A double-blind controlled crossover study was conducted on 48 men and 106 women, each treated sequentially with 3 different supplement regimes. The order in which participants were entered into group 1 (1 - 2.7g/d EPA), group 2 (2 - 2.7g/d DHA) and group 3 (3 - 3g/d corn oil, 0g EPA/DHA) was randomised. Participants were provided with 3x1g capsules to be taken 3x per day for 10-weeks with a 9-week washout phase between each sequential treatment phase. Fatty acids present in RBC membranes and O3I were measured at baseline and at the end of each of the three phases of treatment.

• Results

Both EPA and DHA supplementation caused a significantly increased O3I compared with the corn oil control (+5.6% and +3.3%, respectively; $p<0.0001$); the effect of DHA supplementation was greater than the effect of EPA supplementation ($p<0.0001$). The proportion of docosapentaenoic acid (DPA) present in RBC membranes was increased in participants taking EPA (+2.5%, $p<0.0001$) but decreased in participants taking DHA (-0.8%, $p<0.0001$), compared to control proportions. Women had a higher O3I at baseline compared to men (6.3% vs 5.8%, respectively; $p=0.011$) and the tendency of DHA and EPA to increase the O3I was more pronounced in men than in women (=2.6% vs +2.2%, respectively; $p=0.0537$).

• Conclusion

A more pronounced increase in O3I was observed following supplementation with DHA compared with EPA, suggesting that DHA may have greater potential to reduce the risk of coronary events. The long-term impact on risk, requires further investigation.

Study Summary

Efficacy and tolerance of systemic enzyme therapy in the treatment of acute thrombophlebitis–a randomised double-blind controlled trial

Baumueller M and Rau S

J Phlebol Lymphol. 2018;11(1):7-12.

https://www.pulsus.com/scholarly-articles/efficacy-and-tolerance-of-systemic-enzyme-therapy-in-the-treatment-of-acute-thrombophlebitisa-randomised-doubleblind-controlled-tr-4286.html

• Background

Acute thrombophlebitis, inflammation of the veins as a result of thrombus. Systemic enzyme treatment (SET) has been proposed as a potential treatment option. The aim of this study was to investigate the safety and efficacy of SET in the treatment of thrombophlebitis.

• Methods

A double-blind randomised study was carried out to compare resting pain associated with thrombophlebitis in patients taking SET (n=50) or placebo (n=50). The use of analgesia was permitted however the use of compression therapy was not. Pain, adverse events (AE) and symptoms associated with thrombophlebitis were monitored on days 4, 7 and 14 following commencement of treatment, with resting pain on day 7 as the primary outcome.

• Results

Patients taking SET experienced a greater reduction in resting pain and less pain under pressure, compared to placebo, on all days tested. Specifically, patients taking SET had reduced resting pain compared to placebo, after 7 days of treatment (64% vs 29% respectively; $p<0.0001$). Other symptoms related to thrombophlebitis, including skin redness, hyperthermia, phlebitis cords and sensation of tightness, were all lessened in patients taking SET, compared with placebo. Fewer AE, all of which were either mild or moderate in severity, were reported in the SET group compared with the placebo group, suggesting a favourable safety profile. AEs in the placebo group were predominantly associated with analgesic, reenforcing the need for treatments that can reduce analgesia use.

• Conclusion

SET, in the absence of compression therapy, is a safe and efficacious option in the treatment of thrombophlebitis.

Study Summary

Polyphenols from grape and blueberry improve episodic memory in healthy elderly with lower level of memory performance: a bicentric double-blind, randomised, placebo-controlled clinical study

Bensalem J, Dudonné S, Etchamendy N, Pellay H, Amadieu C, Gaudout D, Dubreuil S, Paradis ME, Pomerleau S, Capuron L, Hudon C, Layé S, Desjardins Y and Pallet V

J Gerontol A Biol Sci Med Sci. 2018 Jul 19. doi: 10.1093/gerona/gly166.

https://www.ncbi.nlm.nih.gov/pubmed/30032176

• Background

Polyphenols may have potential as a supplement to reduce the impact of age-related cognitive decline. The aim of this study was to examine if a grape and blueberry extract (PEGB) which is rich in polyphenol could impact on the memory of healthy 60 – 70 years old healthy elderly participants.

• Methods

A randomised, double-blind study compared the effect of PEGB supplementation against placebo in 215 elderly participants over a 6-month period. The PEGB supplement was administered at a dose of 600mg/day, of which 258mg consisted of flavonoids. Assessments included the CANTAB Paired Associate Learning (PAL) test, to evaluate visuospatial learning and episodic memory, verbal episodic and recognition memory (VRM) and working memory (SSP). Urinary excretion of flavonoids was also monitored.

• Results

Evaluation of the entire population, demonstrated that PEGB supplementation resulted in a significant improvement in VRM free recall, but no significant improvement in PAL responses. The cohort was stratified according to memory performance (PAL) at baseline; participants with advanced cognitive decline at baseline (decliners) were found to have responded well to PEGB supplementation and demonstrated improved VRM delayed recognition after 6-months of supplementation. Decliners were also found to have increased urinary excretion of polyphenol metabolites. The concentration of polyphenol metabolites detected in the urine, and acting as biomarkers for PEGB, were associated with the observed memory improvements.

• Conclusion

PEGB supplementation was found to improve visuospatial and episodic memory in elderly participants, in particular in participants with advanced impaired cognitive function.

Study Summary

Effective alternative to constipation medication in nursing home residents: Libera study

Sobrón Monge I, Imaz González C, Lacarra Jiménez E, Barbosa Robledo A, López Gómez B, Pérez García V, Barcons Vilardell N.

Rev Esp Nutr Hum Diet. 2017; 21(2): 164-73
https://doaj.org/article/89cb859f32c04c708d4f350773b1a86b

• Background

Laxatives are often prescribed in the treatment of constipation but alternatives may be available. This study explored the efficacy of providing desserts rich in fiber and sorbitol on relief of constipation in the elderly.

• Methods

A single-center prospective study was conducted in elderly residents of a nursing home, who required laxatives to treat constipation. The number of days of pharmacological treatment for constipation was recorded for the week prior to the start of the study and this information acted as the baseline measurement. Each patient was given a dessert high in fiber and sorbitol (High-Fibre® Resource Fruit Puree) daily for 7 weeks. The number of days when a laxative was required was monitored and compared with baseline values.

• Results

Forty participants with a median age of 88.5 years (range 72-101 years) were enrolled into the study. Adherence to the protocol was over 94%. Consumption of the desserts resulted in fewer days per week when laxatives were required (3.5 days/week less than baseline) and a 40% reduction in pharmacological intervention for constipation. In addition, gastrointestinal discomfort was reduced and the number of bowel movements increased by 2 per week. The effects were associated with individuals who consumed more than 5 desserts per week, those over 85 years, individuals with poor oral health, and those not suffering from malnutrition or food disorders.

• Conclusion

Provision of a dessert high in fiber and sorbitol may provide a safe and effective alternative to prescription of laxatives, in the elderly.

Study Summary

Nutritional status and healthcare resource use after implementation of a nutritional program for home-based neurological patients with disabilities

Blanco B, Lopez B, Ferrandez M and Gomez N

Clinical Nutrition, 2018 September 37:S108-109. Congress abstract: 40th ESPEN Congress, Madrid, Spain, 1-4 September 2018

https://www.clinicalnutritionjournal.com/article/S0261-5614(18)31691-1/fulltext

• Background

Patients with chronic conditions being cared for at home are at greater risk of being under-nourished resulting from undiagnosed diseases, medication and poor nutrition. Here, we evaluate if the implementation of a nutritional program and subsequent care provision by the Hospital Home Unit of Hospital General Universitario of Elda (Spain), could positively influence the nutritional status of patients as well as the utilisation of healthcare resources.

• Methods

A retrospective analysis of patients records of 100 home-based neurological patients with disabilities was carried out. All patients were participants in the nutritional plan between 2015 and 2017. Nutritional status was assessed 6 months prior and following the implementation of the nutritional plan, using the Malnutritional Universal Screening Tool (MUST) and Mini Nutritional Assessment (MNA®). Outcome measures included body mass index (BMI), weight gain, nutritional parameters and healthcare resource utilisation (hospital admission, length of stay and emergency visits).

• Results

Mean patient age was 78.3 years. Most common diagnoses included acute cerebrovascular accident (15.0%), cerebral haemorrhage (12.0%) and Alzheimer's/dementia (45%). Prior to the nutritional plan, MUST assessment identified 95% of patients as being at risk of malnutrition; MNA identified 71.2% of patients as malnourished with a further 28.8% at risk of malnutrition (mean MNA score of 14.4). Following implementation of the nutrition plan, 52% of the subjects recorded an increase in mean weight (0.56kg; 2.0 SD) and BMI (0.23 kg/m2; 0.8 SD). Nutritional parameters were also reported to be improved after initiating their nutritional plan ($p<0.01$). In addition, a higher proportion of patients required a hospital stay or an emergency visit in the 6 months prior to implementation of the nutritional plan (70% and 79% respectively) compared with during the NP (11% and 28% respectively). Importantly, we have also detected a 94.1% reduction in the hospital length of stay from 7.6 to 0.5 days per patient.

• Conclusion

Implementation of a nutritional plan in home-based patients with neurological conditions improved their nutritional status and reduced healthcare resource utilisation.

Study Summary

Application of the 'Geriatric 8 screening tool' (G8) in cancer patients: a systematic overview of primary studies

Strauß T, Torbahn G, Sieber CC, Volkert D and Kiesswetter E

Internist 2018 · 59 (Suppl 1): S27
https://doi.org/10.1016/j.clnu.2018.06.2065

• Background

A thorough investigation into the general status of an aged individual when planning a new treatment, includes assessment of their psychosocial and functional resources as well as their general health. This can be achieved via completion of the Comprehensive Geriatric Assessment (CGA) tool and its use in conjunction with the Geriatric 8 (G8) screening tool, can help to identify patients with frailty.

• Methods

A systematic review of the published literature was conducted to explore the utility of the G8 when planning treatment options in elderly cancer patients according to a previously published protocol. The databases, Medline, Embase, Central and CINAHL were searched. Clinical trials were also identified from clinicaltrials.gov, International Clinical Trials Registry Platform (ICTRP) of WHO and German Register Clinical Studies (DRKS). Primary studies investigating patients with cancer, in whom the G8 tool was applied, were included. Identification of appropriate studies for inclusion and data extraction was carried out by two independent reviewers; any disagreement was resolved by discussion or by a third person.

• Results

Of 4683 identified studies, 35 were included. Patients were typically 72-83 years. Six studies exclusively reported patients with cancer, whereas in 7 studies treatment options were provided (e.g. chemotherapy, surgical intervention). Impairment (defined as G8<14) was reported in 29 studies and the proportion of impaired individuals varied widely (range 25.6% to 90.8%). Other scales to assess frailty were used in 28 studies and differences were observed dependent on which scale was adopted.

• Conclusion

Although the G8 has been compared with other tools in many studies the high heterogeneity between studied populations limits interpretation.

Study Summary

Patients' and professionals' preferences in terms of the attributes of home enteral nutrition products in Spain. A discrete choice experiment

Olveira G, Martínez-Olmos M, Fernández de Bobadilla B, Ferrer M, Virgili N, Vega B, Blanco M, Layola M, Lizán L, Gozalbo I

European Journal of Clinical Nutrition (2018) 72:272–280
https://www.ncbi.nlm.nih.gov/pubmed/29259337

• Background

Patient compliance to home enteral nutrition (HEN) depends on the preference over certain attributes of the feed by both physicians and patients. In this study, we compare these preferences using a discrete choice experiment (DCE).

• Methods

A discrete choice experiment (DCE) was designed to evaluate participant preferences for different HEN attributes. Participants chose between two hypothetical scenarios presented as 8 choices. Attributes included 'tolerability', 'adaptation to comorbidities', 'nutrition and calories', 'handling' (relating to the container), 'connections' (relating to tubing) and 'information' (i.e. on the packaging). The relative importance (RI) for each of the attributes was calculated. The importance of product features was also explored using a 5-point Likert scale.

• Results

148 patients and 114 physicians completed the DCE. The attributes ranked as most important to patients were 'adaptation to comorbidities' (33%) and 'tolerability' (33%), both given an RI score of 33% and 'nutrition and calories' (26%). Younger patients (<75 years) were more concerned about 'tolerability' whereas elderly patients (>75 years) were more concerned with 'handling' related attributes. Physicians perceived 'tolerability' and 'nutrition and calories' to be more important than patients (p=0.002). Product features related to the packaging such as easy-handling bags (85.1 vs. 64.9%; p = 0.001), container material (69.3 vs. 57.1%; p = 0.003), and reusable containers (79.8 vs. 70.3%; p = 0.01), were considered important or very important in a higher proportion of physicians compared to patients.

• Conclusion

Although physicians' and patients' perceptions of HEN attributes were broadly aligned, some differences were identified. Amalgamation of both perspectives when prescribing HEN, may improve patient satisfaction, adherence and outcomes.

Study Summary

Rasch analysis in the development of the NutriQoL® questionnaire, a specific health-related quality of life instrument for home enteral nutrition

Apezetxea A, Carrillo L, Casanueva F, de la Cuerda C, Cuesta F, Irles J, Virgili M, Layola M and Lizán L

Journal of Patient-Reported Outcomes (2018) 2:25
https://www.ncbi.nlm.nih.gov/pubmed/29888746

• Background

Home enteral nutrition (HEN) is used to help patients who are cared for at home to ingest the appropriate amount of nutrients and calories. This aim of this study was to develop and test a patient-reported tool, to assess health-related quality of life (HRQoL) in a heterogeneous population of patients receiving HEN, regardless of their medical conditions and the method of administering enteral nutrition.

• Methods

A provisional draft of the questionnaire was developed based on findings from a review of the published literature, focus groups and semi-structured interviews. Responses to the provisional questionnaire were analysed according to the Rasch methodology, by assessing the appropriateness of responses, evaluation of the differential item functioning (DIF) and statistic evaluation of infit and outfit (item fit statistics).

• Results

165 responses were assessed to the provisional 43 items included in the questionnaire. Four items were deemed inappropriate for inclusion as they were deemed to be not relevant to >50% of respondents. Seven items were not sufficiently differentiated and poorly categorised and were also removed. Pairwise DIF analysis, conducted on patients grouped by underlying disease and methods of HEN administration, identified 11 items to be removed from the questionnaire. Fit statistics identified an additional four items which were not consistent with the Rasch model and did not belong to any of the questionnaire dimensions. Removal of these items, resulted in a final 17-item questionnaire, hereafter named NutriQoL®.

• Conclusion

NutriQoL is an effective tool to measure and monitor the HRQoL in patients receiving HEN, regardless of different diseases and any method of administration.

Study Summary

Efficacy of TRPA1/M8 agonists to improve the kinematics and the neurophysiology of swallow response in patients with oropharyngeal dysphasia

Alvares-Berdugo D, Tomsen N, Rofes L, Bolivar M, Arreola V, Nascimento V, Martin A, Ortega O, Gosoniu L, Clave P and Michlig S

Congress abstract: 8th European Society for Swallowing Disorders (ESSD), Dublin, Ireland

NO LINK TO THIS CONGRESS ABSTRACT AVAILABLE

• Background

Dysphagia has previously been passively managed, by modifying bolus viscosity. New, active treatments are emerging, such as pharyngeal sensory stimulation through TRP agonists, which may improve the swallow response. The aim of this study was to assess the pharyngeal response to the TRPA1/M8 agonist in patients with neurological diseases or aging.

• Methods

A 3-arm double blind randomised study was conducted on 58 patients with swallow safety impairment as a result of ageing, stroke or neurodegenerative disease (NCT02193438). Patients were given nectar viscosity boluses supplemented with 3 different TRPA1 agonists: 756.6M cinnamaldehyde and 70M zinc (CIN-Zn), 1.6mM citral (CIT) or 1.6mM citral with 1.3mM isopulegol (CIT-ISO). Outcomes included the swallow response, swallow safety and efficacy, analysed by videofluoroscopy (VFS) both prior to and during administration of the interventional bolus. Latency and amplitude of pharyngeal sensory cortical evoked potentials (PSEP) were also analysed by electroencephalography to assess the somatosensory effect of the agonists.

• Results

Treatment with CIN-Zn significantly reduced the penetration-aspiration score ($p=0.009$), the number of penetrations into the airways ($p=0.039$) and reduced the latency of the PSEP at its P2 peak. CIN-Zn and CIT both significantly reduced the time to laryngeal vestibule closure ($p=0.002$ and $p=0.023$, respectively) and upper oesophageal sphincter opening ($p=0.007$, $p=0.035$, respectively). Treatment with CIT-ISO had no significant effects on swallow kinematics and increased the latency of the PSEP.

• Conclusion

Stimulation of TRPA1 with CIN-Zn and CIT resulted in an improvement in swallow response. CIN-Zn resulted in additional improvements in swallow safety. These results suggest that it may be possible to develop treatments to actively target dysphagia through the use of TRPA1 agonists.

Study Summary

Application of the mini-nutritional assessment (MNA)® in cancer patients: a systematic overview of primary studies

Torbahn G, Strauß T, Sieber CC, Volkert D, Kiesswetter E

Internist 2018:59(Suppl 1): S31
DOI 10.1007/s00108-018-0419-y

• Background

The mini nutritional assessment (MNA®) is a tool that can be used to identify nutritional status and the risk of malnutrition. The MNA has been previously validated in elderly patients and in patients with cancer.

• Methods

A systematic review was carried out according a previously published protocol using the databases, Medline, Embase, Central and CINAHL. Relevant clinical studies were also identified using the study registries Clinicaltrials.gov, International Clinical Trials Registry Platform (ICTRP) and the German Register of Clinical Trials (DRKS). Studies reporting cancer patients and the use of MNA were included. Relevant studies were identified, and data was extracted by two independent reviewers. Any disagreement was resolved through discussion or by a third person.

• Results

Of 4683 studies identified by the search strategy, 104 were included in the review. Of these, 64 studies reported the long version (long-form, LF) and 23 reported in the short version (short-form, SF) of the MNA. Seven versions reported both LF and SF versions. Four studies reported modified versions of the MNA, adapted for use among Asian populations. In a further 6 studies the version of the MNA used was not reported. 21 studies reported a patient population over 65 years of age.

Study Summary

Use of Mini Nutritional Assessment (MNA®) in oncological patients – an evidence map

Torbahn G, Strauß T, Sieber CC, Volkert D and Kiesswetter E

Clinical Nutrition, 2018 September 37:S122, Congress abstract: 40th ESPEN Congress, Madrid, Spain, 1-4 September 2018

https://www.clinicalnutritionjournal.com/article/S0261-5614(18)31738-2/fulltext

• Background

The mini nutritional assessment (MNA®) tool can be used to determine the nutritional status of patients, in particular, to screen for patients at risk of malnutrition. MNA can be used across many different clinical indications and settings. The aim of this study was to explore the use of MNA in patients with cancer.

• Methods

A systematic review of the literature was carried out by searching through Medline, Embase, the Cochrane library and CINAHL in June 2017. In addition, references from the identified studies as well as online clinical study registries were also searched. Relevant studies were identified with predefined inclusion criteria, and data was extracted by two independent reviewers using a pilot standardised data extraction form.

• Results

111 studies were included in the analysis of which 71 reported mixed cancer types, 32 with specific cancer and with cancer type that were not extractable. The use of MNA Long Form and MNA Short Form was reported in 86 and 25 studies respectively. The mean age of patients reported in the studies ranged from 28 to 86 years. The percentage of malnutrition was between 0% to 70% in 76 studies. Mean MNA score range of 12 to 25 were reported in MNA Long Form (18 studies) and 9 in MNA short form (1 study). Specific oncologic treatment approaches (e.g. chemotherapy, surgery) were specified in 36 studies. MNA was used to predict outcomes (29/111), to explore associations with other measures (e.g. quality of life, 26/111) and in comparison with other nutritional assessment tools (4/111).

• Conclusion

Published studies suggests that the MNA is a widely used tool in the assessment of risk malnutrition in cancer patients both over and under the age of 65 years.

Study Summary

The exerkine apelin reverses age-associated sarcopenia

Vinel C, Lukjanenko L, Batut A, Deleruyelle S, Pradère J, Le Gonidec S, Dortignac A, Geoffre N, Pereira O, Karaz S, Lee U, Camus M, Chaoui K, Mouisel E, Bigot A, Mouly V, Vigneau M, Pagano A, Chopard A, Pillard F, Guyonnet S, Cesari M, Burlet-Schiltz O, Pahor M, Feige J, Vellas B, Valet P, and Dray C

Nat Med. 2018 Sep;24(9):1360-1371

https://www.ncbi.nlm.nih.gov/pubmed/30061698

• Background

Sarcopenia is an age-related degenerative condition defined by loss of muscle strength and mass which leads to increasing frailty, disability and increasing needs for medical institutionalization for affected elderly individuals.

• Methods

Studies in normal mice investigated age-related changes in expression of the endogenous peptide, apelin. Mice deficient in apelin or its receptor (APLNR) were also investigated. The physical, cellular and biochemical response of apelin and APLNR to exercise was explored in both mice and humans.

• Results

An age-related reduction in apelin was identified in the muscle tissue of both humans and mice. Mice deficient in apelin or its receptor were found to have marked deficiencies in muscle function as they aged, further supporting the role of apelin in age-related sarcopenia. The biochemical response to apelin supplementation included an increase in mitochondriogenesis, autophagy and triggered anti-inflammatory mediators localised in myofibres. Apelin also improved the regenerative capacity of muscle tissue via a stimulatory effect on muscle stem cells. A correlation was found between apelin levels in aged human individuals and their physical performance, suggesting that exercise has a beneficial effect on apelin signaling and muscle function.

• Conclusion

Apelin has an important role in the progression of sarcopenia. Apelin may provide a new target both as a diagnostic tool to identify early sarcopenia, as well as potential for pharmaceutical intervention to reduce age-associated muscle weakness.

Study Summary

Use of health resources and healthcare costs associated with nutritional risk: The FRADEA study

Martínez-Reig M, Aranda-Reneo I, Peña-Longobardo L, Oliva-Moreno J, Barcons-Vilardell N, Hoogendijk E and Abizanda P

Clinical Nutrition, August 2018 37(4):1299-1305
https://www.ncbi.nlm.nih.gov/pubmed/28592356

• Background

Malnutrition in the elderly is highly prevalent and has clear clinical implications, however its economic impact has not been properly investigated. This study explored whether costs associated with hospitalisation, visits to medical specialists, emergency department (ER) visits and overall hospital healthcare could be predicted by nutritional status.

• Methods

Frailty and dependence in Albacete (FRADEA), A cohort study, was carried out in Albacete City, Spain. Patients aged 70 or over were contacted at random and invited to participate. Those who consented (n=827) completed the mini nutritional assessment short-form (MNA-SF®) at baseline, in which scores of 0-7 indicated malnutrition, 8-11 indicated nutritional risk, and 11-14 indicated normal nutrition. Subjects' use of hospital healthcare services and associated costs were recorded at follow up. Generalised linear models (GLM) were used to estimate the impact of malnutrition on healthcare costs (also including costs associated with specialist consultation, emergency care and hospitalisation) and were adjusted for demographic variables including age, sex, comorbidities, pharmacological requirements and their incapacity to perform basic daily activities.

• Results

Mean, overall healthcare costs were €1922 per subject, per year, two-thirds of which (67.2%) was associated with hospitalisation. Malnourished subjects (those with MNA-SF scores of 0-7) had higher annual healthcare costs compared with subjects who were at nutritional risk (MNA®-SF between 8 and 11) or those with adequate nutrition (MNA®-SF between 12 and 14) (€3492 vs €2744 and €1542, respectively). When adjusted for demographic variables, subjects with malnutrition or nutritional risk incurred €714/year more in healthcare costs and were 1.72 times more likely to be hospitalised (OR 1.72, 1.22-2.43) compared with patients with normal nutritional status.

• Conclusion

Malnutrition, as measured by the MNA-SF, can be used to predict healthcare resource utilisation and associated costs, in elderly subjects (those aged 70 and over).

Study Summary

Vitamin B12 deficiency and impaired expression of amnionless during aging

Pannérec A, Migliavacca E, De Castro A, Michaud J, Karaz S, Goulet L, Rezzi S, Ng T, Bosco N, Larbi A and Feige J

J Cachexia Sarcopenia Muscle. 2018 February 9(1):41-52
https://www.ncbi.nlm.nih.gov/pubmed/29159972

• Background

Vitamin B12 deficiency, often caused by poor nutrition, is associated with many age-related conditions and is known to affect the musculo-skeletal system. The aim of this study was to explore the impact of vitamin B12 deficiency on the development of frailty in the elderly.

• Methods

From a subset of the Singapore Longitudinal Aging Study, 238 subjects were stratified by age and degree of frailty, according to the Fried criteria. Molecular mechanisms were explored through measurement of plasma methyl-malonic acid (MMA), a marker which is increased during vitamin B12 deficiency, and amnionless, a protein essential in the intestinal uptake of dietary vitamin B12. The uptake and excretion of vitamin B12 were also explored in the ileum, kidney and liver of a rat model of natural aging under conditions of controlled nutrition.

• Results

A statistically significant increase in MMA was observed in subjects with increasing age and frailty, indicating functional vitamin B12 deficiency (p=0.25; p=0.00013). Lower levels of vitamin B12 were observed in the aged rat model, caused by factors other than nutritional intake; expression of amnionless was reduced in the ileum and kidney of aged rats suggesting reduced intestinal uptake and renal reabsorption of vitamin B12. Circulating amnionless was identified in serum where its concentration increased with age; amnionless concentrations were inversely correlated with vitamin B12 in rats (p=0.0042) and positively correlated with MMA in human subjects (p=0.00068).

• Conclusion

Aging and frailty were found to be associated with vitamin B12 deficiency, caused by factors other than dietary intake. A decrease in the efficiency of intestinal uptake and renal reabsorption was associated with aging. It may be possible to detect changes in vitamin B12 availability through use of serum amnionless as a biomarker.

Study Summary

Special need for and use of texture-modified foods for nursing home residents

Lam P

Congress abstract: 8th European Society for Swallowing Disorders (ESSD) Annual Congress, Dublin, Ireland, September 2018

NO LINK TO THIS CONGRESS ABSTRACT AVAILABLE

Individuals who are long-term residents of nursing homes typically have complex medical needs with many comorbid conditions often accompanied by frailty, disability and dementia. Many individuals are at risk of otopharyngeal dysphagia (OD), which can exacerbate their risk of malnutrition and further worsen their health status.

This increased risk of malnutrition suggests that long-stay residents should be regularly and comprehensively assessed. A personalised patient plan is required to address the individual needs and goals of this heterogenous population. Different plans could focus on prevention, treatment or palliative aspects of care.

Current provision of nutritional support is suboptimal, as evidenced by the high prevalence of malnutrition in nursing homes, in up to 66.5% of residents. Failure to achieve nutritional goals can exacerbate existing medical conditions including OD. Several obstacles have been identified including a lack of investment in diet quality, staffing shortages, leading to reduced assistance with eating and drinking both between and during meal times, insufficient instrumentation and training. There is also a current lack of consensus regarding the diagnosis and management of OD and malnutrition in this population. Above all, there are insufficient drivers to encourage care providers to make changes regardless of their challenging nature.

The aim of the study was to present evidence-based recommendations relating specifically to the management of nursing home residents who require texture modified diets, who are at high risk for OD, aspiration pneumonia and malnutrition. The resulting white paper will be aimed at physicians, nurses, dietitians, nutrition/food service managers and all members of multi-disciplinary teams providing care within the nursing home setting.

Study Summary

Occlusal support, dysphagia, malnutrition and activities of daily living in aged individuals needing long-term care: a path analysis.

Wakabayashi H, Matsushima M, Ichikawa H, Murayama S, Yoshida S, Kaneko M and Mutai R.

J Nutr Health Aging. 2018;22(1):53-58
https://www.ncbi.nlm.nih.gov/pubmed/29300422

• Background

Tooth loss is common in elderly individuals, reducing the number of occluding teeth and the ability to chew. The aim of the study was to investigate four inter-related variables, occlusal support, dysphagia, malnutrition and activities of daily living (ADL) in elderly individuals, using a path analysis methodology.

• Methods

354 participants aged >65 years residing in long-term care facilities, acute care facilities or in their own home, were enrolled. All patients had dysphagia or potential dysphagia. The Dysphagia Severity Scale, the modified Eichner index, the Mini Nutritional Assessment Short-Form and the Barthel index were completed for each participant. Path analysis was conducted to estimate the direct, indirect and total effects of each of the four main variables.

• Results

Mean patient age was 83 years and 66.7% were female (236/354). 216/354 (61%) of patients had functional occlusal support with or without dentures. Only 34/354 (9.6%) had a normal nutritional status, whereas 166 (46.9%) were malnourished and 154 (43.5%) at risk of malnutrition. 73 patients (20.6%) had normal dysphagia. 119 patients (33.6%) displayed dysphagia without aspiration and 162 (45.8%) with aspiration. Median Barthel index score in the total population was 30. Path analysis demonstrated that occlusal support directly impacted on dysphagia (standard coefficient=0.33) and that in turn, dysphagia was directly associated with malnutrition (standard coefficient=0.5). Both dysphagia and malnutrition were directly linked with impairments in ADL (standard co-efficient=0.57; 0.22).

• Conclusion

The results of the study demonstrated that occlusal support was directly associated with dysphagia; this could lead to malnutrition and ADL in an elderly population.

Study Summary

Benefits of a specialised oral supplement in chronic wound healing: a prospective, controlled, and randomised study

Mehl AA, Damiao AOMC, Viana SDDO and Andretta CP

Clinical Nutrition 2018:37;S31

https://www.sciencedirect.com/science/article/pii/S0261561418314407

• Background

Chronic wounds have a considerable impact on healthcare resource and are a significant burden for the patients. Given the role of micronutrients in the healing process, the aim of this study was to investigate the effects of a specific oral nutritional supplement on the healing rate of chronic wounds.

• Methods

A randomised controlled study was carried out on 30 patients with chronic wounds. At baseline, patients were randomised to either receive a standard nutritional supplement or to receive a specialised high protein, high energy supplement containing, arginine, proline, zinc, selenium and high levels of vitamins A, C and E (Novasource®Proline, 200ml twice daily). Wound surface area and perimeter were measured at baseline and weekly for 4 consecutive weeks.

• Results

The 30 patients had 50 wounds, equally randomised between the two arms (both groups contained 15 patients and 25 wounds). 78% of wounds were up to 50cm^2, 14% 50-150cm^2 and 8% were larger than 250cm^2. Patients taking the specialised nutritional supplement had a significantly greater reduction in wound area compared with patients who received the standard supplement (p=0.004) between week 1 and week 2 of the study. The nutritional supplement did not affect blood pressure, glucose control or renal function. The mean weekly distance of healing from the wound edge of 1.85mm in diabetic patients and 3.0mm in non-diabetic patients were measured. These values are higher than expected in similar patient populations.

• Conclusion

The rate of reduction in wound area may be accelerated when patients are given a specialised nutritional supplement compared with a standard supplement.

Study Summary

Development of a non-invasive device for swallow screening in patients at risk of oropharyngeal dysphagia: results from a prospective exploratory study

Steele CM, Mukherjee R, Kortelainen JM, Pölönen H, Jedwab M, Brady SL, Brinkman Theimer K, Langmore S, Riquelme LF, Swigert NB, Bath PM, Goldstein LB, Hughes RL, Leifer D, Lees KR, Meretoja A and Muehlemann N

Dysphagia 2019 (Epub ahead of print)
https://doi.org/10.1007/s00455-018-09974-5

• Background

Dysphagia is prevalent in many at risk population including the elderly, patients who have experienced stroke and those in intensive care. Existing bedside screening tools are suboptimal in early diagnosis of dysphagia. The aim of this study was to evaluate a new algorithm to detect swallowing impairment using an accelerometer-based dysphagia detection system (DDS).

• Methods

A multicenter, prospective study was carried out in 344 individuals in the USA who were considered at risk for dysphagia. A dysphagia detection system, based on dualaxis accelerometry signals were collected during swallows of barium stimuli of varying consistencies (thin, mildly, moderately and extremely thick). Multiple swallows were recorded per individual. Concurrent videofluoroscopy (VFSS) was captured and was used to confirm the extent of the dysphagia. The accelerometry data was used to train the signal processing classifying process, using linear disciminant analysis. The ability of the resulting algorithm to correctly detect impaired swallowing safety, with an area under receiver operating characteristic curve (AUC) of >80% compared to VFSS, was tested.

• Results

When swallowing the thin consistency bolus, impaired swallowing safety was detected in 7.2% of the swallows overall; this involved individual swallows in 19.7% of participants. Swallowing impairment was reduced with increasing thickness of bolus. The DDS was able to correctly identify swallowing impairment with a mean AUC of 81.5%, satisfying the aim of the study. The sensitivity of the algorithm was 90.4% and the specificity was 60.0%.

• Conclusion

The DDS was able to detect impaired swallowing safety in at risk populations and requires further validation.

Study Summary

Hospital costs impact of post ischemic stroke dysphagia: database analyses of hospital discharges in France and Switzerland

Muehlemann N, Jouaneton B, de Leotoing L, Chale J, Fernandes J, Kagi G, Sarikaya H and Arnold M

PLoS ONE 14(1): e0210313.
https://doi.org/10.1371/journal.pone.0210313

• Background

Patients who have suffered a stroke, can experience post-stroke dysphagia; this population are at risk of a higher rate of complications and mortality. The aim of this study was to investigate whether post-stroke dysphagia increased hospital length of stay (LOS) and costs.

• Methods

A retrospective review of databases in France (French Medical Information Service Program) and Switzerland (Swiss Office federal de la statistique database 2012) was conducted to compare LOS following stroke with or without dysphagia. Stroke and dysphagia were identified using diagnostic codes. The databases contained data relating to 62,297 relevant hospital events in the public sector in France and 6,037 in Switzerland. Data were also adjusted to correct for differences in demographics (age and sex) and confounding variables (motor complications or sensory complications).

• Results

8.4% of post-stroke hospital stays in Switzerland and 4.2% in France were associated with dysphagia. The difference in incidence observed, may be a result of inconsistencies between the diagnostic coding systems used in the two countries. A longer LOS was observed in patients with post-stroke dysphagia in both France and Switzerland (23.7 and 14.9 days, respectively) compared with stroke patients who did not have dysphagia (11.8 days and 8.9 days, respectively). Post-stroke dysphagia resulted in increased costs in both countries with increases of €3000 or CHF14,000 respectively. This association between post-stroke dysphagia and increased LOS was independent of demographic variables and sensory or motor complications.

• Conclusion

Post-stroke dysphagia is associated with longer hospital stay and increased costs.

Study Summary

A systematic scoping review on the consequences of stress-related hyperglycaemia

Olariu E, Pooley N, Danel A, Miret M and Preiser J

PLoS One. 2018 Apr 6;13:e0194952
https://www.ncbi.nlm.nih.gov/pubmed/29624594

• Background

Acutely ill patients being cared for in intensive care units (ICU), commonly develop stress-related hyperglycaemia (SHG). There is a growing understanding that SRG is associated with poor outcomes. The aim of this study was to review the current literature on this topic.

• Methods

A systematic review of observational studies reporting SHG along with outcomes including mortality, infection rate, length of stay, duration of ventilation, acquired weakness as well as the need for blood transfusions, or renal replacement therapy was carried out. Studies published between January 2000 and December 2015 were identified following a search of Medline, Embase, and the Cochrane Library, according to the Joanna Briggs methodology.

• Results

3063 studies were identified, of which 43 contained relevant information, relating to over 536,000 patients. Wide variation was observed with the definition of SHG, treatment protocols (including methods of blood glucose measurement and monitoring) and outcome reporting. Most studies (40/43) compared outcomes in patients with, or without SHG; an association between hyperglycaemia and increased mortality was identified in 14 of the 38 studies that reported this outcome, with odds ratios ranging from 1.13 to 2.76. An association between hyperglycaemia and increased length of ICU stay was identified in one of the 23 studies which reported this outcome. Hyperglycaemia was also identified as an independent risk factor for infection, in five studies.

• Conclusion

An association between SHG and poor outcomes was steadily reported but SHG is currently poorly defined and there is little consistency in the measurement, monitoring and reporting of this condition. Standardisation is required to better understand SHG and develop new approaches to its management.

Study Summary

Early introduction of a semi-elemental formula may be cost saving compared to a polymeric formula among critically ill patients requiring enteral nutrition: a cohort cost–consequence model

Curry A, Chadda S, Danel A and Nguyen D

Clinicoecon Outcomes Res. 2018 Jun 5;10:293-300

https://www.ncbi.nlm.nih.gov/pubmed/29892200

• Background

Patients in intensive care units (ICU) who require enteral nutrition (EN) can develop gastrointestinal (GI) intolerance which is associated with poor outcomes. Semi-elemental EN has been used to limit the impact of GI intolerance. The aim of this study was to investigate the cost implications of GI intolerance as well as cost benefits related to early use of semi-elemental formulations in the ICU.

• Methods

A cost-consequence model, based on data from an observational study from the US, compared the financial impact of EN with and without development of GI intolerance. The financial impact of early use of semi-elemental EN, compared with standard formula, was also explored. Standardised costs of ICU care were derived from published literature and costs of EN reflected the cost of the formulae (US price lists). Threshold analysis was used to identify the number of patients in whom intolerance should be avoided before the semi-elemental formula would become cost saving across a cohort of patients.

• Results

31/100 patients in the ICU receiving EN were predicted to develop GI intolerance requiring a median length of ICU stay of 14.4 days compared with 11.3 days in patients without GI intolerance. Avoidance of these additional days in ICU through the use of semi-elemental formula would be cost effective if as few as 7% of patients who developed intolerance, were prevented from doing so through the use of semi-elemental EN.

• Conclusion

Cost-consequence modelling, based on US data, suggests that use of semi-elemental EN instead of standard EN would be cost effective if it causes >7% reduction in incidence of GI intolerance.

Study Summary

Enhanced recovery after surgery: does the provision of an immune-modulating protein supplement improve post-operative outcomes?

Bilbo A, Kavanaugh E, Martin K, Adams D and Morgan K

Congress abstract: ERAS 2018, New Orleans, USA, Nov 8-10, 2018

http://erasusa.org/congress/Program/2018/P18.cgi

• Background

Poor nutritional status is known to adversely affect post-operative outcomes, including length of hospital stay (LOS), surgical site infections (SSI) and the likelihood of hospital readmission. The aim of this study was to assess whether the response to nutritional supplementation was affected by method of funding through comparing patient 'self-pay' funding with grant funding (free to patient).

• Methods

A cross sectional study was carried out in a single centre in the USA. Clinical outcomes, including LOS, SSI and readmission rates, were derived retrospectively. All patients had been instructed to drink an immune-modulating protein supplement (Impact AR®, Nestle™) 3-times daily for 5 days prior to surgery. Patients were divided into those who had been expected to self-pay for the supplement (n=120) and those who had received grant-funded supplements (n=120).

• Results

71.6% of patients receiving grant-funded supplements, reported full compliance with the protocol; 83% of patients in total, drank at least two thirds of their prescribed supplement. A significantly lower LOS was observed in patients who received grant-funded supplements compared with those who were expected to self-pay (6.37 vs 8.3 days respectively, p=0.03). A lower incidence of readmission (14.2% vs 32.5%) and SSI (15.1% vs 29.2%) were also observed in patients receiving grant-funded nutritional supplementation compared with self-pay.

• Conclusion

Provision of nutritional supplements, at no cost to the patient is beneficial in reducing LOS, SSI and rate of readmission compared with 'self-pay' protocols. The cost of the nutritional supplements may be offset by potential savings arising from a reduction in post-operative complications.

Study Summary

Effect of preoperative immunonutrition on postoperative short-term outcomes of patients with head and neck squamous cell carcinoma

Aeberhard C, Mayer C, Meyer S, Mueller SA, Schuetz P, Stanga Z and Giger R

Head Neck. 2018 May;40(5):1057-1067

https://www.ncbi.nlm.nih.gov/pubmed/29368455

• Background

Many patients with head and neck squamous cell carcinoma (HNSCC) develop a poor nutritional status which may negatively affect clinical outcomes. This study explored whether peri-operative immunonutrition could influence clinical outcomes.

• Methods

A retrospective comparative study was carried out in a single centre, before and after adoption of perioperative immunonutrition in the management of patients with HNSCC undergoing elective surgery for their condition. Outcomes of interest included length of hospital stay (LOS), incidence of infections and incidence of overall complications. Regression models were adjusted to account for variables including socio-demographic factors, risk factors, tumour characteristics and comorbidities.

• Results

411 patients were included in the study, 209 in the control group (treated prior to initiation of immunonutrition) and 202 in the intervention group (who received immunonutrition as an adjunct to their surgical management). Hospital LOS was significantly shorter in patients given immunonutrition, compared with the control group (6 vs 8 days; adjusted mean difference of 25.65 days; $p<0.001$). Patients receiving immunonutrition. had significantly lower local infection (7.4% vs 15.3%; adjusted odds ratio 0.3; $p=0.006$).

• Conclusion

Peri-operative immunonutrition can result in shorter LOS and reduced incidence of local infection in patients with HNSCC.

Study Summary

Immunonutrition and pre-surgical wellness, critical elements in the pathway improved outcomes, reduced surgical site infection, length of stay, and readmission independents of enhanced recovery enhancing a proactive culture of safety

Tran B, Gupta V, Strange N and Wooden W

Congress abstract: Annual Congress of Enhanced Recovery and Perioperative Medicine, Washingtom DC, April 27-19, 2017

http://aserhq.org/wp-content/uploads/2017/07/19_ASER_Tran.pdf

• Background

Pre-surgical wellness programs aim to improve outcomes by reducing the rate of post-surgical complications. A Pre-operative Wellness Enhanced Rapid Recovery (POWERR) program was developed, consisting of pre-surgical education, support, and provision of a wellness tool-kit. The aim of this study was to explore outcomes following expansion of the POWERR program in a single institution in the USA.

• Methods

A retrospective chart review of patients who had received the POWERR tool kit was carried out. The tool kit consisted of a 5-day supply of an immunonutritional supplement, smoking cessation, chlorhexidine bath soap, and mupirocin pre-treatment. Outcomes of interest included length of stay (LOS), length of ICU stay, mortality, and surgical site infection (SSI) and were compared to values prior to implementation.

• Results

Following the implementation of the POWERR program, a decrease in LOS was observed consistently across all surgical services, compared with prior to implementation, with over 8000 days of hospital stay collectively recovered since implementation. Compared with pre-implementation, a decrease in LOS index (1.142 vs 1.063), mortality index (1.33 vs 0.97) and mean LOS in the ICU (6.22 days vs 5.99) were observed. The rate of SSI after key high risk surgeries were reduced post-implementation compared with pre-implementation, in colectomy (7.89% vs 1.72%), enterectomy (6.25% vs 0%), gastrectomy (17.14 vs 7.14%), hepatectomy (6.74% vs 2.33%,), pancreatectomy (5.15% to 1.75%) and proctectomy (11.11% vs 0%). Decreases in deep SSI were also observed post-implementation following hepatectomy and pancreatectomy.

• Conclusion

Implementation of the POWERR program dramatically improved post-surgical outcomes following an institution-wide implementation.

Study Summary

Advancing surgical outcomes by providing patients with core elements and standardised preoperative wellness education

Tran B, Gupta V, Strange N and Wooden W

Congress abstract: Annual Congress of Enhanced Recovery and Perioperative Medicine, Washingtom DC, April 27-19, 2017

http://aserhq.org/wp-content/uploads/2017/07/19_ASER_Tran.pdf

• Background

Between 20-50% of patients experience post-surgical infections resulting in significant morbidity and cost. Pre-surgical interventions have been shown to reduce complications. The aim of this study was to report outcomes following initiation of a wellness 'tool-kit' provided to patients during pre-operative screening.

• Methods

A retrospective chart review was conducted in a single institution in the USA. Patients listed for elective surgery, between late 2015 and throughout 2016, attended a Peri-operative Wellness Enhanced Rapid Recovery (POWERR) educational program which consisted of advice regarding exercise and smoking cessation, education about their surgery and provision of the POWERR tool kit (5-day supply of an immunonutrition drink, containing arginine, omega-3 fatty acids and nucleotides incentive spirometer (IS), chlorhexidine soap bath, and mupirocin). The POWERR program was provided free of charge. Compliance to the tool kit was assessed on the day of surgery. Outcomes included length of stay (LOS), surgical site infections (SSI), catheter-associated urinary tract infections (CAUTI), Central-line associated blood stream infections (CLABSI) as well as infections associated with specific organisms (MRSA, VAE, *C. difficile*).

• Results

91% of patients received at least one component of the POWERR program. With an overall compliance rate of 57% (47% compliance with immunonutrition, 50% for IS, 53% for chlorhexidine bath soap and 68% for mupirocin). In patients who were compliant with the POWERR program, a significant decrease in post-surgical complications ($p<0.05$) was observed and the global harm event rate reduced by 39%.

• Conclusion

Compliance with the POWERR program reduced post-surgical complications and global harm event incidence.

Study Summary

Effects of immunonutrition on inflammatory markers and clinical outcomes: a meta-analysis

Periman S, Ochoa J, Brooks L, Ivashchenko AV, Tran ZV

Congress Abstract: ASPEN 2018

https://onlinelibrary.wiley.com/doi/full/10.1002/jpen.1150

• Background

Poor nutritional status is known to impair outcomes following surgery. Immunonutritional supplements, which include arginine, omega-3 fatty acids and nucleotides, have been shown to improve post-surgical outcomes. The aim of this meta-analysis was to explore the impact of immunonutrition on the immune system and clinical outcomes.

• Methods

Randomised studies comparing the immunonutritional supplement IMPACT® (Nestle Health Science, Bridgewater, NJ) with other nutritional formulae were identified. Primary analyses included the measurement of inflammatory markers, blood loss and length of stay (LOS).

• Results

45 studies, most commonly reporting gastrointestinal procedures, were included in the analysis. Compared with alternative nutritional products, levels of interleukin-6 (IL-6, reported in 5 studies), and C-reactive protein (CRP, reported in 4 studies) were reduced by 44.7pg/ml and 45.7mg/ml respectively in patients given immunonutrition. Blood loss was also reduced on average by 15.1ml and LOS reduced by 0.44 days. Higher levels of IL-6 correlated with longer LOS; an increase of 1pg/ml correlated with an extra 0.15 hospital days. Reduced IL-6 levels measured in patients given immunonutrition were not significantly associated with a reduction in LOS (R^2=0.60, p=0.22). Comparison of the timing of administration of immunonutrition demonstrated a benefit of peri and post-operative use (p=0.04). LOS was generally found to reduce over time (since 1995) however the reduction in LOS attributable to immunonutrition, over time, was negligible.

• Conclusion

Immunonutrition can modify innate immunity through a reduction of post-operative IL-6 and CRP. Longer LOS were associated with high levels of IL-6 suggesting that IL-6 may have potential as a predictor of poor post-surgical outcomes.

Study Summary

Improving surgical outcomes in patients undergoing major gastrointestinal and gynecologic surgery with aggressive perioperative immunonutrition

Desai A, Schwartz GH and Bashaw C

Congress abstract: ASPEN Nutrition Science and Practice Conference, Las Vegas, USA, January 22-25, 2018

https://www.nutritioncare.org/Abstracts/

• Background

Inadequate nutrition can contribute to post-surgical complications. The aim of this study was to investigate the effect of immunonutrition in patients with gastrointestinal (GI) or gynecological (GYN) cancer.

• Methods

Patients newly diagnosed with GI or GYN cancer were screened for malnutrition based on a screening tool adapted from the ASPEN guidelines (criteria including severity of ascites, oedema, weight loss, oral intake, fascial fat loss/muscle wasting and skin integrity). Patients who met with 2 or more of the criteria received 500-1000ml per day of an immunonutrient blend product containing arginine, fish oil, nucleotides and antioxidants, for 5-day before and after surgery. Outcomes included length of stay (LOS), post-operative complications and the rate of readmission and were compared with benchmark statistics specific for GI and GYN cancer, including costs of care obtained from NIS/HCUP databases.

• Results

35/51 (65%) screened patients satisfied two or more criteria and were given immunonutrition. Median LOS was 5 days (vs 8.5 days in the benchmark comparative data), post-operative complications were observed in 26% (vs 27.27%) and readmission rate was 8.5% (vs 14.77%). In the 35% of patients who were screened but were not given immunonutrition, worse outcomes were observed compared with the group who received immunonutrition (LOS, 6 days; complications, 40%; readmission, 20%). The observed 1-day decrease in LOS observed in patients taking immunonutrition versus those who were not (5 vs 6 days) would extrapolate to an institute-wide cost saving of $100,136.

• Conclusion

A protocol to identify patients with malnutrition and their treatment with immunonutrition, is cost effective through reduction in LOS, complication rate and readmission rate.

Study Summary

Impact of a novel preoperative patient-centered surgical wellness program

Kelley KE, Fajardo AD, Strange NM, Harmon CA, Pawlecki K, Sieber M, Walke N, Fadel WF, Wooden WA, Sadowski J, Birdas TJ, Stevens LH, Rozycki GS and Schmidt CM

Ann Surg. 2018 Oct;268(4):650-656

https://www.ncbi.nlm.nih.gov/pubmed/30138164

• Background

Post-surgical hospital acquired infections (HAI) are a major source of morbidity and demand a significant amount of clinical resource. The aim of this study was to assess whether provision of a wellness bundle to patients prior to surgery, has potential to improve postoperative outcomes by reducing the incidence of HAI.

• Methods

A single centre study compared a group of surgical patients receiving a wellness bundle (n=12396) to a historic cohort of patients who had received no bundle (n=9202). The wellness bundle, consisting of chlorhexidine bath solution, immunonutrition supplements, incentive spirometer, topical mupirocin for the nostrils, and smoking cessation information, was provided during a pre-operative screening session at an urban medical centre. Outcomes between groups were compared using the Fischer's exact test, logistic regression and Poisson regression.

• Results

Patients in both groups had similar demographics, comorbidities and were undergoing a similar profile of surgical procedures. Patients provided with the wellness bundle, showed a high degree of compliance to individual components of the bundle (80% mupirocin, 72% immuno-nutrition, 71% chlorhexidine bath, 67% spirometer). Post-operative follow-up demonstrated that patients who had received the wellness bundle had a lower incidence of surgical site infections, Clostridium difficile infections and catheter associated urinary tract infections.

• Conclusion

A pre-operative program, consisting of a 'wellness bundle' provided at pre-surgical screening, has the potential to dramatically reduce HAI in surgical patients.

Study Summary

Preop nutrition-enhanced recovery after surgery protocol for thoracic cancer resections decreases hospital days and charges

Robinson L, Tanvetyanon T, Grubbs D, Garcia Getting R and Patel S

Journal of Thoracic Oncology;13:S648–S649. Congress Abstract: IASLC, 19th World Conference on Lung Cancer, Toronto, Canada, 23-26 September 2018

https://www.jto.org/article/S1556-0864(18)31978-6/fulltext

• Background

Adequate pre-operative nutritional status can influence post-operative outcomes. The aim of this study was to compare the impact of the nutrition-enhanced recovery after surgery (N-ERAS) protocol compared with a pre-implementation control cohort, in patients with thoracic cancer.

• Methods

A retrospective comparative study was carried out in 113 patients undergoing surgical resection for thoracic cancer in a single institution. Over a 12-month period all patients were offered a pre-operative nutritional support program comprising of daily probiotics, an immunonutritional drink for 5-days pre-surgery and a drink high in complex carbohydrates provided the night before surgery (the N-ERAS protocol). A historic control included 121 patients undergoing matching surgery performed by same surgical team, in the 12 months immediately preceding the initiation of N-ERAS. Outcomes included length of stay (LOS) and costs.

• Results

No significant differences in demographics were apparent between historic control and N-ERAS groups with the same mean albumin (4.3gm/dl), similar post-bronchodilator %FAV (86.7 vs 89.4, respectively) and similar Charlson co-morbidity index (4.3 vs 4.8, respectively). No empyemas, wound infections or reoperations were required in either group and all patients survived. All patients complied with the N-ERAS protocol with no safety concerns reported. Compared with the historic control, the N-ERAS group had improved outcomes including shorter LOS (median 4 vs 3 days), faster return of bowel function (mean 1.3 vs 1.1 days) and lower total hospital costs ($47403 vs $ 42979) This $4424 (9.3%) saving per patient equated to a cohort wide annual saving of $499912.

• Conclusion

A pre-operative nutritional support program was successful in reducing post-operative LOS and costs in the surgical management of patients with thoracic cancer.

Study Summary

The effect of immunonutrition on veterans undergoing major surgery for gastrointestinal cancer

Lewis S, Pugsley M, Schneider C, Rakita S and Moudgill L

Federal Practitioner 2018; S49-S56

https://www.mdedge.com/fedprac/avaho/article/165715/colon-and-rectal/effect-immunonutrition-veterans-undergoing-major

• Background

Provision of omega-3-fatty acids to modulate the immune system, known as immunonutrition, is hypothesised to improve post-operative outcomes in patients undergoing oncological surgery. The aim of this study was to assess the effect of immunonutrition on outcomes following surgery for gastrointestinal cancer, in a veteran population.

• Methods

A single-centre, prospective, randomised study was carried out in 108 veteran patients undergoing elective surgery for gastrointestinal cancer. All patients continued with their normal diet but received either an immunonutritional supplement (n=54) or a standard supplement (n=54) to be taken 3-times daily for 5 days before surgery. Incidence of post-surgical complications were recorded as the primary outcome. Compliance and tolerance to the supplements, duration of hospital and ICU stay were also explored.

• Results

No demographic differences were observed between the two groups. Both supplements were well tolerated with mean adherence to both supplements of 86%. A higher proportion of patients taking the standard supplement experienced post-operative complications compared with those taking the immunonutritional supplement (52% vs 31%, p=0.02). The difference in post-operative infections was not significantly different (33% vs 20% respectively, p=0.12). Only minimal differences in the mean length of hospital stay (9.3 vs 9.4 days, respectively) or ICU stay (3.0 vs 2.5 days, respectively) were observed.

• Conclusion

The provision of an immunonutritional supplement reduced the overall incidence of post-operative complications in patients undergoing surgery for gastrointestinal cancer, compared with provision of a standard nutritional supplement.

Study Summary

Pre-op nutrition: making an "impact"

Heynen K and Stauffacher T

Congress abstract: American Society for Enhanced Recovery (ASER), San Francisco, 2018

https://aserhq.org/wp-content/uploads/2018/03/23_ASER_Heynen.pdf

• Background

Pre-operative immunonutrition has been shown to improve post-operative outcomes following several specific types of surgical procedure. The aim of this study was to explore the impact of pre-operative immunonutrition on outcomes following total joint replacement in a single institution in the USA.

• Methods

A comparative study was carried out to compare patients undergoing total joint replacement who received pre-operative immunonutrition (n=77) and a matched retrospective cohort who did not receive immunonutrition (control, n=77). The control group were selected from all previous surgeries conducted at the same institution by matching for type of total joint replacement, surgeries conducted in the same quarter of the year, surgeries conducted by the same surgeon, and patients with similar pre-operative American Society of Anaesthesiologists (ASA) score. Immunonutrition consisted of a drink which included arginine, omega-3 fatty acids, and dietary nucleotides. Outcomes of interest included length of hospital stay (LOS), incidence of post-operative infection and readmission rate within 90 days of the surgical procedure.

• Results

Compared with control, patients who received immunonutrition had marginally improved LOS (2.41 vs 2.26 days), post-operative infection (1.30% vs 0%) and readmission rate (12.99% vs 10.39%).

• Conclusion

Positive outcomes were observed in patients who received immunonutrition prior to total joint replacement.

Study Summary

Effects of arginine-based immunonutrition on inpatient total costs and hospitalisation outcomes for patients undergoing colorectal surgery

Banerjee S, Garrison LP, Danel A, Ochoa Gautier JB, Flum DR

Nutrition. 2017 Oct;42:106-113

https://www.ncbi.nlm.nih.gov/pubmed/28734748

• Background

Arginine-based immunonutrition has been hypothesised to reduce infectious complications and length of hospital stay (LOS) related to surgical procedures. The aim of this study was to evaluate the effects of immunonutrition on port-surgical resource utilisation and costs, in a cohort of patients who had undergone colorectal surgery.

• Methods

A retrospective evaluation of two healthcare databases, the Surgical Care and Outcomes Assessment Program (SCOAP), and the Comprehensive Hospital Abstract Reporting System (CHARS), was carried out. Data represented 722 adult patients who had undergone colorectal surgery involving an anastomosis (index procedure), in a Washington state hospital that had participated in the 'Strong for Surgery' initiative. The intervention group had received immunonutrition (n=151) and the control group had not (n=565). Outcomes were predicted using a generalised linear model, adjusted for variables including patient demographics and comorbidities, within a multivariate regression framework.

• Results

Patients receiving immunonutrition were significantly less likely to be readmitted and required significantly fewer hospital days over the 180-day period following the index procedure. Significant reductions in the proportions of patients developing infection and venous thromboembolism were reported in the intervention group. Costs associated with the index procedure and all follow up costs to 180 days were consistently lower in the group of patients who received immunonutrition, although these differences were not statistically significant.

• Conclusion

Arginine-based immunonutrition may have potential in reducing resource utilisation following colorectal surgery. Further evaluation is required to assess whether these findings are transferable into other settings.

Study Summary

Systematic review and meta-analysis of the evidence for oral nutritional intervention on nutritional and clinical outcomes during chemo(radio)therapy: current evidence and guidance for design of future trials

de van der Schueren MA, Laviano A, Blanchard H, Jourdan M, Arends J and Baracos VE

Ann Oncol. 2018 May 1;29(5):1141-1153
https://www.ncbi.nlm.nih.gov/pubmed/29788170

• Background

Patients with cancer often suffer from nutritional deficiency and malnutrition. This has a negative effect on their quality of life as well as impacting on their tolerance to treatment, clinical outcomes and survival. The aim of this study was to conduct a systematic review of randomised controlled trials (RCTs) to explore the benefit of different nutritional interventions.

• Methods

RCTs exploring the impact of dietary interventions in cancer patients, were identified. Interventions included dietary counseling (DC), high-energy oral nutritional supplements (ONS) or ONS supplemented with protein and n-3 polyunsaturated fatty acids (PUFA). Meta-analyses were carried out to explore the overall impact as well as the impact of these individual interventions on body weight.

• Results

11 studies were identified. Overall, nutritional interventions during chemo(radio)therapy improved body weight (+1.31kg, 95%CI 0.24-2.38, p=0.02). DC with or without ONS had no significant effect on body weight (+0.80 kg, 95% CI -1.14 to 2.74, P = 0.32). Provision of PUFA resulted in a significant increase in body weight (+1.89 kg, 95% CI 0.51-3.27, P = 0.02) and improved quality of life. Evidence was limited and was insufficient to draw conclusions about the effect of nutritional interventions on tolerance to treatment, or survival.

• Conclusion

Nutritional interventions, in particular PUFA enriched ONS, have a beneficial effect on body weight during chemo(radio)therapy which may be due to modulation of cancer-related metabolic alterations. The lack of impact of DC with or without ONS may be due to lack of compliance, leading to insufficient nutritional intake. Further evidence is needed, in particular relating to the effect of nutritional interventions on clinical outcomes and survival.

Study Summary

Fluctuations of nutrition-associated markers after decompressive hemicraniectomy in middle cerebral artery occlusion patients

Kutsuna N, Makita K, Goto K, Hirayama K, Kido G and Kagawa Y

Adv Exp Med Biol. 2018;1072:33-38

https://www.ncbi.nlm.nih.gov/pubmed/30178320

• Background

Cerebral infarction following middle cerebral artery occlusion has serious implications and a high rate of mortality. Decompressive hemicranectomy (DHC) is the preferred surgical intervention, based on good outcomes reported in several randomised studies. Although malnutrition following ischaemic stroke is known to worsen outcomes, little is known about the impact of nutritional state in the immediate period after DHC.

• Methods

A preliminary study involving 4 patients was carried out. Enteral nutrition (Peptamen® AF, Nestle) was given within 48 hours of surgery. Blood samples were taken preoperatively and on postoperative days 1, 3, 7, 10 and 14, to analyse markers of nutrition, including prealbumin, transferrin, retinol binding protein (RBP) and serum albumin.

• Results

Compared with preoperative levels, concentrations of prealbumin, RBP and transferrin all decreased by postoperative day 3, although only with transferrin was the decrease statistically significant ($p<0.05$). Compared with day 3, all three markers were significantly increased by day 14 ($p<0.05$). The levels of serum albumin were significantly reduced between days 3-7 compared to pre-operative levels ($p<0.05$) and the total serum protein measured was also significantly lower on post-operative day 3. The dip in nutritional markers observed at postoperative day 3 was also observed with total cholesterol and LDL cholesterol. Conversely, an increase in C-reactive protein was measured at this time point.

• Conclusion

Nutritional markers fluctuated significantly around day 3 following DHC. This may represent a post-operative hypercatabolic phase which starts to normalize after postoperative day 3. Further investigation into the impact of enteral feeding during this post-operative phase is needed.

Study Summary

How prevalent are gastro-intestinal problems in the long-term feeding of patients with a neurological condition?

Parry S

Congress abstract: 38th ESPEN congress, Copenhagen 17-20th September 2016

https://www.clinicalnutritionjournal.com/article/S0261-5614(16)30732-4/fulltext

• Background

Patients with severe neurological damage or an advanced neurodegenerative condition may require long-term enteral feeding. Anecdotally, the tolerance of this patient population to enteral feeding is low and it is hypothesised that neurological damage may lead to loss of coordination of digestive function. The aim of this study was to explore the incidence of gastrointestinal (GI) complications in neurological patients who are exclusively enterally fed.

• Methods

A retrospective chart review was conducted for 60 patients either with a brain injury or medium/late stage neurodegenerative disease, chosen at random from a neuro-rehabilitation centre. All patients had been exclusively enterally fed for a period of 12 weeks. Patients receiving antibiotics were excluded from the study. Due to the limited ability of patients to communicate physical discomfort, measurement of feeding tolerance was based on incidence of diarrhoea, vomiting, regurgitation and constipation; and patient pain/discomfort was not recorded.

• Results

Feeding intolerance was reported in 17/60 (28%) patients. The most common problem was diarrhoea, reported by 13/60 (22%) patients and accounting for 76% of all GI-related complications. Other problems included vomiting (experienced by 9/17 patients, 15%), constipation, (4/60, 7%) and feed regurgitation (5/60, 9%). Abdominal bloating, usually a common cause of abdominal discomfort, was less frequently noted (1/60 patients, <2%).

• Conclusion

This study suggests that approximately one-fourth of patients who require enteral feeding due to a neurological condition experience intolerance to their feeding. This may be an underestimate, due to the inability of patients to express discomfort from symptoms such as abdominal bloating or wind.

Study Summary

Nutritional consequences of intestinal dysmotility in mitochondrial disease

Hynd P, Ng YS, Gorman G, Turnbull D, Feeney C, Schaefer A and McFarland R

Congress Poster: ASPEN 2016

NO LINK TO THIS CONGRESS ABSTRACT AVAILABLE

• Background

There is growing recognition that mitochondrial disease affects the gastrointestinal (GI) system causing symptoms including constipation and intestinal dysmotility. Although seemingly common, these symptoms are not routinely recognised nor properly managed, potentially leading to malnutrition. The aim of this study was to investigate the incidence of GI complications in patients with mitochondrial disease.

• Methods

A questionnaire was developed and posted to 190 patients in the UK, identified either through the MRC Mitochondrial patient cohort or by approaching patients during routine clinic appointments. All patients had the most common form of mitochondrial disease (m.3243A>G mutation). Constipation was defined by the Rome III diagnostic criteria.

• Results

86/190 (45%) patients completed and returned the questionnaire. 65% of respondants had functional constipation; in over one-third of cases, constipation was untreated. Patients who completed the diet and life-style questionnaire reported adopting high fibre (24/36 patients) or low fibre (8/36) diets or increased physical activity (4/36). Other common GI symptoms included abdominal distension (84%), pain (56%) and reflux/nausea/vomiting (42%). Weight loss was reported in 9 (14%) patients however only 2 of these received high calorie dietary advice. Poor nutritional intake was reported, due to early satiety or loss of appetite (54% of patients), reduced food intake (43%) and inability to consume a full meal (58%) however only 4/190 (2%) of patients received enteral feeding.

• Conclusion

The high incidence of GI complications and poor nutritional intake in patients with mitochondrial disease are under-reported and sub-optimally managed. Earlier enteral feeding, currently viewed as a last resort, should be considered in patients at risk of malnutrition.

Study Summary

Use of a multiple-analyte test in assessing patients with diarrhoea

Moshiree B, Cash B, Saad R, Feuerstadt P, Barnett R, Pruthi J, Levenson S, Krause R, Fleisher M, Iyer R, Princen F, Renshaw M, Chen H, McFarland J, Mimms L, Everts-van der Wind A, Ginsburg P, Bray K, and Lembo A

Congress abstract: ACG 2018, Pennsylvania, USA, October 5–10, 2018

https://www.eventscribe.com/2018/ACG/PosterSpeakers.asp?goToLetter=M&

• Background

Diarrhoea can be a symptom of many different conditions, leading to difficulties in determining the most appropriate treatment. A new test was developed to analyse a range of different biomarkers associated with common causes of persistent diarrhoea. The aim of the study was to explore whether the battery of tests was able to differentiate between different causes of diarrhoea.

• Methods

A prospective, multi-centre study was carried out on 395 adult patients who had experienced diarrhoea for a minimum of 4-weeks' duration. Diagnoses were made by gastroenterologists according to their local clinical protocols; physicians were blinded to the test results. Blood and stool specimens were tested in a central location for bile acid analytes (7α-hydroxy-4-cholesten-3-one; 7C4), inflammatory markers (fecal calprotectin, FCP; C-reactive protein, CRP), markers for coeliac disease, as well as viral, bacterial and parasitic pathogens.

• Results

44.8% of patients returned a positive result in one or more of the variables tested, most commonly 7C4 (21% of patients), FCP (14%), CRP (8%) and bacterial contamination with *C. difficile* (5%). Stratification of test results against clinical diagnosis revealed additional information that would be of benefit in refining diagnoses and determining the most appropriate course of further investigation. For example, a subset of patients with diarrhoea-predominant irritable bowel syndrome had elevated inflammatory markers or 7C4, suggesting undetected inflammation or bile acid malabsorption in these patients. Observations such as these may trigger further investigation or specific intervention.

• Conclusion

The battery of tests for common causes of diarrhoea may be of benefit in supporting early diagnosis and guiding further investigation in patients with persistent diarrhoea.

Study Summary

Serum concentrations of 7α-hydroxy-4-cholesten-3-one are associated with bile acid diarrhoea in Crohn's disease

Battat R, Duijvestein M, Vande Casteele N, Singh S, Dulai P, Valasek M, Mimms L, McFarland , Hester K, Renshaw M, Jain A, Sandborn W and Boland B

Clin Gastroenterol Hepatol. 2018 Nov 15. doi: 10.1016/j.cgh.2018.11.012. (E-pub ahead of print)

https://www.ncbi.nlm.nih.gov/pubmed/30448597

• Background

Patients with Crohn's disease (CD) who have undergone ileal resection (IL) often have bile acid malabsorption leading to bile acid diarrhoea (BAD). 7α-hydroxy-4-cholesten-3-one (C4), a bile acid precursor, is increased during bile acid malabsorption. The aim of the study was to explore the correlation between BAD and serum levels of C4 in patients with CD.

• Methods

Patients with CD who had undergone IR (n=26) and who had not (n=21) and patients with ulcerative colitis (UC, n=37) were evaluated. Clinical, endoscopic and histological presence of ileitis, and details of diarrhoeal symptoms were evaluated. Serum concentrations of C4 and fibroblast growth factor 19 (FGF19) were compared. BAD was defined as diarrhoea along with a serum concentration of FGF19 <60 pg/ml. Area under the receiver operating curve (AUROC) analysis was used to identify the C4 cut-off concentration associated with BAD.

• Results

Compared with patients with UC (11.8 ng/ml), patients with CD who had undergone IR had higher levels of C4, regardless of the presence of ileitis (100.0 ng/ml with ileitis, p<0.0001; 51.6 ng/ml without ileitis, p<0.001). Levels of C4 in patients with CD who had not undergone IR were similar to levels in patients with UC (p=0.71), regardless of the presence of ileitis (p=0.34). Cut-off concentration of C4 >48.3 ng/ml identified patients with BAD to 90.9% sensitivity, 84.4% specificity and AUROC 0.94. C4 concentrations correlated with daily number of bowel movements (r=0.41, p=0.004) and correlated inversely with FGF19 concentrations (r=-0.72, p<0.0001).

• Conclusion

Increased serum C4 above 48.3 ng/ml can be used to identify patients with CD-related diarrhoea attributable to bile acid malabsorption.

Study Summary

FRI-462 - FIBROSpect® NASH serum test identifies advanced liver fibrosis in patients with nonalcoholic steatohepatitis: results of a validation study

Abdelmalek M, Guy C, Diehl AM, Li X, Mimms L, Hester K, Jain A and Loomba R

Journal of Hepatology, 2018; 68:S571-S572

https://www.sciencedirect.com/science/article/abs/pii/S0168827818314004

• Background

Hepatic fibrosis is a major predictor for liver-related complications in patients with nonalcoholic steatohepatitis (NASH) and is usually confirmed by liver biopsy. The aim of this study was to refine and validate a non-invasive serum-based test for liver fibrosis, against liver biopsy findings.

• Methods

A cohort study was initially carried out in 396 patients with NASH. Serum samples were obtained on the same day as liver biopsies and were tested using the FIBROSpect NASH assay (Prometheus Laboratories Inc, San Diego) which identified concentrations of the serum biomarkers alpha2-macroglobulin, hyaluronic acid and tissue inhibitor of metallo-proteinase-1 (TIMP-1). Serum results were trained against biopsy results to refine the assay. The predictive value of the serum assay was then validated in an independent, multi-centre cohort of 640 patients with NASH.

• Results

In the validation study (n=640) mean patient age was 49.6 years; 39% of patients were male. Patients were categorised according to stage of fibrosis, as determined by biopsy, from stage 0 (33% of patients), 1 (26%), 2 (20%), 3 (18%) and 4 (3%). Collectively, 21% of patients had advanced hepatic fibrosis (defined as stage 3 or 4); this was similar to the reported literature. Comparing the serum assay against biopsy-proven fibrosis grade, resulted in an AUROC of 0.86 (95% CI: 0.82-0.89). In terms of the ability to identify patients with advanced fibrosis, the sensitivity of the assay was 80% (95% CI: 72–86%) and the specificity was 76% (95% CI: 72–79%).

• Conclusion

The FIBROSpect NASH serum assay test can non-invasively identify patients with advanced hepatic fibrosis, with robust sensitivity and specificity.

Study Summary

A noninvasive method to assess mucosal healing in patients with crohn's disease

Sandborn WJ, Abreu MT and Dubinsky MC

Gastroenterology & Hepatology 14 (5) Supplement, May 2018. Also presented as a poster at ACG, Orlando, Oct 13-18, 2017

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6018319/pdf/GH_14_5_Supp2.pdf

• Background

The principle goal in the management of Crohn's disease (CD) is mucosal healing, typically monitored by ileocolonoscopy, an intervention poorly tolerated by patients. The aim of this study was to assess the ability of a new, non-invasive serum biomarker test, to accurately reflect disease severity.

• Methods

A retrospective analysis was carried out on 748 serum samples obtained from 396 adult patients with CD, at or within 30 days of ileocolonoscopy (training set). Serum samples were tested for a wide range of biomarkers, whose expression were modelled against CD endoscopic index of severity (CDEIS) scores to identify biomarkers most strongly associated with CD severity. Biomarker expression were combined into a single score, the mucosal healing index (MHI), that correlated with disease severity. The predictive ability of the identified suite of biomarkers was validated on 412 serum samples from 112 independent patients (validation set).

• Results

Mathematic modelling of the training set samples, identified a suite of 13 biomarkers that correlated with CDEIS; angiopoietin; carcinoembryonic antigen-related cell adhesion molecule (CEACAM), C-reactive protein (CRP), extracellular matrix metalloproteinase inducer (EMMPRIN), interleukin; matrix metalloproteinase (MMP), serum amyloid A (SAA), transforming growth factor (TGF) and vascular cell adhesion molecule (VCAM). These were assessed using the Monitr test. Analysis of samples in the validation set demonstrated accuracy of 90%, negative predictive value of 92% and positive predictive value of 87%.

• Conclusion

The Monitr test is a non-invasive test which may be of benefit in the monitoring of mucosal healing in patients with CD and may minimise the need for repeated endoscopic procedures.

Study Summary

A model utilising week-6 infliximab trough levels predicts one-year persistent remission in infliximab-treated pediatric IBD patients

Singh N, Arora Y, Yakub J, Cook-Wiens G, Hester K, Kondragunta V, Jain A, Rabizadeh S and Dubinsky M

Gastroenterology, 2018 154; S-825

https://www.gastrojournal.org/article/S0016-5085(18)32815-4/abstract

• Background

Patients with inflammatory bowel disease (IBD) can be treated with infliximab (IFX). Trough concentration of IFX at 14-weeks have been associated with durability of IFX response. The aim of this study was to explore whether IFX concentrations during induction can predict longer-term response to treatment.

• Methods

A prospective study was carried out on 56 paediatric patients with IBD initiating treatment with IFX. Blood samples taken at each infusion were analysed for IFX concentration, anti-IFX antibodies (ATI), albumin, C-reactive protein (CRP), erythrocyte sedimentation rate (ASR) and haematocrit. The incidence of steroid-free persistent remission was determined after 54 weeks of IFX treatment and of the associations between IFX and ATI concentrations at weeks 6 and 14 were evaluated.

• Results

Median age was 13 years. Patients in persistent remission at 54 weeks had higher IFX concentration compared with patients not in remission, at week 6 (32.8 ug/ml vs 4.3 ug/ml, $p<0.0001$) and at week 14 (12.5 ug/ml vs 2.9 ug/ml $p<0.0001$). Of patients who developed ATI during the induction phase, none went on to prolonged remission by week 54. Conversely, a significantly higher proportion (73%) of patients who remained ATI-free achieved prolonged remission ($p<0.0001$). Week 6 IFX trough concentration predicted persistent remission (area under curve [AUC] 0.9) more strongly than week 14 concentration (AUC 0.87). When other week 6 variables including ATI, CRP, albumin and ESR were added to the statistical model, AUC improved to 0.94.

• Conclusion

A strong association was observed between persistent remission and week 6 trough levels of IFX in paediatric patients newly initiating this treatment.

Study Summary

Vedolizumab levels during induction are associated with long-term clinical and endoscopic remission in patients with inflammatory bowel disease

Yarur AJ, Bruss A, Patel A, Beniwal-Patel P, Fox C, Naik SU and Stein D

Gastroenterology, 2018: 154; S1:827–828.

https://www.gastrojournal.org/article/S0016-5085(18)32821-X/fulltext

• Background

Vedolizumab (VDZ) can be used to manage Crohn's disease (CD) and ulcerative colitis (UC). The aim of this study was to explore the association between serum VDZ levels (SVL) during induction of VDZ therapy and subsequent remission in patients with CD and UC.

• Methods

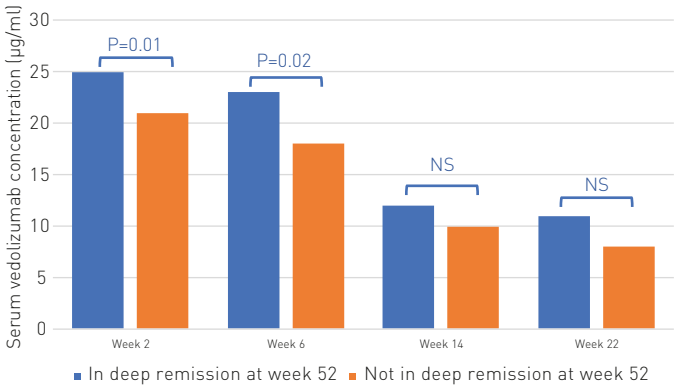
A prospective cohort study was carried out in 53 patients with active CD (n=25) or UC (n=28) starting VDZ treatment. SVL was measured using the Anser® VDZ assay at weeks 2, 6, 14 and 22 following drug initiation. C-reactive protein (CRP), serum albumin and fecal calprotectin (FC) were also measured. Disease status was monitored using Harvey-Bradshaw Index (HBI) for CD and Mayo Clinical Score for UC along with endoscopy. Primary outcome was deep remission at week 52 (HBI<5 or MAYO<3).

• Results

Patients who achieved deep remission at week 52 (21/53; 40%) had higher SVL at weeks 2, 6, 14 and 22 compared with patients who did not achieve deep remission. The difference at weeks 2 and 6 were statistically significant (p=0.01 and 0.02, respectively). Combination treatment with immunomodulators did not influence SVL (p>0.05 at all time points). A positive correlation between baseline albumin levels and SVL was observed at week 2 (not significant) and week 6 (p=0.003). A significant negative correlation was observed between baseline FC and SVL at week 2 and 6 (p<0.001 and 0.03, respectively). Non-response to VDZ was observed in 19 (36%) patients leading to discontinuation.

• Conclusion

Serum VDZ levels during the early induction phase correlate with remission at 52 weeks. Therapeutic drug monitoring in the early induction phase may help to improve outcomes.



Serum VDZ levels (SVL) were significantly higher at weeks 2 and 6, in patients who attained deep remission by week 52 compared with patients who did not.
NS, not significant

Study Summary

Disease-specific antibodies and proteomic markers allow for early detection of asymptomatic ibd years before diagnosis – results from the predicts (Proteomic Evaluation and Discovery in an IBD Cohort of Tri-Service Subjects) study

Torres J, Petralia F, Sato T, Wang P, Telesco S, Choung RS, Strauss R, Laird R, Porter CK, Plevy S, Princen F, Murray JA, Riddle MS and Colombel JF

Gastroenterology 154: S1;152-153. Congress Abstract: Digestive Disease Week 2018

https://www.gastrojournal.org/article/S0016-5085(18)30925-9/fulltext

• Background

Symptomatic inflammatory bowel disease (IBD) is preceded by an asymptomatic phase during which anomalies in immune pathways may emerge. This is hypothesised to occur many years before symptoms manifest. Several small studies have previously reported increases in biomarkers believed to be associated with emergent IBD. The aim of this study was to rigorously evaluate the ability of a wide variety of biomarkers to accurately predict the emergence of Crohn's disease (CD) and ulcerative colitis (UC).

• Methods

Individuals with multiple serum samples taken prior to the diagnosis of IBD (as confirmed by ICD9 and CPT codes), whose samples were stored in the Department of Defense Serum Repository, were identified. Three preclinical samples were obtained for patients who developed CD, (n=200), UC (n=200) and age/gender matched controls who remained healthy (n=200). Samples were tested for antibodies (Serological panel: ASCA IgA, ASCA IgG, Anti-OmpC, Anti-Cbir1, Anti-FlaX, Anti-Fla2 and pANCA) and 1129 protein markers using a Somalogics panel and the predictive performance of these markers assessed alone or in combination using univariate and multivariate analyses and evaluated via receiver operating characteristic (ROC) curves.

• Results

The earliest samples from patients who developed CD or UC predated diagnosis by a median of 5.9 and 7.1 years, respectively. The analysis of the biomarkers is on-going.

• Conclusion

The evaluation of biomarkers in a preclinical phase that predates emergence of IBD by several years is feasible and analysis is on-going. Identification of molecular changes predictive of IBD may allow accurate prediction of disease and could facilitate preventative strategies.

Study Summary

Low infliximab levels and anti-infliximab antibodies increase the risk of loss of response to infliximab in pediatric IBD, a prospective study

Zitomersky N, Chi L, Liu E, Tollefson S, Bender Stern J, Naik S, Rufo PA, Snapper SB and Bousvaros A

Gastroenterology 154; S1:S-60 Congress abstract: Digestive Week, Washington, USA, 2-5 June 2018

https://www.gastrojournal.org/article/S0016-5085(18)30657-7/fulltext

• Background

Inflammatory bowel disease (IBD) can be treated with infliximab (IFX), however 25%-50% of patients experience a loss of response (LOR) to the treatment over time. This may be due to low IFX concentrations leading to the formation of neutralising antibodies to IFX (ATI). The aim of this study was to explore the relationship between low IFX levels, development of ATI and long-term remission.

• Methods

A prospective cohort study was carried out on 226 paediatric patients with IBD initiating IFX. Patients were followed up for a mean of 59 months. Blood samples, taken at the beginning of the study and then repeatedly at a median interval of 7 months, were tested for IFX and ATI concentrations using the Anser® IFX assay. The primary outcome was the incidence of loss of response, determined by discontinuation of IFX. Relationships between potential risk factors and LOR were evaluated using Cox proportional hazard ratio (HR) models.

• Results

LOR was experienced by 38 (17%) patients. IFX concentrations below 3.5 µg/ml increased the risk of LOR by 2.8 times and ATI of >3.1 in the early stages of the study increased the risk of LOR by 4.3 times ($p<0.001$). Variables that had no influence on LOR included BMI, age, sex and combination of IFX with other treatments. Patients with IFX <3.5 µg/ml were 11 times more likely to develop detectable ATI ($p<0.0001$) and the risk of detectable ATI was significantly decreased when IFX concentrations were increased by as little as 1 µg/ml (13% decrease, $p<0.0001$).

• Conclusion

Dosing adjustment in early treatment to prevent low IFX concentrations may prevent development of ATI and may protect the response to IFX.

Study Summary

High anti-TNF drugs trough levels are not associated with the occurrence of adverse events in patients with inflammatory bowel diseases.

Bodini G, Demarzo MG, Saracco M, Coppo C, Baldissarro I, Jain A, Savarino E, Savarino V and Giannini EG

Gastroenterology 2018: 54, Supplement 1, S-367

https://www.gastrojournal.org/article/S0016-5085(18)31540-3/abstract

• Background

Patients with inflammatory bowel disease (IBD) can be treated using anti-TNF biologic treatments including adalimumab (ADA) and infliximab (IFX). Patients can experience loss of response (LOR) to these treatments in a manner believed to be associated with low drug trough concentrations; increased dose is often the first compensatory measure. The aim of this study was to explore potential associations between ADA or IFX trough concentrations and the incidence of adverse events (AEs) in patients treated with biologic monotherapy and combination therapy.

• Methods

A study was carried out on 113 patients with IBD treated with either IFX or ADA. Biologics were administered along with an immunomodulatory therapy in 24% of patients. Trough levels of ADA or IFX were measured using a homogeneous mobility shift assay (Prometheus Laboratories, San Diego, United States) within 1 week of a reported AE.

• Results

103 AEs (79% infections, 13% dermatological reactions) were reported over a median follow up of 16 months. Trough concentrations were obtained for 88/103 AEs (85%). No significant differences were observed in the median AE-related trough concentrations in patients receiving biologic monotherapy or combination therapy with an immunomodulator (6.2 vs 6.9 mcg/mL; p=0.42). Cut-off trough concentrations of up to 15 mcg/mL for IFX and 10 mcg/mL for ADA were not statistically significantly associated with a higher incidence of AEs.

• Conclusion

Patients with higher trough concentrations of ADA or IFX were at no greater risk of AEs compared to patients with lower tough concentrations and this finding was consistent in patients receiving either monotherapy or combination therapy with immunomodulators. The physician's decision to increase dosage should not be driven primarily by concerns relating to AEs.

Study Summary

The clinical utility of a multi-marker serum test for assessment of ulcerations in infliximab treated patients with Crohn's disease

de Bruyn M, Bessissow T, Kondragunta V, Jain A, Arijs I, Van Assche GA, Ferrante M, Opdenakker G and Vermeire S

Gastroenterology 2018:154, Supplement 1, Page S-597

https://www.gastrojournal.org/article/S0016-5085(18)32169-3/pdf

• Background

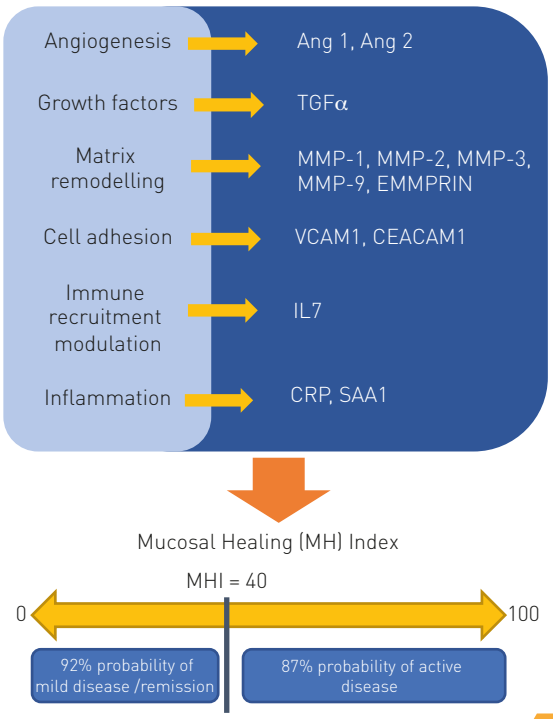
Mucosal healing (MH) in Crohn's disease (CD) is typically assessed with ileocolonoscopy, an invasive and expensive procedure. Recent studies have suggested that adoption of a mucosal healing index (MHI) score based on 13 serum markers (Ang1, Ang2, CEACAM1, VCAM1, TGFb, CRP, SAA1, MMP-1, -2, -3, -9, EMMPRIN and IL-7) may provide an alternative approach. The aim of this study was to validate the MHI in two cohorts of patients treated with infliximab (IFX).

• Methods

In cohort 1 (n=104), serum samples were obtained after a median of 32-weeks after initiation of IFX. In cohort 2 (n=65), serum samples were taken before initiation of IFX and after a median of 23 weeks of treatment. All samples were taken within 30 days of ileocolonoscopy, during which the extent of MH was determined (complete MH, absence of ulceration; partial MH, 50% improvement; no MH, no improvement). The MHI was based on 13 markers and expressed on a scale of 1-100 (MHI<40, low severity; MHI>40, moderate/high severity).

• Results

In cohort 1 and 2, respectively, no MH (42% and 34%), partial MH (18% and 32%) and complete MH (39% and 34%) were observed following treatment with IFX. In both cohorts significantly lower MHI scores were reported in patients with complete MH versus no MH ($p<0.001$ and $p=0.009$, respectively). High proportions of patients in both cohorts with MHI scores >41 had ulceration (78% and 88%, respectively). IFX treatment resulted in decreased MHI scores in 85% of patients.



• Conclusion

The MHI may be a useful tool to assess ulceration in patients with CD and has been validated in two independent patient cohorts.

Study Summary

Pharmacokinetic dashboard-driven infliximab dosing in IBD: a prospective interventional study

Dubinsky M, Phan BL, Lega S, Tse S, Kline MR, Novack DE and Mould D

Gastroentrology 154, Supplement 1, S-820. Congress abstract: Digestive Diseases Week, 2018

https://www.gastrojournal.org/article/S0016-5085(18)32802-6/fulltext

• Background

Treatment of inflammatory bowel disease (IBD) with on-label dosing of infliximab (IFX) is often suboptimal, leading to loss of response. The aim of this study was to explore a prototype pharmacokinetics (PK) dashboard to establish individualised induction and maintenance dosing regimens for IFX.

• Methods

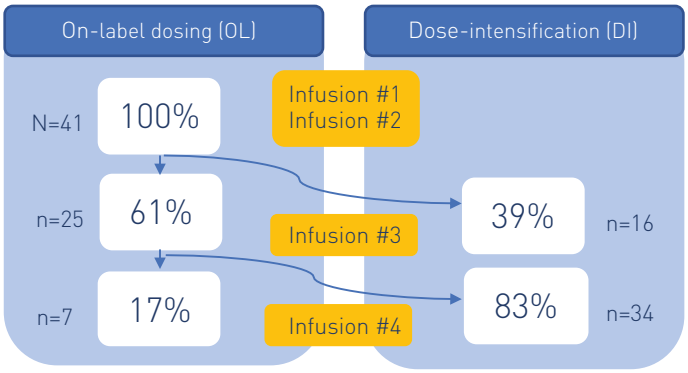
41 patients with IBD were assessed. Two dosing regimens were possible, on-label (OL, 5 mg/kg) and dose intensification (DI). The DI regimen consisted of a 5 mg/kg dose at infusions 1 and 2 with dose escalation at infusions 3 and 4 according to the prediction from the PK dashboard. Clinical data (sex, weight, type of IBD) and lab data (albumin, C-reactive protein) were input into the dashboard software and PK predictions were then generated using Bayesian PK algorithms to calculate the dose required for a minimum target concentration of 17 µg/mL by the third infusion and 10 µg/mL by the fourth infusion.

• Results

OL dosing at week 6 was prescribed for 61% (25/41) of patients. 17% of patients remained on the OL dosing regimen at week 14 with the remaining 83% requiring DI. Of these patients, 32% remained on the 5 mg/kg dose with escalated dosing frequency and 68% required both dose (10 mg/kg) and frequency escalation to maintain the target concentration. Mean IFX in the OL and DI groups were monitored at week 2 (43 vs 32 µg/mL; p=0.05) week 3 (29.4 vs 22.3; p=0.07) and week 4 (8.1 vs 13.1; p=0.02). Remission rates were 86% and 79% in the OL and DI groups respectively.

• Conclusion

On-label IFX dosing achieves minimum target IFX concentrations in only a minority of patients. The use of a PK dashboard to guide individualised dosing escalation led to a more optimal IFX exposure.



Study Summary

Benefit of combination therapy with infliximab and immunomodulators in Crohn's disease is primarily driven by pharmacokinetics

Elman J, Ungaro RC, Phan BL, Colombel JF and Dubinsky M

Gastroenterology 54, Supplement 1, S-821. Congress abstract: Digestive Disease Week, 2018

https://www.gastrojournal.org/article/S0016-5085(18)32804-X/fulltext

• Background

Treatment of Crohn's disease (CD) with a combination of infliximab (IFX) and the immunomodulator azathioprine (AZA) has been shown to be more effective than treatment with either IFX or AZA alone. The aim of this study was to explore whether this observation is due to pharmacokinetic interaction or synergy between IFX and immunomodulators.

• Methods

A retrospective chart-based analysis of 283 patients (>16 years) with CD, receiving IFX for >6 months and with IFX concentrations obtained within 8 weeks of first infusion, was carried out. Disease severity was measured using the Montreal classification. Patients treated with IFX as a monotherapy or in combination with immunomodulators were compared. Outcomes included remission (defined using physician global assessment, CRP <5mg/ml and no use of steroids within 3 weeks), and concentrations of IFX (split into quartiles) and antibodies to IFX (ATI).

• Results

185 (65%) patients were receiving IFX monotherapy and 98 (35%) combination therapy with an average duration of therapy of 46 and 41 months respectively. No difference in severity of disease was observed between groups. No difference in development of ATI was observed. Combination therapy was associated with a decreased incidence of clinical remission (OR, 0.61, 95% confidence interval 0.37-0.99). However, when data were stratified according to IFX concentrations, rates of clinical remission did not differ significantly between patients receiving either monotherapy and those on combination therapy in each quartile.

• Conclusion

When accounting for IFX concentrations, remission rates were not significantly different between patients receiving IFX monotherapy and those receiving IFX in combination with immunomodulators. This suggests that immunomodulators may influence the PK of IFX.

Study Summary

Proactive infliximab monitoring following reactive testing is associated with better clinical outcomes than reactive testing alone in patients with inflammatory bowel disease

Papamichael K, Vajravelu RK, Vaughn BP, Osterman MT and Cheifetz AS

Crohns Colitis. 2018 Jun 28;12(7):804-810

https://www.ncbi.nlm.nih.gov/pubmed/29590345

• Background

Patients with inflammatory bowel disease (IBD) can be treated with infliximab (IFX) however loss of response (LOR) is seen in some patients. Evidence is emerging that proactive therapeutic drug monitoring, where drug titration is used to achieve target IFX trough concentrations, may improve outcomes and protect against LOR. The aim of this study was to explore long-term outcomes following proactive drug monitoring.

• Methods

A retrospective multi-centre cohort study was carried out in 102 consecutive patients with IBD, who were receiving IFX maintenance therapy and had received reactive testing. Patients were divided into group A, who received proactive infliximab monitoring after reactive testing, (n=33), and Group B, who received reactive testing alone (n=69). Outcomes included treatment failure (defined as drug discontinuation as a result of LOR or serious adverse event) using time to event analysis, and healthcare resource utilisation (IBD-related surgery and hospitalisation).

• Results

Patients were followed for a median duration of 2.7 years. Patients in Group A (n=33), receiving proactive monitoring experienced significantly less treatment failure (hazard ratio 0.15; 95% confidence interval 0.05-0.51; p=0.002) and significantly fewer hospitalisations related to IBD (hazard ratio 0.18, confidence interval 0.05-0.99; p=0.007).

• Conclusion

Proactive infliximab monitoring following reactive testing results in reduced risk of treatment failure and reduced resource utilisation, in particular fewer hospitalisations related to IBD, compared with reactive testing alone.

Study Summary

Outcomes of dose escalation and drug level monitoring in patients with inflammatory bowel disease treated with vedlizumab

Scoville EA, Izmaylov ML, Bennett A, Evers L, Annis K, Garrett A, Duley C, Adams DW, Dalal RL, Beaulieu D, Schwartz DA and Horst SA

Gastroenerology 2018: 154, Supplement 1, S-829–S-830: Congress abstract: Digestive Diseases Week

https://www.gastrojournal.org/article/S0016-5085(18)32826-9/fulltext

• Background

Inflammatory bowel disease (IBD) can be treated with the biologic drug vedolizumab (VZB) but patients can experience loss of response (LOR), leading to treatment discontinuation. Dose escalation is commonly used to counteract LOR. The aim of this study was to identify factors associated with dose escalation in patients receiving VZB.

• Methods

A retrospective analysis was carried out on 397 patients managed in a tertiary care setting who received VZB between 2014 and 2016.

• Results

During a median follow-up of 572 days, 169/397 (42.6%) patients who received VZB required dose escalation, with the majority receiving an increased dose every 4 weeks. Median time to dose escalation was 220 days overall, significantly earlier in patients with ulcerative colitis (n=44, 192 days) compared with patients with Crohn's disease (n=125, 261 days, $p<0.01$). Analysis of VZB trough concentration demonstrated that the majority of patients (86%) who required dose escalation had levels <12.7µg/ml. VZB levels correlated with serum albumin ($p<0.001$) but not C-reactive protein (CRP). 63/169 (37%) patients discontinued VZB at a median of 180 days after dose increase but the remainder of patients were able to continue with therapy. Multivariate analysis identified that co-administration with immunomodulators in CD and pancolitis in UC predicted the need for dose escalation; these factors may reflect the underlying severity of disease in this group of patients. No other factors were associated with dose escalation.

• Conclusion

Dose escalation was required in a high proportion of patients receiving VZB for the treatment of IBD. This was not linked with treatment discontinuation. Most patients who required dose escalation had VZB trough levels below 12.7 µg/ml.

Study Summary

The association of serum 7a-hydroxy 4 cholesten-3-one (7C4) with bile acid diarrhoea in patients with inflammatory bowel disease

Battat R, Duijvestein M, Vande Casteele N, Singh S, Renshaw M, McFarland J, Chen H, Jain A, Sandborn WJ and Boland BS

Gastroenterology 154, Supplement 1, S-393. Congress abstract: Digestive Disease Week 2018

https://www.gastrojournal.org/article/S0016-5085(18)31609-3/fulltext

• Background

Diarrhoea associated with inflammatory bowel disease (IBD) can be caused by bile acid malabsorption (BAM) following ileal resection. BAM also causes an increase in the bile acid precursor 7 a-hydroxy-4- cholesten-3-one (7C4). The aim of this study was to explore whether 7C4 levels were related to bile acid diarrhoea (BAD) in IBD.

• Methods

A retrospective study was conducted on 26 patients with Crohn's disease (CD) who had undergone ileal resection and 11 patients with ulcerative colitis (UC). Outcomes included diarrhoeal symptoms, disease severity, remission, as well as serum 7C4 measured by liquid chromatography and mass spectrometry (Prometheus Laboratories, San Diego, CA, USA).

• Results

Higher concentrations of 7C4 were measured in serum of patients who had undergone ileal resection vs those who had not (107.5 vs 28.4 ng/mL, p<0.0001) and patients experiencing diarrhoea vs those without diarrhoea (133.5 vs. 70.3 ng/mL, p=0.001). Among the subset of patients with ileal resection, those experiencing diarrhoea had higher levels of 7C4 compared to those without (132.1 vs. 84.6 ng/mL, p=0.04). The sensitivity and specificity of different cut-off 7C4 concentrations were explored; 50 ng/ml (73% sensitivity, 52% specificity, AUC 0.71) was more sensitive (p=0.02) compared with 100 ng/mL (63% sensitivity, 73% specificity AUC 0.71). In patients with remission confirmed by endoscopy, use of the >50 ng/mL threshold of 7C4 (sensitivity 100%, specificity 73%, AUC 0.90) was associated with the presence of diarrhoea (22% vs 0% of patients, p=0.04).

• Conclusion

Incidence of BAD is associated with 7C4 concentrations in patients with IBD. A threshold of >100 ng/mL of 7C4 may be appropriate for confirmation for suspected BAD. A threshold of >50ng/mL may be appropriate as a screening test for BAD in IBD patients with ER.

Study Summary

Mucosal healing and bacterial composition in response to enteral nutrition versus steroid based induction therapy – a randomised prospective clinical trial in children with Crohn's disease

Pigneur B, Lepage P, Mondot S, Schmitz J, Goulet O, Doré J and Ruemmele FM

J Crohns Colitis. 2018 Dec 12. doi: 10.1093/ecco-jcc/jjy207. [Epub ahead of print]
https://www.ncbi.nlm.nih.gov/pubmed/30541015

• Background

Induction of remission, and mucosal healing in Crohn's disease (CD) is efficiently achieved through exclusive enteral nutrition (EEN) and evidence suggests that EEN may be even more efficacious than corticosteroids (CS) in inducing mucosal healing without the side effects associated with CS. The aim of this study was to compare EEN (with Modulen IBD) and CS, in particular the anti-inflammatory effects and changes to the gut microbiota observed following treatment.

• Methods

A prospective randomised study was carried out on 19 paediatric patients with new-onset CD (Harvey Bradshaw Index, HBI>5), aged between 6 and 17 years. Patients were given either CS (n=6) or Modulen IBD®(n=13). HBI, faecal microbiota, biomarkers of inflammation and CD endoscopic index of severity (CDEIS) were recorded at week 0, and 8. Remission was defined as HBI <5.

• Results

After 8 weeks of treatment, clinical remission was achieved in 100% (13/13) of patients given Modulen IBD as EEN, compared with 83.3% (5/6) of patients given CS. The rate of mucosal healing was markedly higher following EEN compared with CS (89% vs 17%). No differences in biological markers were observed between groups. In patients given EEN, changes in gut microbiota included a shift towards a higher proportion of Clostridium bacteria, including a significant increase in Ruminococcus compared with patients treated with CS (p=0.049).

• Conclusion

Although both CS and EEN are capable of inducing remission in children with CD, treatment with EEN showed a more pronounced rate of mucosal healing which was associated with changes in gut microbiota.

Study Summary

Effects of two preoperatory weight loss diets on hepatic volume, metabolic parameters, and surgical complications in morbid obese bariatric surgery candidates: a randomised clinical trial

Contreras A, Sanjaume A, Jaime M, Soler A, Pereferrer F, López A, Tomás B, Del Castillo Déjardin D and Salas-Salvadó J

Obes Surg. 2018 Dec;28(12):3756-3768

https://www.ncbi.nlm.nih.gov/pubmed/30109669

• Background

Patients undergoing bariatric surgery are at high risk for post-surgical complications, including those related to increased liver volume often associated with morbid obesity. Pre-operative dietary strategies may be effective in reducing incidence of complications related to liver volume.

• Methods

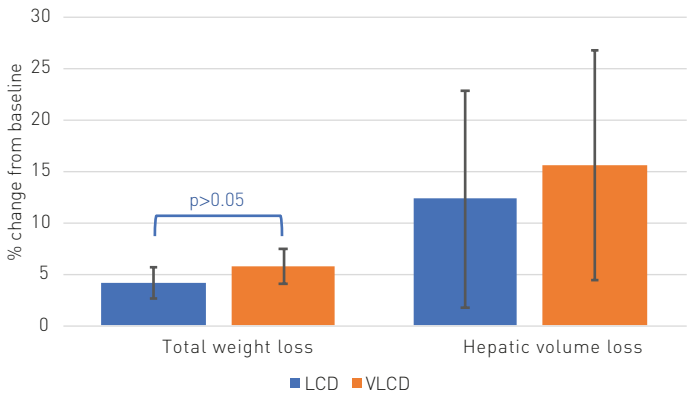
A parallel randomised study was conducted in 86 patients with morbid obesity to compare the effect of a very low calorie diet (VLCD) and a low calorie diet (LCD) for 21 days prior to bariatric surgery. Changes in hepatic volume were measured and biochemical and anthropometric variables were assessed. Incidence of surgical complications and duration of hospital stay were recorded post-operatively

• Results

Patients adhered well to both diets although patients were less tolerant of the VLCD than the LCD. Hepatic volume was reduced to a similar extent in both groups following the 21-day protocol. Patients with greater hepatic volume at baseline (>3L) had a more pronounced reduction in hepatic volume than patients with smaller initial hepatic volume (<3L; p<0.001). A significantly greater weight loss was observed following VLCD (5.8% loss) compared with LCD (4.2%, p=0.004). No differences in the incidence of surgical complications, length of hospital stay, or biochemical parameters were observed between groups.

• Conclusion

VLCD has a greater impact on pre-operative weight loss compared with LCD in patients with morbid obesity but was not found to impact significantly on percent reduction in liver volume, duration of hospital stay or incidence of post-operative complications.



Study Summary

A health economic model to assess the cost effectiveness of OPTIFAST® for the treatment of obesity in the United States

Nuijten M, Marczewska A, Araujo Torres K, Rasouli B and Perugini M

J Med Econ. 2018 Sep;21(9):835-844

https://www.ncbi.nlm.nih.gov/pubmed/29678127

• Background

The direct and indirect costs of obesity are substantial, given the high prevalence of obesity in the Unites States, however the cost-effectiveness of weight-loss strategies require clarification. The OPTIFAST® Program is a clinically effective and well tolerated behavioral intervention for obesity that includes a low-calorie, total meal replacement diet. This study evaluated US payors' potential cost savings from providing reimbursement for the OPTIFAST® Program, compared to no intervention or pharmacological intervention.

• Methods

Patients with class I and II obesity (BMI 30-39.9 kg/m^2) or class III obesity (BMI>40 kg/m^2) undergoing a 3-year program of weight loss using the OPTIFAST® Program, those being prescribed pharmacological intervention for weight loss (liraglutide 3 mg or naltrexone/bupropion) and patients receiving no intervention were assessed. Cost savings were estimated using an event-driven decision analytic model that included the risk of obesity-related complications. Information used in the model was derived from clinical studies, published articles, national population statistics and US price lists. Costs were calculated in US dollars.

• Results

The OPTIFAST® Program led to overall cost savings per class I and II patient, compared with liraglutide ($9285 saving), naltrexone/bupropion ($685) and no intervention ($1951). Scenario analysis explored projected cost savings up to a 10-year time horizon and found that an OPTIFAST® program could be cost-saving for patients with class III obesity and those with obesity and type 2 diabetes compared with all comparators as well as against bariatric surgery, over this longer time frame.

• Conclusion

Reimbursement for the OPTIFAST® Program can result in cost-savings for US payors compared with no intervention and compared with pharmacological intervention in patients with obesity.

Study Summary

OPTIFAST® meal replacement program for the treatment of obesity: a cost-effectiveness assessment from the employer perspective in the USA

Perugini M, Marczewska A, Araujo Torres K, Rasouli B and Nuijten M

Congress abstract: ISPOR 2018

NO LINK TO THIS CONGRESS ABSTRACT AVAILABLE

• Background

The direct and indirect costs of obesity in the workplace are substantial, however the cost-effectiveness of weight-loss strategies in the working population requires clarification. The aim of this analysis was to evaluate potential cost savings over 3 years of a medically supervised behavioral intervention that includes total meal replacement (the Optifast® Program) compared to no intervention or pharmacological intervention, from the perspective of a US-based, self-insured employer.

• Methods

Employees with class I and II obesity (BMI 30-39.9 kg/m^2) or class III obesity (BMI>40 kg/m^2) participating in the OPTIFAST® Program for 1 year, those being prescribed pharmacological intervention for weight-loss (liraglutide 3 mg or naltrexone/bupropion) and patients receiving no intervention were assessed. Cost savings were estimated using an event-driven decision analytic model, that included loss of productivity as a result of obesity-related conditions including myocardial infarction, hypertension, angina pectoris and type-2 diabetes. Information was derived from clinical studies, published journal articles, national population statistics and US price lists. Costs were calculated in US dollars.

• Results

The model predicted cost savings of $9488 per person on the Optifast® Program compared with no intervention (costs $47,884 vs $57,372 respectively). In comparison with pharmacological intervention with liraglutide ($61,688 costs) or naltrexone/bupropion ($53,890 costs), the Optifast® Program was predicted to save $13,804 and $6,006, respectively. Use of the Optifast® Program was predicted to have an even greater cost savings in employees with class III obesity and in longer-term scenarios (5 years and 10 years).

• Conclusion

The Optifast® Program may provide significant cost-savings for self-insured employers in the US through minimization of costs associated with loss of productivity caused by obesity-associated conditions.

Study Summary

Effectiveness of a total meal replacement program (OPTIFAST® program) compared with a reduced-energy food-based diet plan on weight loss: results from the OPTIWIN study

Ard J, Auriemma A, Coburn S, Lewis K, Loper J, Matarese L, Periman S, Pories W and Rothberg A

European Journal of Obesity, 5;S1:337, 2018. Congress abstracts, 25th European Congress on Obesity, Vienna, Austria, May 23–26, 2018

https://www.karger.com/Journal/Issue/277249

• Background

Dietary interventions, such as the Optifast® Program, that include total meal replacement may be more effective for weight loss and maintenance than interventions based on food-based (FB) diets. However, evidence from long-term, randomised studies is lacking.

• Methods

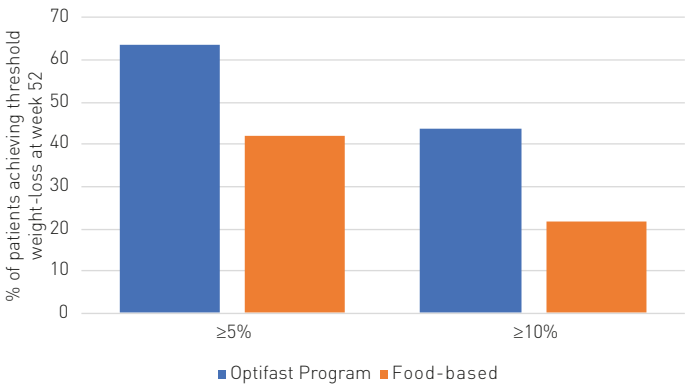
The OPTIWIN study is a 52-week, randomised, multicenter study comparing weight loss and related health outcomes in 330 adults with obesity (BMI 30-55 kg/m^2) who were randomised to the Optifast® Program or a food-based diet and lifestyle (FB) program. Co-primary outcomes were percent change in baseline body weight at 26 and 52 weeks. Analyses were conducted in the modified intent-to-treat population which included participants with baseline data and at least one other follow up measurement.

• Results

At baseline, mean body weight was 108.4 kg. Relative weight loss at 26 and 52 weeks was significantly greater in the Optifast® Program group (12.2% and 10.3%,) compared with the FB program group (5.9% and 5.5% p<0.01 for both timepoints). At 52 weeks, a higher proportion of participants in the Optifast® Program achieved greater than 5% or 10% weight loss (63.7% and 43.7% of patients respectively) compared with participants in the FB program (42% and 21.7%, respectively p<0.01). Similar proportions of participants discontinued the Optifast® and FB programs (29.3% vs 31.9 of patients).

• Conclusion

Individuals participating in the Optifast® Program lost a higher percentage of body weight at 26 and 52 weeks compared with participants in a FB program. Additionally, higher proportions of individuals in the Optifast® Program achieved clinically significant weight loss compared to a food-based weight-loss program.



Study Summary

Effectiveness of a total meal replacement program (OPTIFAST® program) on weight loss: results from the OPTIWIN study

Ard JD, Lewis KH, Rothberg A, Auriemma A, Coburn SL, Cohen SS, Loper J, Matarese L, Pories WJ and Periman S

Obesity (Silver Spring). 2018 Nov 13. doi: 10.1002/oby.22303

https://www.ncbi.nlm.nih.gov/pubmed/30421863

• Background

A behavioral intervention, such as the Optifast® Program, that includes total meal replacement can improve weight loss in individuals with obesity. The aim of this study was to compare the effectiveness of the Optifast® Program (OP) and a reduced-energy, food-based diet and lifestyle intervention (FP).

• Methods

A 52-week randomised trial was carried out on participants aged between 18 and 70 years with a BMI between 30-55 kg/m^2. Participants received either OP (n=135) or FB (n=138) which included a 26–week weight loss phase, followed by a 26-week weight-maintenance phase. Outcomes, measured at baseline and at 26 and 52 weeks included body weight, body composition (dual energy x-ray absorptiometry) and adverse events. Repeated measures multivariable linear mixed models were used to compare outcomes between groups. Data analysis was performed in participants known to have started the assigned intervention and who had at least one postbaseline assessment of body weight (modified intent-to treat, mITT).

• Results

The mITT population included 273 participants (83% of randomised participants) with a mean age of 47 years, of whom 82% were female. Baseline BMI was 39 kg/m^2. At 26 weeks, percentage weight loss from baseline was greater in the OP group (12.4%) compared with the FB group (6.0%, p<0.001). Significantly greater weight loss in the OP group was maintained at 52 weeks (10.5% vs 5.5%; p<0.001). Analysis of body composition demonstrated greater loss of fat mass in OP participants compared with those randomised to FB. Rates of serious adverse events did not differ between groups.

• Conclusion

Participation in the Optifast® Program resulted in greater initial and sustained weight loss compared with a reduced-calorie, food-based diet.

Study Summary

Effect of total meal replacement program compared with a reduced-energy food-based diet plan on glycemic status—results from the OPTIWIN Study

Rothberg AE, Ard JD, Auriemma A, Coburn SL, Lewis KH, Loper J, Laura E. Matarese LE, Periman S and Pories WJ

Diabetes; 67:S1. Congress poster: American Diabetes Association, 2018

http://diabetes.diabetesjournals.org/content/67/Supplement_1/298-LB

• Background

Obesity increases the risk of type 2 diabetes. Weight loss can help to resolve dysglycaemia and reduce the need for pharmacological glycaemic control. The aim of this study was to present additional analysis of the OPTIWIN study, to explore whether the Optifast® Program, an obesity intervention that includes total meal replacement, influenced glycaemic control compared with a reduced-calorie, food-based diet and lifestyle program.

• Methods

A prospective multicenter study was carried out for 52 weeks in adults with obesity who were randomised to participate in either the Optifast® Program or a reduced-energy (-500 to -750kcal/day) food-based (FB) program based on the Diabetes Prevention Program. The effects on glycemic outcomes were investigated.

• Results

273 patients were eligible for inclusion in the analysis. At baseline, the proportions of participants in the Optifast® and FB programs with diabetes (9.6% vs 14.5%, respectively) and prediabetes (42.2% vs 35.5%, respectively) did not differ significantly. At baseline, mean fasting blood glucose was similar in both groups (5.6 mmol/L); however at week 26, participants in the Optifast® Program had significantly lower fasting blood glucose levels compared with participants in the FB program (5.2 vs 5.5 mmol/L, p=0.02). At week 52, participants in the Optifast® Program had a significantly greater improvement in HbA1c compared with those participating in the FB program (p=0.04). At 26 weeks, the proportion of participants with diabetes remission was higher in the Optifast® Program group compared with the FB group although the difference did not reach statistical significance (p=0.07).

• Conclusion

The Optifast® Program improved glycaemic outcomes in individuals with obesity, compared with a food-based program.

Study Summary

Effectiveness of a total meal replacement program compared with food based diet plan on body composition: the OPTIWIN study

Matarese LE, Ard JD, Auriemma AM, Coburn SL, Lewis K, Loper JF, Periman S, Pories WJ, and Rothberg AE

Congress abstract, Obesity Week, Nashville, USA, Nov 11-15, 2018

https://obesityweek.com/abstract/effectiveness-of-a-total-meal-replacement-program-compared-with-food-based-diet-plan-on-body-compositionthe-optiwin-study/

• Background

Obesity interventions that include total meal replacement (TMR) are successful in reducing body weight, however some concerns exist around the changes in body composition that accompany rapid weight loss. The aim of this study was to compare body composition in participants in the Optifast® Program, a behavioral intervention that includes TMR, and those participating in a food-based diet and lifestyle intervention.

• Methods

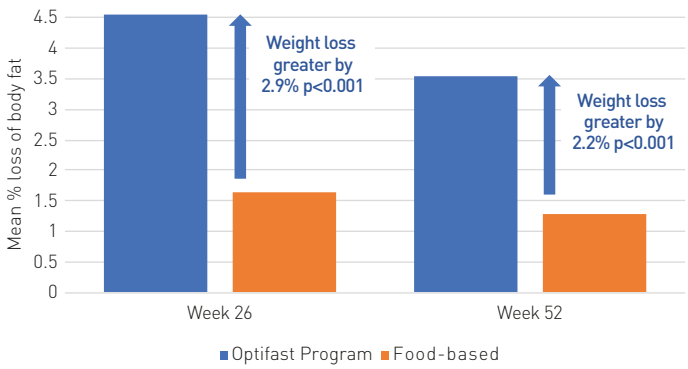
Data obtained as part of the OPTIWIN study were investigated. Obese individuals were randomised to participate in either the Optifast® Program or a food-based diet and lifestyle program, based on the Diabetes Prevention Program, for 52 weeks. Body composition (body fat and lean body mass) was measured by dual-energy X-ray absorptiometry (DEXA) at baseline and after 26 and 52 weeks.

• Results

273 participants were eligible for inclusion in the analysis. Significantly greater weight loss was observed in the Optifast® Program compared with the FB program. Mean waist circumference in the Optifast® Program group decreased 3.6 cm more than in the FB program group at 26 weeks and 3.4 cm more by 52 weeks ($p<0.01$ at both timepoints). The mean reduction in percent body fat was significantly greater in the Optifast® Program group compared with the FB program group at both 26 weeks (4.55% vs 1.63% reduction respectively, difference of 2.9%, $p<0.01$) and 52 weeks (3.53% vs 1.28% reduction respectively, difference of 2.2%, $p<0.01$). The proportion of weight lost from lean body mass was not significantly different between groups at either time point.

• Conclusion

Participants in the Optifast® Program experienced greater improvements in waist circumference and percent body fat at 26 and 52 weeks than participants in a food-based diet and lifestyle program. The proportion of weight lost from lean body mass was similar between groups.



Study Summary

Optifast® increases weight loss response compared with food-based diet plan: the OPTIWIN study

Ard JD, Auriemma AM, Coburn SL, Lewis K, Loper JF, Matarese LE, Periman S, Pories WJ and Rothberg AE

Congress abstract: Obesity Week 2018, November 11-15, 2018, Nashville, USA

https://obesityweek.com/abstract/optifast-increases-weight-loss-response-compared-with-food-based-diet-planthe-optiwin-study/

• Background

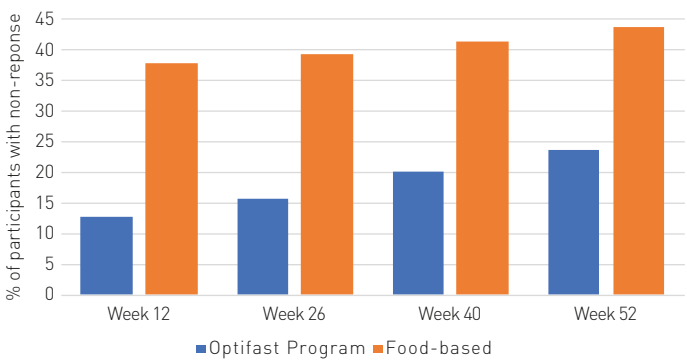
Some degree of non-response occurs with all weight-loss interventions. Weight-loss programs that include total meal replacement (TMR), such as the Optifast® Program, have reduced variability in daily caloric intake compared with programs based on reduced-energy food-based diets. The reduced variability in energy intake may improve rates of non-response The aim of this study was to compare the rates of non-response to the Optifast® program and a food-based diet and lifestyle program.

• Methods

Data obtained as part of the OPTIWIN study, a prospective multicenter study, were investigated. Participants were randomised to either the Optifast® Program or a reduced-energy, food-based diet and lifestyle (FB) program. Weight loss from baseline was measured at 26 and 52 weeks. The percentage of non-responders (defined as participants with <3% weight loss) was compared between groups.

• Results

Significantly greater weight loss was observed in the Optifast® Program group versus the FB group at 52 weeks. Higher proportions of participants in the Optifast® Program achieved clinically relevant weight loss compared with participants in the FB program (at 52 weeks, 10% weight loss was achieved by 44% vs 22%; 15% weight loss was achieved by 30% vs 12%, respectively). The proportion of non-responding participants was significantly lower in the Optifast® Program compared with the FB program at 26 weeks (15.6% vs 39.1%, respectively) and 52 weeks (23.7% vs 43.5%, respectively). The likelihood of non-response to the Optifast® Program was 60% lower compared to the FB program at 52 weeks (odds ratio 0.4, p=0.0017).



• Conclusion

The Optifast® Program significantly reduces the likelihood of non-response, compared to a food-based diet and lifestyle program.

Study Summary

Sleep and quality of life of patients with glycogen storage disease on standard and modified uncooked cornstarch

Rousseau-Nepton I, Huot C, Laforte D, Mok E, Fenyves D, Constantin E and Mitchell J

Mol Genet Metab. 2018 Mar;123(3):326-330
https://www.ncbi.nlm.nih.gov/pubmed/29223626

• Background

Individuals with hepatic glycogen storage diseases (GSDs) rely on specific nutritional intervention and avoidance of a fasting period, to maintain glycaemic control. Uncooked cornstarch (UCCS) has been important in prolonging euglycemia overnight, however sleep disturbances remain common. A new modified UCCS, Glycosade® was developed with the aim of prolonging euglycemia. This study investigated whether the provision of Glycosade could improve sleep quality, and quality of life (QoL).

• Methods

A prospective cohort study was carried out in nine adult patients with GSD to compare the quality and quantity of sleep of the patients over one month when given standard UCCS and for 1 month after a switch to modified UCCS (Glycosade®). The switch to modified UCCS was carried out under controlled conditions in a hospital setting. Sleep and QoL were evaluated via patient-completed questionnaires, sleep diaries and actigraphy. Blood glucose was monitored using a continuous glucose monitor (CGM).

• Results

Glycosade was observed to reduce the number of sleep disturbances compared to standard UCCS. QoL was not affected, with normal levels recorded both before and after the switch from standard to modified UCCS. Longer duration of euglycaemia with Glycosade, was confirmed through CGM monitoring.

• Conclusion

Improved sleep quality and longer duration of overnight euglucaemia were observed in patients taking Glycosade®. This modified UCCS may present an alternative option for individuals with GSD.

Study Summary

The challenges of vitamin and mineral supplementation in children with inherited metabolic disorders: a prospective trial

Daly A1, Evans S, Chahal S, Surplice I, Vijay S, Santra S and MacDonald A.

J Hum Nutr Diet. 2016 Aug;29(4):434-40

https://www.ncbi.nlm.nih.gov/pubmed/26781762

• Background

The dietary management of inborn errors of metabolism involves the restriction of protein, fat or carbohydrate. This can impact on nutritional intake and increase the risk of nutritional deficiencies. The aim of this study was to evaluate a new comprehensive vitamin and mineral supplement (Fruitivits®, Vitaflo Ltd) on micronutrient status, when used in combination with a restrictive diet.

• Methods

An open prospective study design, assessing 14 children, for a 26 week study duration was carried out. All participants had dietary restrictions including low protein (n=8, 57%), regular daytime cornstarch and overnight glucose polymer tube feeds (n=4, 29%), low fat (n=1, 7%) and modified Atkins diet (n=1, 7%). Data was collected at baseline and after 12 and 26 weeks of supplementation and included blood biochemical analysis, anthropometry and food frequency questionnaires.

• Results

Compared with levels at baseline, folate, vitamin E, plasma selenium, whole blood selenium and total vitamin D were all significantly improved by week 26 ($p<0.05$). No other nutritional markers were affected. Use of the provided supplements was lower than prescribed with 37% of the product unused throughout the course of the study.

• Conclusion

Children with inborn errors of metabolism who require dietary restriction are at risk of nutritional deficiencies. Although statistical significant improvements in some nutritional biomarkers were observed, adherence to the vitamin and mineral supplement was lower than prescribed and alternative approaches are still required.

Study Summary

The challenge of nutritional profiling of a protein-free feed module for children on low protein tube feeds with organic acidaemias

Daly A, Evans S, Ashmore C, Chahal S, Santra S and MacDonald A.

J Hum Nutr Diet. 2017 Jun;30(3):292-301

https://www.ncbi.nlm.nih.gov/pubmed/28294445

• Background

Individuals with organic acidaemias (OA) are managed by restriction of protein intake, commonly involving enteral tube feeding. In children, the use of standard formulae suitable for enteral feeding are not appropriate in this population as the protein content is too high. Typically, preparation of enteral feed for children with OA is achieved via combination of several feed ingredient 'modules'. The proportions of each module need to be calculated and carefully measured to ensure adequate and safe nutrition. The aim of this study was to assess the efficacy of a premeasured, protein-free module (Basecal®, Vitaflo LTD), compared to standard practice.

• Methods

15 children with OA, over 12 months old, weighing between 11.6 and 31 kg and who required enteral feeding, participated in the study. Their normal feed (either a protein-free infant feed or modular ingredients) were replaced gradually by the investigational feed, ensuring that energy and protein intake were unchanged, in order to maintain metabolic stability. Measurements were taken at baseline and after 26 weeks of provision of the investigational feed. Dietary intake, anthropometry and nutritional biochemistry were measured.

• Results

Following the switch to the premeasured protein-free module, statistically significant increases in magnesium, sodium, vitamin D, docosahexaenoic acid and arachidonic acid were observed, compared with measurements taken prior to the switch ($p<0.05$). Analysis of the composition of prepared feeds demonstrated deviations from the expected composition, largely due to inaccurate feed preparation by caregivers.

• Conclusion

Nutritional intake and biochemistry were improved through adoption of a premeasured protein-free module for enteral feeding, although errors in preparing the feed remained an issue.

Study Summary

Glycomacropeptide in children with phenylketonuria: does its phenylalanine content affect blood phenylalanine control?

Daly A, Evans S, Chahal S, Santra S and MacDonald A

J Hum Nutr Diet. 2017 Aug;30(4):515-523

https://www.ncbi.nlm.nih.gov/pubmed/28111827

• Background

Individuals with phenylketonuria (PKU) require dietary management which includes protein-substitutes, which has traditionally been phenylalanine-free and based on L-amino acids (Phe-free LAA). An alternative is casein glycomacropeptide (CGMP) which contains a residual amount of phenylalanine. The aim of this study was to monitor the impact of CGMP-amino acid (CGMP-AA) protein substitute on blood phenylalanine control.

• Methods

A prospective pilot study was carried out, for 6 months, on 22 children with PKU. Patients were given either CGMP-AA or Phe-free LAA based on individual preference. Patients given Phe-free LAA received their usual L-AA protein substitute throughout the study. Patients in the CGMP-AA group were either partially or wholly transitioned from Phe-free LAA, dependent on blood phenylalanine concentration. The proportion of CGMP-AA provided was titrated to maintain phenylalanine in the target range. Outcome measures included the measurement of phenylalanine, tyrosine, and Phe:Tyr ratio and were compared with each patient's own blood results from the previous year.

• Results

Median age was 11 years (range 6-16 years). Twelve patients received CGMP-AA, 9 Phe-free L-AA; one patient was withdrawn from the CGMP-AA group. Within the CGMP-AA group there was a significant increase in blood phenylalanine (317 µmol/L vs 275 µmol/L; p=0.02), decrease in tyrosine (40 µmol/L vs 50 µmol/L; p=0.03) and an increase in Phe:Tyr ratio (8:1 vs 4.9:1; p=0.02). No significant differences in phenylalanine concentrations, tyrosine or Phe:Tyr ratios (p=0.9) between the two groups were observed. Acceptance of the CGMP-AA was higher with the children compared with the Phe-free LAA.

• Conclusions

Children taking CGMP-AA maintained blood phenylalanine concentrations within the target range, however there was a deterioration in blood phenylalanine control. CGMP requires careful monitoring when used in the dietary management of children with PKU.

Study Summary

Weaning practices in phenylketonuria vary between health professionals in Europe

Pinto A, Adamsb S, Ahringc K, Allend H, Almeidae MF, Garcia-Arenash D et al

Molecular Genetics and Metabolism Reports, in press
https://www.sciencedirect.com/science/article/pii/S2214426918301150

• Background

Weaning in PKU has additional challenges when compared to infants without PKU. During weaning, the natural protein from breast milk or standard infant formula is replaced by solid foods. A phenylalanine (Phe)-free second stage L-amino acid protein substitute (PS) is used to gradually replace the protein source from Phe-free infant formula. The aim of this study was to explore different approaches to weaning of PKU infants across Europe.

• Methods

A cross-sectional, online questionnaire was sent to European health care professionals experienced in the care of infants with metabolic disorders. The questionnaire was composed of 31 open and multiple-choice questions. Countries were grouped into broad geographical regions for analysis.

• Results

The majority (85%) of centres started weaning between 17- and 26-weeks, with fewer recommending weaning after 26 weeks (12%) and some before 17 weeks (3%). First solid foods were low-Phe vegetables (59% of centres) and fruit (34%). 51% of centres introduced Phe-containing foods before 26 weeks and 48% after 26 weeks. Centres located in Northern and Southern Europe most commonly used a Phe exchange system to allocate dietary Phe whereas centres from Eastern Europe and the majority from Germany and Austria, tended to calculate most Phe containing food sources. Some centres used a combination of methods. 41% of centres introduced a-more concentrated second stage PS between 26-36 weeks (typically Northern and Eastern Europe, Germany and Austria) and 37% from around 12-months of age (typically Southern Europe).

• Conclusion

Variations in approaches to weaning of infants with PKU are apparent across geographical regions in Europe. The long-term impact of different weaning strategies is an important consideration for longer term adherence and these different approaches need further prospective investigation.

Study Summary

Safety and efficacy of long-term use of extended release cornstarch therapy for glycogen storage disease types 0, III, VI, and IX

Ross KM, Brown LM, Corrado MM, Chengsupanimit T, Curry LM, Ferrecchia IA, Porras LY, Mathew JT, Dambska M and Weinstein DA.

Journal of Nutritional Therapeutics, 2015, 4, 137-142

http://www.lifescienceglobal.com/media/zj_fileseller/files/JNTV4N4A5-Weinstein-OA.pdf

• Background

Individuals with glycogen storage disease (GSD) experience hypoglycemia as a response to fasting. A waxy-maize extended release cornstarch, developed to prolong euglycaemia overnight, has been available in the USA since 2012. The aim of this study was to investigate the long-term safety and efficacy of this modified cornstarch, specifically in patients with ketotic forms of GSD

• Methods

An open prospective study was carried out in 16 patients. The response of patients to the modified, extended release cornstarch was monitored in a preliminary investigation. Patients in whom an improvement in metabolic control of greater than 2 hours, compared with their previous trial, were given the option of continuing with the intervention for up to 12-months. Biochemical analysis was carried out at baseline and at 12 months.

• Results

Patients with GSD type 0, III, VI and XI were enrolled. All patients responded well to the modified cornstarch and entered into the long-term phase. At baseline, the mean duration of overnight fasting was 4.9 hours. This was significantly prolonged to 9.6 hours following the initiation of the modified extended release cornstarch ($p<0.001$). Markers of metabolic control did not differ between baseline and following 12-months of treatment.

• Conclusion

Modified extended release cornstarch increased the duration of overnight fasting, thus reducing the likelihood of hypoglycaemia events, reducing sleep disruption. This may potentially improve on quality of life whilst maintaining metabolic control.

Study Summary

An examination of biochemical parameters and their association with response to ketogenic dietary therapies

Schoeler NE, Bell G, Yuen A, Kapelner AD, Heales SJR, Cross JH and Sisodiya S

Epilepsia. 2017 May;58(5):893-900

https://www.ncbi.nlm.nih.gov/pubmed/28369834

• Background

One option for patients with drug resistant epilepsy is the adoption of a ketogenic diet (KD), however accurate predictors of response to this intervention have not been identified to date. This study explored the hypothesis that correlations exist between specific biochemical markers and the extent of the anti-seizure effect of KD in individual patients.

• Methods

Biochemical analyses were carried out using routine blood samples taken prior to the initiation of KD and after 3-months. 215 children and 13 adults participated in the study. Responders to KD were identified as those individuals who experienced >50% reduction in seizures at 3 months. Data relating to b-hydroxybutyrate, acetoacetate, non-esterified fatty acids, free carnitine and acylcarnitine profile, glucose, and glucose-ketone index (GKI) were stratified according to whether patients were categorised as responders or non-responders.

• Results

Baseline levels of acetyl carnitine were significantly higher ($p<0.007$) in responders compared with non-responders. No association was observed between acetyl carnitine and KD response at the 3-month time point. A non-significant trend was observed for higher concentrations of free carnitine and other acylcarnitine esters, propionyl carnitine and b-hydroxybutyrate, measured in KD responders compared to non-responders both at baseline and at 3-months. No meaningful differences were observed in any of the other biochemical parameters tested.

• Conclusion

Carnitine fractions, specifically acetyl carnitine levels prior to commencement of KD are associated with a positive anti-seizure response. These findings are consistent with the current understanding that KD in drug-resistant epilepsy might exert its effects via alterations in energy metabolism.

Table. Acetyl carnitine concentrations were significantly higher at baseline in patients who responded to ketogenic diet compared with non-responders.

	Responders	Non-responders	p-value
Median concentration of acetyl carnitine at baseline, µmol/L (range)	12.15 (2.74-40.7)	15.05 (3.59 – 32.5)	< 0.007

Study Summary

The role of ketogenic diets in the therapeutic management of adult and paediatric gliomas: a systematic review

Martin-McGill KJ, Srikandarajah N, Marson AG, Tudur Smith C and Jenkinson MD

CNS Oncol. 2018 Apr;7(2):CNS17

https://www.ncbi.nlm.nih.gov/pubmed/29658772

• Background

Glioma progression is dependent on brain glucose. Previous studies have suggested that a switch to a ketogenic diet, reducing the availability of glucose as an energy source in the brain, may restrict glioma progression and improve outcomes. The aim of this study was to review the published evidence to assess the effectiveness and acceptability of ketogenic diets in humans.

• Methods

A systematic search protocol was adopted, searching for relevant data on seven separate databases. Papers identified in an initial search were reviewed independently by two authors who determined whether studies were eligible for inclusion according to pre-defined criteria. Study quality was assessed and data relating to overall survival, progression-free survival and patient acceptability of the ketogenic diet were extracted independently and agreed by both authors.

• Results

Six studies, representing 39 patients met the eligibility criteria and were included in the analysis. No randomised clinical trials were identified and all six studies were case series or case reports. These types of study carry with them an inherent risk of bias. All studies reported both overall and progression-free survival; no studies reported patient acceptance of the ketogenic diet intervention. The evaluation was not able to establish the effectiveness of a ketogenic diet in this population.

• Conclusion

There is a very limited evidence base describing the effectiveness and acceptability of ketogenic diets in the treatment of gliomas, preventing evidence-based decision making. Further high-quality investigation is needed.

Summary of Study Protocol

Ketogenic diets as an adjuvant therapy in glioblastoma (the KEATING trial): study protocol for a randomised pilot study

Martin-McGill KJ, Marson AG, Tudur Smith C, and Jenkinson MD

Pilot Feasibility Stud. 2017 Nov 28;3:67

https://www.ncbi.nlm.nih.gov/pubmed/29209515

• Background

Glioblastoma has an incidence of 2-3 per 100,000 per year and is the most common form of brain tumour, in adults. Management typically involves radiotherapy, chemotherapy (temozolomide) and surgical resection. However, response to treatment is poor, achieving a median survival rate of only 12-14 months. Given that glioma cells are highly dependent on glycolytic pathways, and that evidence suggests glucose restriction can limit their growth, an alternative approach to medical therapy is the ketogenic diet, with the purpose of establishing ketones as the major energy source for the body. Prior publications reporting on the utilisation of the KD with glioblastoma describe a variety of approaches in application. There is no agreement on optimal dietary composition, implementation method or timing for inclusion of the KD within traditional treatment plans. The aims of this pilot, randomised clinical study were to investigate and compare the practical use of two different versions of the KD, to determine their efficacy, tolerability and acceptability in the management of adults with glioblastoma within the UK healthcare system, and to provide information on the most appropriate dietary interventions for future related research in this group of patients.

• Methods

This paper describes the protocol for a prospective randomised (1:1) pilot study to be carried out in 12 patients in the UK, newly diagnosed with glioblastoma and following surgical resection. Diets to be evaluated are the modified ketogenic diet and the medium chain triglyceride ketogenic diet. Patient outcomes will be assessed at 12 weeks and 12 months following commencement of the allocated version of the ketogenic diet. Outcomes will include quality of life and food acceptability, gastrointestinal side effects, changes to biochemical markers (including glucose and ketone levels) and anthropometric measures. The feasibility of the study design will be assessed, by monitoring retention and recruitment rates, ability to enroll patients prior to commencement of chemotherapy, intervention time, dietary compliance and adjustments. Results will be used to design and power future clinical studies.

• Trial registration

ISRCTN71665562 and NCT03075514.

Study Summary

The safety of Lipistart®, a medium-chain triglyceride based formula, in the dietary treatment of long-chain fatty acid disorders: a phase I study

MacDonald A, Webster R, Whitlock M, Gerrard A, Daly A, Preece MA, Evans S, Ashmore C, Chakrapani A, Vijay S and Santra S

J Pediatr Endocrinol Metab. 2018 Mar 28;31(3):297-304

https://www.ncbi.nlm.nih.gov/pubmed/29425111

• Background

Children with long-chain fatty acid β-oxidation disorders (LCFAOD) can be managed using specialist infant formulae in which medium chain triglyceride (MCT) mostly replaces long-chain triglyceride (LCT). A new specialist formula has been developed and requires investigation of its safety and efficacy in children.

• Methods

An open-label, 21-day, phase I clinical study was carried out on 6 children with LCFAOD. All children were aged between 7 and 13 years and were previously well-controlled. Specific forms of LCFAOD included very long chain acyl CoA dehydrogenase deficiency (VLCADD, n=2), long chain 3-hydroxyacyl CoA dehydrogenase deficiency (LCHADD, n=2) and carnitine acyl carnitine translocase deficiency (CACTD, n=2). A new MCT-based formula (Lipistart®, Vitaflo), containing 30% energy from MCT, 7.5% LCT and 3% linoleic acid, was compared with conventional high-MCT feed (Monogen®, Nutricia), containing 17% energy from MCT, 3% from LCT and 1.1% from linoleic acid. Participants were given the conventional feed for 7 days before being switched to the new formula for 7 days and switched back to the conventional feed for the final 7 days. The parameters monitored included vital signs, blood biochemistry, electrocardiogram (ECG), weight, height, dietary intake and any symptoms specifically associated with LCFAOD, such as muscle pain.

• Results

5/6 participants completed the study. The new formula had minimal effect on tolerance, free fatty acids, acylcarnitines, 3-hydroxybutyrate, creatine kinase, blood glucose or liver enzymes. No changes in ECG results were reported. Median daily volume of both feeds was 720ml (intakes ranging from 500-1920ml). No LCFAOD-specific symptoms were reported by any children throughout the study.

• Conclusion

This trial is the first reported safety study for a LCFAOD-specific formula. The new formula was safe and well tolerated, in the short-term, in children with LCFAOD.

Study Summary

Fifteen years of using a second stage protein substitute for weaning in phenylketonuria: a retrospective study

Evans S, Daly A, MacDonald J, Pinto A and MacDonald A.

J Hum Nutr Diet. 2018 Jun;31(3):349-356

https://www.ncbi.nlm.nih.gov/pubmed/28940742

• Background

Management of phenylketonuria (PKU) principally consists of a low phenylalanine (Phe) diet by limiting ingestion of protein and supplementing with Phe-free amino acids. For infants with PKU during the weaning period a second stage Phe-free protein substitute (PS) is introduced in a semi solid format to ensure adequate intake of non-Phe protein which would otherwise be provided by food. Presenting the PS in this form helps to encourage appetite for solid foods. Although such Phe-free PS have been available for over 15-years to support weaning, no long-term study has evaluated their use in management of infants with PKU.

• Methods

Data relating to 31 children with PKU who were given a second stage PS during weaning was evaluated retrospectively from the commencement of weaning to their second birthday.

• Results

Weaning of low protein foods started at a median of 17 weeks (range 12-25 weeks) and second stage PS was given from a median of 20 weeks (range 13-37 weeks). Initial weaning PS was the equivalent of 2-4g/day (5-10g of powdered supplement). As the volume of infant PS decreased and the infant gained weight, the amount of second stage PS prescribed increased; between weaning and first birthday, second stage PS intake increased each month by 0.2g/kg/day. Total protein intake was >2g/kg/day from weaning to second birthday. Acceptance of solid food and PS was affected negatively by teething and illness. Introduction of increased variety of textured foods was delayed in 32% of children and was influenced by birth order (firstborn, p=0.05) and food refusal when teething (p=0.02).

• Conclusion

Negative behavior associated with second stage PS was typically associated with illness, teething or food refusal. Improved acceptance of second stage PS was observed in situations where consistent feeding routines and appropriate timings were used.

Study Summary

Dietary management of blood glucose in medical critically ill overweight and obese patients: an open-label randomised trial

Rice TW, Files DC, Morris PE, Bernard AC, Ziegler TR, Drover JW, Kress JP, Ham KR, Grathwohl DJ, Huhmann MB, and Gautier JB

J Parenter Enteral Nutr. 2018 Sep 27

https://www.ncbi.nlm.nih.gov/pubmed/30260488

• Background

Standard enteral nutrition (EN) formulae contain high levels of carbohydrate and can result in hyperglycaemia. The aim of this study was to assess the effect of an alternative EN formula, containing very high-protein and low carbohydrate content on glucose control.

• Methods

A multi-centre, randomised study was carried out in overweight or obese patients, undergoing mechanical ventilation and prescribed 1.5g protein/kg ideal body weight/day. Patients received either the experimental EN formula (37% protein, 29% carbohydrate, n=52) or a control EN formula (25% protein, 45% carbohydrate, n=53). An interim analysis was conducted after enrollment of 105 patients to evaluate the primary objective, the number of glucose events outside the range of >110 and ≤150 mg/dL.

• Results

Between days 1-5 of EN, no differences in protein delivery (1.2 ± 0.4 and 1.1 ± 0.3 g/kg ideal body weight/day; p=0.83) or energy delivery (8.2 ± 6.0 and 12.5 ± 3.7 kcals/kg ideal body weight/day; p<.0001) were observed between groups. No significant difference in the primary outcome, was observed (p=0.54) resulting in study termination. A significant difference in mean blood glucose (126 vs 138 mg/dl respectively; p=0.004) and decreased insulin administration (0.1% vs 10.9%; p=0.048) were observed in the experimental group compared to the control group. A 13% decrease in the number of hyperglycaemic events >150mg/dl (p=0.015) but a 14% increase in the number of events between 80-110mg/dl (p=0.0007), were observed in the group given the experimental EN formula.

• Conclusion

Very high protein, low carbohydrate EN formula can improve glucose control, resulting in fewer severe hyperglycaemic events and a reduced need for insulin.

Study Summary

Modulation of cerebral ketone metabolism following traumatic brain injury in humans

Bernini A, Masoodi M, Solari D, Miroz JP, Carteron L, Christinat N, Morelli P, Beaumont M, Abed-Maillard S, Hartweg M, Foltzer F, Eckert P, Cuenoud B and Oddo M

J Cereb Blood Flow Metab. 2018 Oct 24, doi: 10.1177/0271678X18808947

https://www.ncbi.nlm.nih.gov/pubmed/30353770

• Background

Following traumatic brain injury (TBI), the brains' metabolism can respond by switching to alternative energy sources, such as ketone bodies (KB), as a protective mechanism. Increased metabolism of KB is believed to protect the brain against damage associated with low glucose availability. The aim of this study was to monitor changes in KB metabolism in patients who had received TBI and to explore the impact of fasting or provision of nutrition.

• Methods

KB levels (acetoacetate and b-hydroxybutyrate) in brain interstitial tissue of 34 patients following TBI, were measured using cerebral microdialysis. Patients were either fasted or received stable enteral nutrition.

• Results

Brain KB was significantly reduced in patients who were receiving nutrition compared with fasting patients (34.7 [10th–90th percentiles 10.7–189] mmol/L vs. 13.1 [6.5–64.3] mmol/L, $p<0.001$). A similar observation was made when blood KB was monitored (668 [168.4–3824.9] vs. 129.4 [82.6–1033.8] mmol/L, $p<0.01$). A correlation was identified between brain and blood KB (Spearman's rho 0.56, $p=0.0013$). Higher levels of brain KB were found to correlate with patient age and other brain metabolites indicative of stress, including lactate, pyruvate and glutamate, but not correlate with brain glucose. Provision of medium-chain trigycerides-enriched enteral nutrition resulted in a modest increase in free medium chain fatty acids detected in blood and brain but did not affect blood KB.

• Conclusion

The correlation between brain KB and indicators of metabolic stress support the hypothesis that metabolic stress may trigger the release of KB to act as an alternative metabolic substrate following trauma. Cerebral KB metabolism following TBI was reduced in patients who received post-injury enteral nutrition.

Study Summary

Nutritional ketosis increases NAD+/NADH ratio in healthy human brain: an in vivo study by 31P-MRS

Xin L, Ipek Ö, Beaumont M, Shevlyakova M, Christinat N, Masoodi M, Greenberg N, Gruetter R and Cuenoud B.

Front Nutr. 2018 Jul 12;5:62.

https://www.ncbi.nlm.nih.gov/pubmed/30050907

• Background

The human brain is known to metabolise ketone bodies (KB) under conditions of glycaemic stress, such as trauma, neurological diseases or aging. The role of KB in the brain of healthy individuals is largely unknown. The aim of this study was to explore the metabolic contribution of KB in the healthy human brain and the effect of a ketogenic dietary supplement on this mechanism.

• Methods

Brain metabolites were monitored using a non-invasive, phosphorous magnetic resonance spectroscopy (31P-MRS) technique in healthy young adults before and after ingestion of Peptamen®, an oral nutritional supplement that is high in medium chain triglycerides (MCT) levels. MCT are ketone precursors which are known to raise systemic levels of ketones.

• Results

Following ingestion of Peptamen®, the redox NAD+/NADH ratio in the brain was increased by 18% compared with values before the supplement was given. NAD was increased by 3.4% and NADH was reduced by 13%.

• Conclusion

NAD has an important role in the modulation of metabolism. Its increase in the brain, as a result of nutritional ketosis, suggests that ingestion of a diet rich in ketones may have an NAD sparing effect. This finding may have potential in several clinical scenarios where KB metabolism in the brain may incur greater brain health.

Study Summary

Nutritional interventions in primary mitochondrial disorders: developing an evidence base

Camp KM, Krotoski D, Parisi MA, Gwinn KA, Cohen BH, Cox CS, Enns GM, Falk MJ, Goldstein AC, Gopal-Srivastava R, Gorman GS, Hersh SP, Hirano M, Hoffman FA, Karaa A, MacLeod EL, McFarland R, Mohan C, Mulberg AE, Odenkirchen JC, Parikh S, Rutherford PJ, Suggs-Anderson SK, Tang WH, Vockley J, Wolfe LA, Yannicelli S, Yeske PE and Coates PM

Mol Genet Metab. 2016 Nov;119(3):187-206

https://www.ncbi.nlm.nih.gov/pubmed/27665271

• Background

Primary mitochondrial disorders (PMDs) are rare, and heterogenous conditions, and have been historically managed through the use of dietary supplements. Although this approach is perceived as safe, the hypothetical benefits remain to be proven through rigorous clinical investigation with only a few reports currently published in the literature. The low incidence of these disorders is a barrier to large clinical evaluations.

• Methods

A workshop, sponsored by NIH, the Wellcome Trust, and the United Mitochondrial Diseases Foundation, was held in December 2014, entitled "Nutritional Interventions in Primary Mitochondrial Disorders: Developing an Evidence Base". The aims were to explore the current status of use of nutritional supplements in the management of PMDs, to identify gaps in the evidence base and to identify research opportunities, potentially involving collaboration between different stakeholders, as a means of progressing research in this field.

• Results

Several areas were identified that required further investigation. These included 1) defining the disease, 2) clinical trial design, 3) biomarker selection, 4) mechanistic approaches, 5) challenges in using dietary supplements, 6) standards of clinical care, and 7) collaboration issues. Short- and long-term goals were identified in all 7 areas. Suggestions included development of a natural history study to include all individuals with PMD and establishment of a patient registry to enable and support future clinical research.

• Conclusion

The workshop identified many areas that would benefit from further investigation and through fostering collaborative links, identified potential future routes to overcome the research challenges specific to PMD.

Study Summary

The pleiotropic effects of decanoic acid treatment on mitochondrial function in fibroblasts from patients with complex I deficient Leigh syndrome

Kanabus M, Fassone E, Hughes SD, Bilooei SF, Rutherford T, Donnell MO, Heales SJR and Rahman S

J Inherit Metab Dis. 2016 May;39(3):415-426
https://www.ncbi.nlm.nih.gov/pubmed/27080638

• Background

Patients with mitochondrial disorders may benefit from a ketogenic diet (KD). The cellular mechanism involved and whether KDs are likely to be of equal benefit to patients with different types of mitochondrial disorders is largely unknown. Decanoic acid (C10) is a component of the medium chain triglyceride KD which acts as a ligand for PPAR-γ, implicated in mitochondrial biogenesis. The aim of this study was to investigate the effects of C10 on human fibroblasts with mitochondrial disorders.

• Methods

Primary human fibroblasts were obtained from 6 patients with Leigh Syndrome (LS) and cultured in vitro. Their response to C10 was assessed using mitochondrial respiratory chain enzyme assays, gene expression microarray, qPCR and flow cytometry.

• Results

Fibroblasts from some donors with LS responded to C10 by increasing citrate synthase activity, a cellular mitochondrial marker, in a manner dependent on PPAR-γ. An increase in fatty acid metabolism was suggested by an upregulation in Acyl-CoA Dehydrogenase (ACADVL) and Carnitine palmitoyltransferase I (CPT1). A decrease in glucose metabolism, signaled by a downregulation in puruvate dehydrogenase (PKD3 and PKD4) and an upregulation in PCK2, which blocks glucose metabolism, was observed. C10 also reduced oxidative stress in cells challenged with rotenone. The cells from some subjects did not respond to C10 exposure.

• Conclusion

The effect of decanoic acid on primary fibroblast cells of individuals with LS promoted fatty acid metabolism, while impacting on the regulation of genes involved in glucose metabolism. Not all donors' cells responded to the stimulation with C10: prior in vitro screening may be a useful tool prior to selecting individuals for future clinical trials.

Study Summary

Neuronal decanoic acid oxidation is markedly lower than that of octanoic acid: a mechanistic insight into the medium-chain triglyceride ketogenic diet

Khabbush A, Orford M, Tsai YC, Rutherford T, O'Donnell M, Eaton S and Heales SJR

Epilepsia. 2017 Aug;58(8):1423-1429

https://www.ncbi.nlm.nih.gov/pubmed/28682459

• Background

Individuals with drug-resistant epilepsy can be treated with a ketogenic diet composed of medium chain triglyceride (MCT). The exact mechanism of action is unknown. MCT contains both octanoic (C8) and decanoic (C10) acids. It has been suggested that molecular interactions in the brain with C10 but not C8, may be responsible for the anti-seizure effect of KDs and that accumulation of C10 in the brain may be required. The aim of this study was to investigate the underlying mechanisms leading to C10 accumulation.

• Methods

C8 and C10, were labelled with carbon 13 (C^{13}) and applied to cultured neuronal SH-SY5Y cells in the presence of etomoxir, an inhibitor of carnitine palmitoyltransferase I (CPT1), an enzyme involved in fatty acid metabolism. The β-oxidation rate of C8 and C10 was monitored by detection of C^{13} labelled CO_2.

• Results

Although both C8 and C10 were catabolised by SH-SY5Y cells, β-oxidisation of C10 occurred at a lower rate (20%) compared with C8. β-oxidisation of C10 was highly dependent on CPT1 activity whereas 66% of the β-oxidisation of C8 was independent of CPT1 activity. The known low levels of CPT1 found in neurons is consistent with these observations. The oxidisation of C10 was further decreased in the presence of C8.

• Conclusion

Low expression of CPT1 in neuronal tissue may result in a lower rate of oxidisation of C10 in the brain, potentially leading to its accumulation and anti-seizure effects. As C8 has a sparing effect on C10, this effect may be enhanced by the provision of C10 along with C8, in ketogenic diets.

Study Summary

Nutritional status in children with PKU: glycomacropeptide compared with phenylalanine free-AA

Daly A, Evans S, Chahal S, Santra S, Pinto A, Rocha J, van Spronsen SJ and MacDonald A

J Inherit Metab Dis (2018) 41(Suppl 1): 1. https://doi.org/10.1007/s10545-018-0232-x
https://link.springer.com/journal/10545/41/1/suppl/page/1

• Background

Individuals with phenylketonuria (PKU) require dietary management which includes protein-substitutes. These have traditionally been phenylalanine-free and based on L-amino acids (Phe-free LAA). An alternative is casein glycomacropeptide (CGMP). The aim of this study was to monitor the impact of CGMP-amino acid (CGMP-AA) protein substitutes on micronutrient status in children with PKU.

• Methods

48 children (29 on CGMPAA2 19 on L-AA) all started with 100% L-AA protein substitute at baseline. In the CGMP-AA group subjects partially or wholly replaced Phe-free L-AA with CGMP-AA, replacement was gradual and titrated the blood phe levels. L-AA group consumed 100% L-AA protein substitutes. Micronutrient status was evaluated at baseline and 6 months after introducing cGMP-AA. Samples were tested for zinc, selenium, C-reactive protein, haemoglobin, cell volume, ferritin, vitamin B12 and 25-hydroxy vitamin D.

• Results

At 6 months cGMP-AA group participants consumed a median of 75% protein substitute intake as CGMP, with 25% from L-AA. Compared to the L-AA group, there was a significant increase in selenium concentration between baseline and 6-months in both whole blood and plasma (p=0.0002, p=0.0007) in the CGMP group . In patients treated with CGMP, but not L-AA, ferritin decreased between baseline and 6-months (p=0.0006) although median values remained within the recommended range. All other nutritional markers assessed were within the normal range at 6-months, except for vitamin B12 which had a concentration above the recommended range in both groups.

• Conclusion

Both protein substitutes were successful in maintaining nutritional blood markers within the reference range. An increase in plasma and whole blood selenium was observed in the CGMP group which may indicate superior antioxidant properties of the product.

Study Summary

Prospective study: Glycomacroprotein and conventional amino acid protein substitute in children. Effect on blood phenylalanine and growth

Daly A, Evans S, Chahal S, Santra S, Pinto A, Hogler W, Gingell C, Richa J, van Spronsen FJ and MacDonald A

J Inherit Metab Dis (2018) 41(Suppl 1): 1
https://link.springer.com/journal/10545/41/1/suppl/page/1

• Background

Individuals with phenylketonuria (PKU) require dietary management which includes protein-substitutes. These have traditionally been phenylalanine-free and based on L-amino acids (Phe-free LAA). An alternative is casein glycomacropeptide (CGMP) which contains a residual amount of phenylalanine. CGMP has been reported to potentially provide additional health benefits. The aim of this study was to monitor the impact of CGMP-PS on blood Phe, Tyr, Phe:Tyr ratio, weight, height and BMI z scores.

• Methods

48 children (29 on CGMPAA2 19 on L-AA) all started with 100% L-AA protein substitute at baseline. In the CGMP-AA group subjects partially or wholly replaced Phe-free L-AA with CGMP-AA, replacement was gradual and titrated the blood phe levels. L-AA group consumed 100% L-AA protein substitutes. Micronutrient status was evaluated at baseline and 6 months after introducing cGMP-AA. Nutritional and anthropometric parameters were measured at baseline, 6 and 12-months.

• Results

At the end of 12 months 48% of subjects were able to completely replace their L-AA PS with cGMP-AA as their single source of PS. In the CGMP group cGMP-AA provided a median 75% (30-100%) of the total protein substitute intake with the remaining 25% from L-AA. There was no difference between cGMP and L-AA for blood phe, tyr or anthropometry. In cGMP group there was a significant increase of phe between baseline and 6 months ($p=0.06$) and baseline and 12 months ($p<0.001$). Baseline average Phe: 270µmol/L (170-430), 6m average Phe: 300µmol/L (124-485), 12m average Phe: 300µmol/L (200-490). Patients in the CGMP group, but not in the control group increased in weight ($p=0.0001$) and BMI ($p=0.0001$) between baseline and 12 months.

• Conclusion

A significant rise in blood Phe (within the target treatment range) was observed in children managed with CGMP. CGMP can be used in the management of PKU children with careful introduction and monitoring but may only partially contribute to their protein substitute requirement.

Study Summary

Variability of phenylalanine concentrations over 24 hours using two different protein substitutes and changing dietary phenylalanine intake

Daly A, Evans S, Chahal S, Santra S, Pinto A, Gingell C, Rocha J, van Spronsen FJ, Jackson R and MacDonald A

J Inherit Metab Dis (2018) 41(Suppl 1): 1

https://doi.org/10.1007/s10545-018-0232-x https://link.springer.com/journal/10545/41/1/suppl/page/1

• Background

Individuals with phenylketonuria (PKU) require dietary management including a protein-substitute. Studies have suggested that blood phenylalanine (Phe) variability may be stabilised through the use of glycomacropeptide (CGMP). The aim of this study was to assess blood Phe variability over 24 hours in patients receiving either CGMP or Phe-free L-amino acid (LAA).

• Methods

A 3-arm, randomised, controlled, cross-over study was carried out in 18 children with PKU. Isocaloric intake was maintained. The dietary regimen on each arm was followed by each participant for 14 days: 1. CGMP-AA only (no dietary Phe adjustment), 2. CGMP-AA2 (Phe content of GMP removed from dietary Phe allowance), 3. Phe-free LAA (no dietary Phe adjustment). On days 13 and 14, blood samples were collected every 4 hours for 48 hours and analysed for Phe concentrations.

• Results

The median Phe concentrations over 24 hours were statistically significant between each arm of the study (see Table). CGMP without dietary Phe adjustment does lead to higher blood phenylalanine concentrations in children with PKU, however blood concentrations remained within the target treatment range. No significant difference in the rate of change of Phe levels over the 24-hour period was observed between groups.

• Conclusion

These findings indicate that reducing the dietary phe to compensate for phe contained in CGMP-AA enables a more consistent blood phe profile, although the difference in the rate of change did not reach statistical significance.

Median Phenylalanine concentrations of 4 hourly bloodspots over 24 hours

	CGMP-AA plus dietary Phe	CGMP-AA minus dietary Phe	Phe free L-AA
Median Phenylalanine (range), µmol/L	290 (30-580)	220 (10-670)	165 (10-640)
% Phenylalanine concentrations within target range	44	56	39

Study Summary

Understanding the core principles of a 'modified ketogenic diet': a UK and Ireland perspective

Martin-McGill KJ, Lambert B, Whiteley VJ, Wood S, Neal EG, Simpson ZR and Schoeler NE, on behalf of the Ketogenic Dietitians Research Network (KDRN)

Congress abstract: 6th Global Symposium on Ketogenic Therapies for Neurological Disorders. Korea 5-9 October 2018

NO LINK TO THIS CONGRESS ABSTRACT AVAILABLE

• Background

Ketogenic diets can be used in the treatment of refractory epilepsy. Anecdotally, centres across the UK and Ireland report using a 'modified' ketogenic diet (MKD). These modifications are poorly defined in the current literature and information about the clinical efficacy of such modifications is scant. The aim of this study was to explore the principles underpinning MKD and to clarify to what extent they differ from conventional ketogenic diets.

• Methods

An online questionnaire, designed by a consensus group of ketogenic dieticians, containing 35 questions relating to the use of MKD, was sent to 39 centres in the UK and Ireland.

• Results

Responses were returned from 18/35 centres, (13 paediatric, 3 adult and 2 mixed centres). The principal determinant of MKD prescriptions was the patients' individual estimated energy requirement. Macronutrient composition was typically 75% fat, 5% carbohydrate with protein *ad libitum*. To achieve carbohydrate and fat targets, weighed portions were most commonly used (carbohydrate lists, 18 centres; fat lists, 13 centres) with a 'household measures' approach less common (carbohydrate lists, 2 centres; fat lists, by 3 centres). 17/18 (94%) of centres adjusted macronutrients over time, most commonly based on seizure frequency and ketone levels (14/18, 83% of centres). Products available on prescription were used when initiating MKD in 10/18 (56%) of centres which increased to 100% of centres as the diets were fine-tuned to individual patient requirements.

• Conclusion

MKD are based on the principles of established ketogenic diets but incorporate novel elements. Further investigation is required to determine the clinical- and cost-effectiveness of MKD.

Study Summary

NICE to know: impact of NICE guidelines on ketogenic diet services nationwide

Whiteley VJ, Martin K, Carroll J, Taylor H and Schoele N

DMCN 59:S4;1-142. Congress abstract: British Paediatric Neurology Association Annual Meeting, London, UK, 3–5 January 2018

https://onlinelibrary.wiley.com/toc/14698749/59/S4

• Background

Patients with drug-resistant epilepsy may benefit from a ketogenic diet. The National Institute for Clinical Excellence (NICE) in the UK published guidelines on the diagnosis and management of epilepsy in 2012 (CG137) which recommended consideration of ketogenic diet for children and young people with drug-resistant epilepsy. The aim of this study was to investigate the impact of the publication of the NICE guidelines on clinical practice in the UK.

• Methods

An online questionnaire was sent to ketogenic dieticians based in the UK and Ireland in 2017. Results were compared to similar questionnaires completed in 2010 and 2000.

• Results

An increase in the number of centres offering ketogenic diets for the management of drug-resistant epilepsy was observed in 2017 (39 centres) compared with provision in 2010 (28) and 2000 (22), equating to a 77% increase since 2000. 7/39 (18%) of centres in 2017 accepted adult referrals compared with only 2/28 (7%) in 2010. Patient numbers being managed by ketogenic diets increased 7-fold, from 101 patients in 2000 to 754 in 2017. In 2017, 31/39 (79%) of centres had a waiting list, ranging from 1-49 patients, with a total of 267 patients waiting for initiation of a ketogenic diet.

• Conclusion

The number of patients managed with a ketogenic diet has increased as more centres have offered these services. The increase in availability of adult services, not currently indicated by the NICE guidelines, is increasingly offered. Demand for the services currently outstrips supply, suggesting that further expansion of centres offering ketogenic diet support, is needed in the UK and Ireland.

Content Ed Net

Content Ed Net GmbH
Allschwilerstrasse 10. CH-4055 Basel. Switzerland
Sales.ch@contentednet.com

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