A practical guide to the use of medium chain triglyceride (MCT) in the ketogenic diet
Introduction

The ketogenic diet (KD) originally devised in the 1920's and 30's and still in worldwide use today uses foods naturally rich in fat as long chain triglyceride (LCT) to provide an abundance of fatty acids for conversion to ketones. However, the diet is challenging to undertake, despite its proven success in the dietary management of drug resistant epilepsy and neurometabolic disorders.

In the 1960's, medium chain triglycerides (MCT) became available for clinical use. Differences in molecular structure between MCT and LCT, and major dietary sources are outlined in Figure 1 and described in section 1.0. To take advantage of the observed greater ketogenic potential of fat comprised of medium chain fatty acids and to try to improve patient acceptability and application of the ketogenic diet, an alternative to the original, Classical regime (CKD) was devised in the 1970's - the medium chain triglyceride KD (MCTKD). Inclusion of MCT oil retained clinical efficacy and importantly, enabled reduction in total fat content and more protein and carbohydrate foods, facilitating greater dietary palatability. A randomised trial of the MCTKD and CKD in children with intractable epilepsy found them comparable in efficacy and tolerability, and concluded both had their place in the treatment of childhood drug resistant epilepsy.

Aside from heightened ketone production, a specific anti-epileptic effect of MCT and of the individual medium chain fatty acids octanoic (C8) and decanoic (C10) has been proposed, resulting from studies of children on the MCTKD. More recently, research has emerged that reinforces and extends these observations, so potentially meriting the inclusion of MCT in combination with LCT as a beneficial and advantageous constituent in all versions of the ketogenic diet in the dietary management of seizures.

The scientific, clinical and dietary aspects of the use of MCT in the KD are outlined in sections 2.0 and 3.0, and a timeline showing the history of use of MCT in the KD in 4.0.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CKD</td>
<td>Classical ketogenic diet</td>
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<td>C8</td>
<td>Caprylic or octanoic acid; ketogenic medium chain fatty acid</td>
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<td>C10</td>
<td>Capric or decanoic acid; ketogenic medium chain fatty acid</td>
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<td>GI</td>
<td>Gastrointestinal</td>
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<td>KD</td>
<td>Ketogenic diet</td>
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<td>LCFA</td>
<td>Long chain fatty acid</td>
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<td>LCT</td>
<td>Long chain triglyceride</td>
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<td>LGIT</td>
<td>Low glycaemic index treatment</td>
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<td>MAD</td>
<td>Modified Atkins diet</td>
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<td>MCF A</td>
<td>Medium chain fatty acid</td>
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<td>MCT</td>
<td>Medium chain triglyceride</td>
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<td>MCTKD</td>
<td>Medium chain triglyceride ketogenic diet</td>
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<td>MKD</td>
<td>Modified ketogenic diet</td>
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For information on the ketogenic diet, Vitaflo products for the use in ketogenic diet and recipes visit the Vitaflo websites:

www.vitaflo.com  www.myketogenicdiet.co.uk/de
www.myketogenicdiet.com  www.myketogenicdiet.co.uk/ie
www.myketogenicdiet.co.uk  www.myketogenicdiet.co.uk/nl

Other Vitaflo resources for the KD can be accessed on the VIA website

www.nestlehealthscience.com/Vitaflo/VIA
1.0 Overview of MCT and LCT

1.1 Dietary sources of MCT and MCFA

A molecule of MCT consists of mixtures of three medium chain fatty acids (MCFA) of 6 - 10 carbons attached to a glycerol backbone:

- C6 (hexanoic or capronic acid)
- C8 (octanoic or caprylic acid)
- C10 (decanoic or capric acid)

MCFA with ketogenic and antiepileptic effects

MCT is present naturally in only a few foods, in small amounts, for example coconuts, animal milks. Proprietary products (oils, emulsions and powders) therefore typically supply MCT in the KD.

Foods - LCT is the main fat present in foods. Naturally occurring MCT is only found in small amounts in coconuts, palm kernels and animal milks and therefore normal dietary intakes are limited. In coconut and palm kernel oils, the proportions of C6, C8 and C10 in the triglycerides are low in comparison to C12, which is the main fatty acid present.

Proprietary MCT oils, emulsions and powders - MCT oils have been available for clinical use since the 1950’s and contain predominantly C8 and C10 fatty acids. They are produced by hydrolysis of coconut or palm kernel oils followed by filtration to remove the C12 fatty acids. The remaining C8 and C10 are then re-esterified with glycerol backbone into triglycerides. The proportions of C8 to C10 are defined during manufacture of the MCT oil and typically expressed as a ratio, e.g. 40:60, 50:50. MCT emulsions (e.g. betaquik® Vitaflor International Ltd) are made by combining these oils with water, and MCT powders (e.g. MCTprocal® Vitaflor International Ltd) by the spray drying of MCT oils onto protein and carbohydrate. A comparison of the fatty acid profiles of coconut oil and an MCT oil with a 60:40 ratio of C8 to C10 MCFA is illustrated in Figure 2.

Note: *C12 (dodecanoic or lauric acid) is sometimes classified as MCFA.

1.2 Assimilation of MCT and LCT

The process of assimilation i.e. the incorporation of nutrients into the body via digestion, absorption and transportation, is different for MCT compared to LCT. This is due to the specific physical structures and unique biological properties of the triglyceride molecules and their constituent fatty acids. When consumed as part of a KD, these features influence the availability of the fatty acids for beta-oxidation to acetyl-CoA and then onwards to ketogenesis. Essentially, due to their shorter carbon chain lengths, the MCFA go through the beta-oxidation pathway more quickly and undergo conversion to ketones more efficiently and rapidly than the LCFA. C8 is thought to drive the ketogenic effect of MCT containing both C8 and C10. It has been shown that C8 is preferentially converted to acetyl-CoA compared to C10, hence it can undergo ketogenesis more rapidly.

1.3 MCT in the KD

MCT oils, emulsions and powders high in C8 and C10 MCFA have a history of safe and efficacious use in the KD (Section 4.0). They are primarily used for the ketogenic and anti-epileptic effects of these fatty acids. To provide MCT in the KD, it is preferable to use these proprietary products rather than coconut oil, as although it is a useful source of fat, it provides only small amounts of C8 and C10 due to its high C12 content.

Clinical, scientific and dietetic evidence, in combination with experience of use, suggests that inclusion of MCT as a source of fat in the KD may:

- Promote and enhance ketogenesis.
- Provide a potential anti-epileptic effect.
- Enhance dietary palatability and acceptability.
- Be helpful in the management of KD-related side effects, e.g. dyslipidaemia, gastroesophageal reflux (GOR), constipation.
2.0 Scientific and clinical basis for the use of MCT in the KD

2.1 For ketogenesis
In the context of the KD, the faster route to ketogenesis of MCT and MCFA in comparison to LCT and LCFA is advantageous. Compared to LCFA, MCFA have been demonstrated to:
- Reach and enter the liver cell mitochondria faster and undergo a more prompt and extensive oxidation to acetyl-CoA via the β oxidation pathway, in particular, C8\textsuperscript{17, 18, 22}.
- Primarily undergo ketogenesis, instead of being stored in adipose tissue as an energy reserve\textsuperscript{2, 33}.
- Be converted to ketones in both regular and ketogenic diets, after oral administration of MCT\textsuperscript{2, 34}.
- Be rapidly converted to ketones within 30 minutes of ingestion of either MCT oil or emulsion, and for blood levels to remain elevated for around 4 hours, in comparison to LCT\textsuperscript{2, 34}.

2.2 For specific, anti-epileptic properties
Based on its ketogenic potential, in combination with LCT, MCT has a role in establishing and maintaining ketosis and low ketone levels (typically monitored on the KD and useful as a marker for dietary compliance), can be equally compared to LCF\textsubscript{A}. In the context of the KD, the faster route to ketogenesis of MCT and MCFA in comparison to LCT and LCFA is advantageous.

2.3 For ketogenesis and absence of seizures
Scientific and clinical basis for the use of MCT in the KD
- Inclusion of MCT, as an addition or substitution of a proportion of total LCT content in a KD may, therefore;
  - Help preserve carbohydrate content or permit an additional amount to be included.
  - Promote dietary acceptability, palatability and adherence.

2.4 To improve ketosis
The requisite high fat, low carbohydrate content of the KD limits the choice and variety of foods permitted. This can have a negative influence on the enjoyment of eating, contributing toward a high discontinuation rate, despite any initial success, especially in adolescents and adults\textsuperscript{34}. Huttenlocher et al developed the MCTKD as a modification of the CKD by replacing a proportion of the LCT content with MCT oil\textsuperscript{34}. This enabled total fat content to reduce from 87-90% to around 75% of daily energy requirement yet still achieve adequate ketosis and dietary efficacy. In addition more protein and carbohydrate could be included which reportedly enhanced overall dietary palatability and acceptability\textsuperscript{44}.

The potential of the MCTKD allows more carbohydrate in the MCTKD can be applied in all the LCT based versions of the KD - CKD, LGIT, MAD and MKD\textsuperscript{35}.

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3.0 Dietary attributes of MCT in the KD

3.1 To enhance dietary palatability and promote acceptability
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3.2 To improve ketosis
- In the CKD
  - Inclusion of MCT may be beneficial as an alternative to increasing the ketogenic ratio, e.g. from 3 to 1 up to 4 to 1 as this involves reducing the amount of carbohydrate and/or adding more LCT\textsuperscript{35}.
- In the modified versions of the KD (LGT, MAD, and MKD)
  - Adding in a measured daily quantity of MCT may avoid further carbohydrate restriction\textsuperscript{35}.
  - In neurometabolic conditions, e.g. Glut-1 DS
    - For those reliant on the KD to supply an alternative energy source to glucose, regular consumption of MCT at specific times during the day may help improve ketosis overall and ensure an adequate supply of ketones to meet energy needs\textsuperscript{35}.

3.3 For rapid ketone production at specific times
- MCT may ‘boost’ ketone production and energy supply at specific times, e.g. for those with Glut-1 DS before exercise.
- MCT taken at bedtime to help maintain ketosis overnight is linked to improved control of nocturnal seizures\textsuperscript{35}.

3.4 For the management of diet related side effects of the KD
- Evidence suggests that in normal human diets, MCT is beneficial in the context of cardiovascular risk factors and health\textsuperscript{17, 37}. On the KD, dyslipidaemia is common, and, although typically self-resolving with time, can be of concern, and warrant manipulation of dietary fat sources. In studies, use of MCT in the KD is associated with more favourable lipid levels, and therefore its inclusion may be helpful in the prevention or management of this condition\textsuperscript{17, 37, 38-41}.
- MCT may help manage GOR. In those with drug resistant epilepsy, when especially in combination with neurological impairment, there is a high incidence of GOR. This condition is often aggravated by a high fat diet\textsuperscript{42}. Use of MCT to promote stomach emptying\textsuperscript{43} and/or as an adjunct to lowering total fat content, may help application and tolerance of the KD in this situation, or if GOR symptoms related to high fat intake manifest once on diet.
- MCT may be helpful in the management of constipation, a common side effect of the KD\textsuperscript{34}. However, care is advised when MCT is given for this (or any other reason) as it can induce diarrhoea and gastrointestinal disturbance in some individuals\textsuperscript{44}. (See also the VitaroFoods resource A practical guide to establishing gastrointestinal tolerance of medium chain triglyceride (MCT) and betaquick in the ketogenic diet).
4.0 History of use of MCT in the KD

4.0.1 1920’s and 30’s
The CKD based on LCT is devised. Its application is efficacious in many children and adults with drug resistant epilepsy11-13.

4.0.2 Late 1930’s
The development and availability of anti-epileptic drugs, e.g. phenytoin, leads to declining use of the KD14.

4.0.3 1960’s
The ability of MCT and individual MCTA C8 and C10 to generate ketones and establish ketonaemia more rapidly and efficiently than LCTA, even in the presence of dietary carbohydrate is recognized5-7.

4.0.4 1970’s
This characteristic is due to the unique physiological properties, functions, and biological features of MCT and its constituent fatty acids. A faster assimilation enhances bioavailability for beta-oxidation to acetyl Co-A, providing a more efficient method of ketone production.

4.0.5 1980’s and onwards
Continued efficacious use of MCTKD is reported, mainly in children11, 12, 13, 14. Practical experience and use of the MCTKD shows 45 – 50% of energy intake from MCT achieves a good balance between adequate ketosis, dietary efficacy, and gastrointestinal tolerance8, 9, 10, although successful use up to 70% is reported11.

4.0.6 1990’s
The development of emulsions of MCT as an alternative to MCT oil aids acceptability and tolerance as part of a KD8.

4.0.7 Today, and into the future...
Use of the KD for the dietary management of drug resistant epilepsy is re-established12.

5.0 References

6.0 Appendices

6.1. Assimilation of fatty acids

The process of assimilation by the body is shown in Figure 4. The length of the carbon chain of the fatty acid molecule determines their digestion, absorption and transportation. The route to ketone production is more rapid for MCT compared to LCT. Figure 5 shows the metabolic pathway of ketogenesis, the production of energy from ketones, produced in preference to glucose when on the high fat KD.

Figure 4 - Comparison of the assimilation of MCT, MCFA, LCT and LCFA by the body.

Figure 5 - Ketogenesis - the conversion of ketones by the body into energy whilst on a KD.

1. The very high fat, low carbohydrate intake on the KD provides an abundant mixture of fatty acids.
2. On arrival in the liver hepatocytes after assimilation (Figure 4), fatty acids undergo beta-oxidation. This results in an excess of acetyl-CoA, which is converted, via ketogenesis, into ketones.
3. The ketones are transported in the blood to tissues and organs e.g. the brain, heart and muscles.
4. Here they are absorbed into the cells and converted back into acetyl-CoA.
5. The acetyl-CoA enters the cell mitochondria and is oxidised via the Kreb’s cycle to produce energy.

Key
- Ketones
- Fatty acids
- Beta-oxidation pathway

Immediate hydrolysis of MCT into constituent MCFA in the mouth and stomach by lingual and gastric lipases.
MCT does not require bile salt emulsification, but undergoes complete hydrolysis by pancreatic and mucosal lipases to glycerol and MCFA.

The larger sized LCT molecules are insoluble and are emulsified with bile salts to facilitate assimilation.

MCFA are transported directly to the liver and the cell mitochondria via the portal blood system. On arrival they undergo beta-oxidation to ketones (ketogenesis, figure 5).

When required for energy, LCFA are mobilised from adipose tissue and muscle and recirculated to the liver for beta-oxidation to ketones (ketogenesis, figure 5).