Nutrition and Functionality: “Key Partners in Ageing”
Chairman: Professor Heike Bischoff-Ferrari

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The Nestlé Nutrition Institute was very pleased to host a satellite symposium at the 19th IAGG World Congress of Gerontology and Geriatrics, held on 7 July 2009 in Paris (France), discussing the various ways that nutrition impacts the functionality of the ageing person. Nutritional status is very often an overlooked aspect in the care for the elderly, with weight loss in the elderly accepted as a “normal” part of ageing. This is despite strong data showing that weight loss is correlated with morbidity and mortality. The expert speakers in this symposium discussed the role of antioxidants, vitamin D and oral nutritional supplements to help optimize the ageing process and preserve or regain functionality, which helps to maintain independence and optimise quality of life in the elderly. The evidence is quite clear that nutrition intake and nutritional status play a key role in promoting healthy ageing.

From left: Professor David R Thomas, Professor Heike Bischoff-Ferrari, Professor Luigi Ferrucci
Nutrition and functionality: What is the link?

The significance of nutrition in maintaining good health and how good nutrition leads to healthy ageing is very challenging to demonstrate. The basic source of food for animals is plants. Plants use sunlight, which is the ultimate source of energy, to synthesize carbohydrates. Carbohydrates, when consumed, release energy within the body. At the cellular level, the mitochondria play a vital role in converting food – mostly carbohydrates and lipids – into energy.

Free radical theory of ageing

During mitochondrial metabolism, very dangerous free radicals (eg, hydroxyl radical) and reactive oxygen species (eg, hydrogen peroxide) are generated. Hydrogen peroxide, in particular, is capable of leaving the mitochondria and attacking other parts of the cell in the cytoplasmic and nuclear environments, where the damage can be extensive. It is believed that the oxidative damage caused by these molecules on DNA, lipids and proteins ultimately leads to ageing and age-related disorders (Figure 1).

Some of the deleterious actions of free radicals may be prevented by antioxidants. These antioxidants may be intrinsically generated enzymes or substances derived from nutritional sources. A chronic state of oxidative stress occurs when there is an imbalance of pro-oxidant and antioxidant systems.

Antioxidant vitamins and functional outcomes

Antioxidant intake may decrease oxidative stress in older people, as reflected by improvements in age-related decline in functional outcomes.

The Aging in the CHIANTI Area (InCHIANTI) study assessed the correlation of plasma concentrations and daily dietary intakes of antioxidants with skeletal muscle strength and physical performance in 986 elderly subjects (≥65 years). Plasma levels of tocochromanols – both α-tocopherol (p=0.003) and γ-tocopherol (p=0.04) – were associated with knee extension strength. Of the dietary vitamins, vitamin C and β-carotene showed positive correlation with knee extension (p=0.02 and p=0.05, respectively) and vitamin C was significantly associated with physical performance (p=0.04).

The association between α-tocopherol and the risk of frailty syndrome was assessed in 827 older persons (≥65 years) from the InCHIANTI study. Low circulating levels of α-tocopherol were found in persons identified as being pre-frail and frail. One longitudinal study evaluated 698 persons (≥65 years) from the InCHIANTI study registry to determine whether a low serum concentration of micronutrients was associated with a subsequent decline in physical function. Results showed a strong correlation for α-tocopherol (p=0.01). These findings suggest that α-tocopherol may be an important micronutrient associated with the prevention of disability and frailty in the elderly.

Similarly, serum carotenoids have also been associated with changes in skeletal muscle strength in the elderly. Hip, knee and grip strength were measured in 628 participants from the InCHIANTI study population (≥65 years) at baseline and at 6 years. Participants in the lowest versus highest quartile of total plasma carotenoids at enrollment were at higher risk of developing poor hip (p=0.004), knee (p=0.005) and grip (p=0.07) muscle strength at the 6-year follow-up visit.

Conflicting data on antioxidant efficacy

There are also inconsistent data on the benefits of administering β-carotenoids. The Alpha-Tocopherol, Beta-Carotene cancer prevention (ATBC) study reported a 17% (95% confidence interval [CI] 2–33%) higher incidence of lung cancer and 8% (95% CI 1–15%) higher total mortality among participants who received β-carotene supplementation compared with nonrecipients, during a 6-year trial period. Post-trial data showed that these differences disappeared when supplementation was stopped.

A recently conducted genome-wide association study found a common variation in the BCM01 gene, which was associated with higher levels of beta-carotene and lower levels of the other carotenoids – lycopene, zeaxanthin and lutein. This suggests that when only one carotenoid is artificially administered, as in the case with supplementation, the absorption of the other carotenoids is prevented because of competition at the absorption level. However, the human body is complex and when presented with different carotenoids in the food, it is able to absorb all the nutrients in a very wide and balanced concentration. Therefore, administering one...
molecule of carotenoid is not likely to have a significant effect on the health of an individual. Ultimately, it is important to remember that it is the overall concentration of nutrients in the food, rather than just single molecules, that will have an impact.

Conclusions

Excessive and unopposed oxidative stress may be the main cause of progressive disability and other adverse manifestations of ageing. Intake of antioxidants may decrease this oxidative stress, but the available data on the benefits of antioxidant supplementation are conflicting. However, antioxidants as part of food are beneficial.

References


Minimising falls and fractures: What role does nutrition play?

Nutrition plays an important role in maintaining functionality in the elderly. Impaired functionality may increase the risk of falls and subsequent fractures, a major adverse event in this population. Older individuals (≥65 years) who had suffered previous falls are particularly prone to recurrent falls, and have a 4-fold increased risk of sustaining fall-related fractures. Furthermore, individuals who sustain a fracture are more likely to suffer subsequent fractures. After the age of 75 years, hip fractures are the most severe and most frequent type of fractures sustained from falls.

Vitamin D supplementation: A desirable strategy for fall and fracture prevention

The key to preventing falls and fractures in the elderly is through early intervention strategies, possibly through a dual impact on bone and muscle. There is now a large body of clinical trial data that shows that vitamin D supplementation is associated with benefits on both of these structural components; on the one hand, vitamin D improves bone mineral density and contributes to fracture reduction, and on the other hand, it increases muscle strength and reduces the risk of falls.

Vitamin D insufficiency in the elderly

The primary sources of vitamin D in humans are skin exposure to sunlight and dietary intake. However, these sources often do not adequately meet vitamin D requirements in older individuals, leading to vitamin D insufficiency and deficiency. In Europe and the US, only <20% and <30% of older persons, respectively, reach the serum threshold level of 75 nmol/L for 25-hydroxyvitamin D, which is required for optimal bone health and fracture reduction. A recent survey of hip fracture patients (>65 years old) in Switzerland found that less than 5% of patients reached this desired serum level, and severe vitamin D deficiency, below 30 nmol/L, was present in 60% of patients.

Several potential reasons exist for the observed high prevalence of vitamin D insufficiency among the elderly. Sun exposure may be insufficient for cutaneous vitamin D production due to:

- Living in northern latitudes
- Winter season
- Having a darker skin tone
- Being institutionalised

Age-related decrease in the capacity of the skin to produce vitamin D

Furthermore, it would be impractical, if not impossible, to meet all of the vitamin D needs through dietary sources, which are largely limited to oily fish, such as salmon and mackerel. Alternatively, vitamin D supplementation may be recommended as an effective means for achieving adequate levels in older persons. In fact, the revised dietary guidelines issued by Health Canada in 2007 recommend a daily vitamin D supplement of 10 μg (400 IU) for adults over the age of 50.

How does vitamin D affect muscle tissue?

Vitamin D receptors (VDR) are present in human muscle tissue. The binding of vitamin D to these receptors may lead to de novo protein synthesis affecting muscle cell growth. The importance of vitamin D in muscle development has been demonstrated in VDR knockout mice, which show a skeletal muscle phenotype with variable and smaller muscle fibres, similar to humans with severe vitamin D deficiency. VDR expression decreases with age. This may in part explain sarcopenia associated with old age and the resultant adverse outcomes, such as muscle weakness, falls and fractures. Generally, muscle weakness is also recognised as a clinical sign of severe vitamin D deficiency, which is reversible with treatment.

There is ample clinical evidence demonstrating the benefits of vitamin D on muscle structure and function. In a small uncontrolled biopsy study in postmenopausal women with osteoporosis, the diameter and relative number of type II muscle fibres increased after 3 months of treatment with 1-alpha-hydroxyvitamin D.
The third National Health and Nutrition Examination Survey (NHANES III) investigated the association between serum 25-hydroxyvitamin D concentrations and lower extremity function — an important predictor of disability, falls and hip fractures in older adults — in 4,100 community-dwelling older individuals (≥60 years) in the US. Lower-extremity function was assessed using an 8-foot walking-speed test and a timed test of five repetitions of rising from a chair and sitting down. A significant positive association was found between 25-hydroxyvitamin D concentrations and these musculoskeletal functions (Figure 2), independent of activity level, gender or calcium intake, suggesting that different subgroups of the elderly population could benefit from maintaining high serum 25-hydroxyvitamin D levels.\textsuperscript{11}

Nonvertebral and hip fracture prevention with vitamin D

The anti-fracture efficacy of oral vitamin D supplementation in older individuals (≥65 years) was assessed in a recently published meta-analysis of 16 double-blind, randomised, controlled trials; the analysis included 12 trials for nonvertebral fractures (n=42,279) and 8 trials for hip fractures (n=40,886).\textsuperscript{13} The analysis detected heterogeneity, where the anti-fracture efficacy of supplemental vitamin D increased significantly with higher received dose (treatment dose x adherence) or higher achieved serum 25-hydroxyvitamin D levels for both fracture endpoints; a higher received dose of 482–770 IU/day of supplemental vitamin D reduced nonvertebral fractures by 20% (pooled relative risk [RR]=0.80; 95% CI 0.72–0.89; n=33,265 from 9 trials) (Figure 3) and hip fractures by 18% (pooled RR=0.82; 95% CI 0.69–0.97; n=31,872 from 5 trials), whereas, no fracture reduction was observed for a received dose of ≤400 IU/day.\textsuperscript{13}

Nonvertebral fracture prevention was present and significant in all subgroups of the older population, most pronounced in community-dwelling older individuals (≥65 years) in the US.\textsuperscript{11}

Figure 2. Dose-response for 25-hydroxyvitamin D levels and lower extremity function\textsuperscript{11}

Figure 3. Nonvertebral fracture reduction at higher received vitamin D dose\textsuperscript{13}

Table 1. Supplemental vitamin D (482–770 IU/day) and nonvertebral fracture reduction – primary subgroup analysis\textsuperscript{13}

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Impact of other micro/macro nutrients on falls and fractures?

Apart from vitamin D, evidence-based data on nutrition and fall and fracture prevention are mainly limited to calcium supplementation. A meta-analysis of prospective cohort studies and randomised controlled trials assessed the impact of calcium intake on hip fracture risk. Poole results from four trials showed no reduction in hip fracture risk with calcium supplementation, and a possible 64% increase in risk (pooled RR=1.64; 95% CI 1.02–2.64; n=6,504 with 139 hip fractures) (Figure 4). Pooled analysis of five clinical trials yielded a neutral effect of calcium supplementation compared with placebo for any nonvertebral fracture (pooled RR=0.92; 95% CI 0.81–1.05; n=6,740 with 814 nonvertebral fractures).

Given the potential adverse effect with respect to hip fractures, calcium supplementation alone should not be considered for fracture prevention in clinical practice, but rather an optimal combination of calcium and vitamin D may be a better strategy. Furthermore, vitamin D given with dairy products – a natural source of calcium – would confer additional benefits as they contain protein, a key component of muscle, for increasing muscle mass and strength.

Conclusions

Vitamin D insufficiency and deficiency are highly prevalent in the elderly. Since vitamin D needs cannot be adequately met with diet or sun exposure, supplementation is essential for maintaining better bone and muscle health. Supplemental vitamin D has been shown to have a dose-dependent benefit on reducing fractures in the elderly. Fracture prevention starts at received vitamin D doses of at least 480 IU/day, with continuous improvements thereafter. The available evidence suggests that a daily dose of 700–1,000 IU/day of supplemental vitamin D should be recommended for fall and fracture prevention in individuals aged 60 years and older.

References


Orange nutritional supplementation: Does it make a difference?

As humans age, there is an overall decline in food intake, referred to as the “anorexia of ageing”, which can contribute to malnutrition and weight loss. Ten percent of older men and 20% of older women have intakes of protein below the US recommended daily allowance (RDA) and 50% of older adults have intakes of vitamins and minerals less than the RDA. Furthermore, 16–18% of community-dwelling elderly persons consume <1,000 kcal/day. Weight loss is a devastating consequence in the elderly, as it carries an increased risk of mortality. Hence, oral nutritional supplementation may be beneficial in older individuals for promoting weight gain and meeting essential nutritional requirements.

Oral nutritional supplements can be divided into two categories:

- Nutritionally complete: Suitable as a sole source of nutrition
- Nutritionally incomplete: Not suitable as a sole source of nutrition, only as a supplement to food intake

Do oral nutritional supplements improve nutritional status and other outcomes?

An observational, prospective, cohort study assessed the impact of administering oral nutritional supplements on the nutritional status of 378 elderly (>70 years) malnourished patients over 12 months. Nutritional status was determined at baseline and throughout the study using the Mini Nutritional Assessment (MNA) scale. Over time, the MNA score improved
significantly more in patients who were routinely prescribed nutritional supplements than in those who rarely received the supplements (p<0.01). In another clinical trial, 80 patients, aged >75 years and at risk of undernutrition, were randomised to receive either oral nutritional supplementation or no supplementation during hospitalisation and after discharge, for a total duration of 60 days. Nutritional status and body weight were assessed at baseline and at the end of study. Oral supplementation maintained body weight throughout the study period while no supplementation resulted in weight loss (Figure 5). The mean percent weight changes from baseline in the two groups were statistically significant (p=0.05). Furthermore, at the end of study, the MNA® scores were higher in the supplemented group than in the control group (p<0.01).

In one study, 59 elderly patients (mean age 82 years) with femoral neck fractures were randomised to receive either a daily oral nutritional supplement or no supplement for a mean of 32 days. Overall, clinical outcomes were much improved in the supplemented group, with lower complication rates and fewer deaths than the control group (Figure 6).

Another study compared the improvements in body composition from liquid nutritional supplementation and placebo over 6 months in 68 elderly subjects (mean age 82 years) with a low body mass index (≤25 kg/m²). After 6 months, the supplement group had gained more weight than the placebo group (p=0.03). The body mass index also improved in the supplemented group compared with the placebo group. Furthermore, supplementation did not affect energy intake from regular meals, suggesting that it resulted in additional energy intake; the daily energy and protein intake contributed by the dietary supplement consisted of 250 kcal and 8.75 g, respectively.

**Do oral nutritional supplements decrease regular food intake?**

A common concern with oral nutritional supplements is their impact on regular food and caloric intake and whether they simply substitute regular food, and thus have no net effect. However, clinical evidence actually shows improvement in caloric intake in elderly individuals treated with such supplements.

A 6-week, randomised, controlled trial conducted in 91 elderly residents of long-term care facilities compared the effects of nutritional supplementation and extra food snacks in between meals. When assessed at weeks 3 and 6, the overall caloric intake was significantly increased in the supplemented group compared with the food-snack group (Figure 7).

Similarly, another randomised controlled study assessed the effect of oral nutritional supplementation on daily energy intake, body weight and nutritional status in 88 nursing home residents (≥65 years) over 60 days. At baseline, subjects were grouped according to their MNA® scores: well-nourished (≥24), at-risk (17–23.5) and malnourished (<17). The well-nourished group (group A) received no supplementation. The at-risk group was randomised to either no oral supplementation (group B) or oral supplementation (group C). The malnourished group received daily oral nutritional supplementation (group D). The total energy intake (kcal) and protein intake (g) on day 60 versus day 0 were significantly increased in both groups that received supplementation (p<0.001), whereas there was very little change in the groups that did not receive any supplements (total energy intake contributed by the dietary supplement consisted of 250 kcal and 8.75 g, respectively).
energy intake in group C, 1,815 vs 1,558 and in group D, 1877 vs 1489; protein intake in group C, 81.1 vs 57.4 and in group D, 85.8 vs 52.9.

A meta-analysis also documented increased daily protein and energy intake with nutritional supplementation in 29 studies that used a variety of methods and formulations.9

Is the timing of the supplement important?

There is insufficient evidence on the effect of timing of nutritional supplementation on outcomes in the elderly. However, one study suggested that administration of supplements between meals instead of with meals may increase energy consumption.10

Meta-analytical studies of protein and energy supplementation

A number of recently published meta-analytical studies have focused on the effectiveness of oral protein and energy supplements versus placebo or no supplementation in improving clinical and nutritional outcomes in older people.

One review included 34 trials that involved 3,021 randomised subjects.9 Nutritional supplementation was associated with a mean weight gain of 2.3% (95% CI 1.9–2.7%). Mortality was reduced in the supplemented group compared with the control group (RR=0.74; 95% CI 0.59–0.92) based on data from 32 trials. However, morbidity was not affected by supplementation.

Another meta-analysis compared the percent weight gain among patients living at home, and in long-term care and hospital-settings.11 Whilst supplemented patients in all three settings showed significant improvements, patients in long-term care and at home benefited the most (Figure 8).11

This meta-analysis also evaluated the survival benefits of nutritional supplementation in specific subgroups of patients. Improved survival was associated with11:

- Low baseline nutrition status
  - The benefit for mortality was statistically significant in undernourished subjects but not in nourished subjects (Figure 9).
- Age >75 years
- Energy intake >400 kcal/day
- Duration of intervention >35 days
- Patient health (being unwell)
- Hospital setting (vs community)
- Presence of geriatric conditions

Thus, nutritional therapy will yield the highest efficacy when specific geriatric populations are targeted. The MNA® will play a pivotal role in nutritional screening for identifying the ideal candidates for nutritional therapy. Future trials should focus on ways to demonstrate improvements in strength, function and quality of life.

Conclusions

Clinical data for oral nutritional supplementation in the elderly demonstrate weight gain and improvements in nutritional status. Nutritional supplementation does not decrease regular food intake, but actually increases protein and caloric intake in elderly persons. Oral nutritional supplements also appear to have a benefit on mortality. This benefit increases when specific subgroups of the elderly are targeted; older, undernourished, and hospitalised subjects, as well as those who are unwell or have geriatric conditions, benefit most. A greater energy intake and longer duration of supplementation also reduce mortality.

References