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Review

Systematic review and meta-analysis of the effects of high protein oral nutritional supplements

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ABSTRACT

Disease-related malnutrition is common, detrimentally affecting the patient and healthcare economy. Although use of high protein oral nutritional supplements (ONS) has been recommended to counteract the catabolic effects of disease and to facilitate recovery from illness, there is a lack of systematically obtained evidence to support these recommendations. This systematic review involving 36 randomised controlled trials (RCT) ($n = 3790$) (mean age 74 years; 83% of trials in patients >65 years) and a series of meta-analyses of high protein ONS (>20% energy from protein) demonstrated a range of effects across settings and patient groups in favour of the high protein ONS group. These included reduced complications (odds ratio (OR) 0.68 (95%CI 0.55–0.83), $p < 0.001$, 10 RCT, $n = 1830$); reduced readmissions to hospital (OR 0.59 (95%CI 0.41–0.84), $p = 0.004$, 2 RCT, $n = 546$); improved grip strength (1.76 kg (95%CI 0.36–3.17), $p < 0.014$, 4 RCT, $n = 219$); increased intake of protein ($p < 0.001$) and energy ($p < 0.001$) with little reduction in normal food intake and improvements in weight ($p < 0.001$). There was inadequate information to compare standard ONS (<20% energy from protein) with high protein ONS (>20% energy from protein). The systematic review and meta-analysis provides evidence that high protein supplements produce clinical benefits, with economic implications.

1. Introduction

The prevalence of disease related malnutrition is common across all health and social care settings including hospitals, care homes, and sheltered housing (Waitzberg et al., 2001; Stratton et al., 2003; Kruizenga et al., 2003; Russell and Elia, 2009; Elia and Russell, 2009a). Overall, more than 3 million people in the UK are malnourished or at risk of malnutrition, with people aged over 65 years accounting for about 1.3 million of these (Elia and Russell, 2009b). Despite this, malnutrition continues to remain undetected and undertreated (Elia and Russell, 2009b) causing a variety of detrimental effects at enormous cost to the individual and healthcare system (Elia and Stratton, 2009). This is because malnutrition not only predisposes to disease, but it also adversely affects disease outcome in a variety of ways. For example, impaired immunity predisposes to infections and the ability of the body to recover from infections, muscle weakness and immobility predispose to falls, venous thromboembolism and pressure ulcers. Malnutrition delays recovery from illness, increases complications, and resource use, such as frequency of hospital admissions and length of hospital stay (Elia, 2006).

Since reduced dietary intake is a major cause of malnutrition, various authorities including NICE (National Institute for Health and Clinical Excellence) (NICE, 2006) recommend improving dietary intake using a range of nutrition support strategies, including dietary counselling, oral nutritional supplements (ONS) and artificial nutritional support. Many of these strategies not only aim to increase energy but also the contribution of protein to total energy intake and there are several reasons for this. First, the intake of protein is believed to be inadequate in a sizeable proportion of the free living population, especially older people (65 years and over), where 20% of the population do not meet the Reference Nutrient Intake (RNI) for protein in the UK (Finch et al., 1998). Inadequate protein intake is even more likely to occur in patients with disease-related malnutrition because appetite is often poor due to the effects of a wide range of diseases, including infective, malignant, and traumatic conditions. Second, patients with disease-related malnutrition tend to be sedentary, ingesting less food with less protein and other nutrients, which means that nutrient deficiencies including protein are more likely to occur (WHO, 2007). If a normal protein intake was to be maintained in the face of reduced energy intake, protein would need to account for a greater proportion of total dietary energy, which should be considered when

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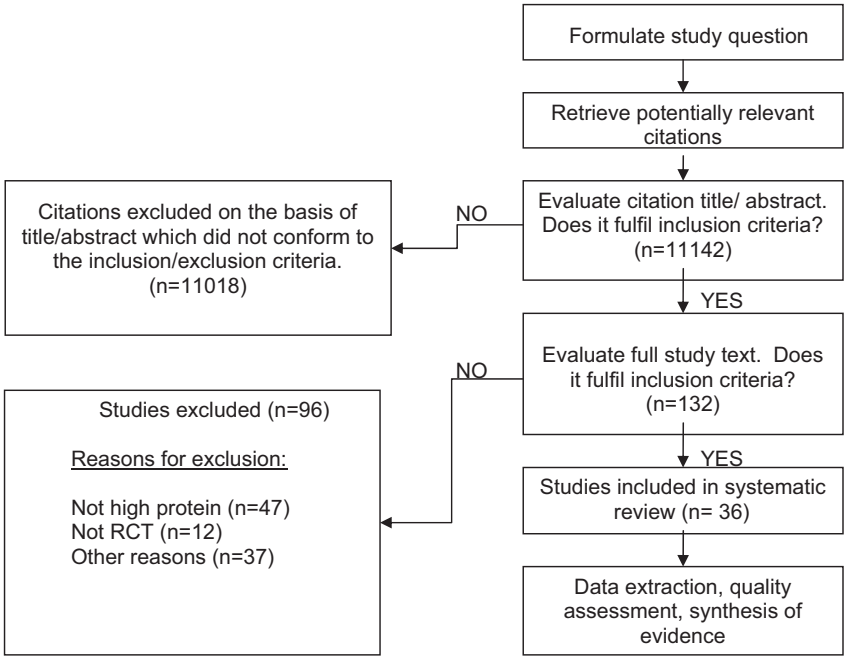

Fig. 1. Summary of systematic review stages and processes.

making recommendations about the composition of dietary intake in disease-related malnutrition. Third, a protein intake above normal may be desirable in patients with illnesses and disabilities for at least two reasons. One reason, is to counteract increased protein losses, which may occur in people with protein losing enteropathy (e.g. Crohn's disease and colitis), transudative wounds including burns, and the catabolic effects of inflammatory disease. The other is the need for protein to encourage repair of damaged tissues, such as wounds, including pressure ulcers, and to facilitate whole body repletion. For example, at a fixed energy intake whole body accretion of lean tissue can be facilitated by increasing protein intake (Elia, 2003).

The above considerations have led to advice to moderately increase the protein content of the diet particularly in older individuals (Paddon-Jones et al., 2008), either by food fortification, protein supplements or by use of commercially available ONS rich in protein to support patients with disease-related malnutrition. There is limited evidence for the clinical effectiveness of dietary advice (Baldwin and Weekes, 2009), however a number of systematic reviews and meta-analyses consistently indicate beneficial clinical effects when using ONS (Stratton and Elia, 2007). None of the previous ONS reviews have specifically investigated the role of high protein supplements (>20% energy from protein) on dietary intake, changes in body composition and functionally/clinically relevant outcomes, such as complications, mortality and length of hospital stay. Given the arguments raised above, beneficial effects might be expected; however, high protein intake has also been implicated in producing some adverse effects like being linked with osteoporosis and renal failure as well as encephalopathy in patients with advanced liver disease (Department of Health, 1992; Institute of Medicine, 2005). Therefore, this systematic review was undertaken to examine whether high protein ONS have beneficial effects in clinical practice and the extent to which these are associated with increased protein intake.

2. Materials and methods

The review was planned, conducted and reported following published guidelines. These include those issued by the Cochrane Collaboration (The Cochrane Collaboration, 2009), the UK National Health Service Centre for Reviews and Dissemination (CRD) (Centre for Reviews and Dissemination, 2009), and the PRISMA guidelines (Moher et al., 2009). Fig. 1 illustrates the principle stages and processes undertaken.

2.1. Identification and selection of studies for the systematic literature review

Potential studies were identified by searching electronic databases that were last accessed 4th January 2010. The databases searched included PubMed, Cochrane, Clinical Evidence Database, National Electronics Library for Health guidelines finder, Turning Research into Practice, Cinahl, and National Service Frameworks. The search terms used included both single words and combinations of words; sip, adult, nutrition, support, oral, feed, supplement, enteral, liquid, formula, protein. Bibliographies were checked and experts were consulted for any additional studies.

Studies available as full papers (conference proceedings were excluded) were deemed eligible if they conformed to the predetermined inclusion and exclusion criteria (Table 1). Only randomised controlled trials (RCT) qualified for review and any other study types were not included. Subjects eligible for inclusion were adults, of any nutritional status (well nourished and malnourished) and based in any setting. No restrictions were placed on sample size. Suitable interventions were those studies using high protein ONS of any consistency (ready made liquid, powder, puddings), for any duration, that contained two or more macronutrients, as well as a range of micronutrients. A high protein oral nutritional supplement was defined as the ONS containing at least 20% of energy provided from protein (Lochs et al., 2006; Regulations (EC) No. 1924/2006, 2006). The intervention could provide some or the entire daily requirement for energy and could be nutritionally complete or incomplete with respect to individual nutrients. No restrictions were placed on studies with regard to year of publication, or type of comparator (e.g. placebo, routine care, normal diet, dietary advice, ONS not high in protein). Throughout the review the comparator arm was termed 'control', unless another ONS was given as the comparator and these were termed 'standard ONS' (ONS not high