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Review

Effectiveness and efficacy of nutritional therapy – A cochrane systematic review☆

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SUMMARY

Background & aims: Disease-related malnutrition has deleterious consequences on patients' outcome and healthcare costs. The demonstration of improved outcome by appropriate nutritional management is on occasion difficult. The European Society of Clinical Nutrition and Metabolism (ESPEN) appointed the Nutrition Education Study Group (ESPEN-NESG) to increase recognition of nutritional knowledge and support in health services.

Methods: To obtain the best available evidence on the potential effects of malnutrition on morbidity, mortality and hospital stay; cost of malnutrition; effect of nutritional treatment on outcome parameters and pharmaco-economics of nutritional therapy, a Cochrane systematic review of the literature was performed by the Croatian Cochrane Branch to answer the following key questions: Q1) Is malnutrition an independent predictive factor for readmission within 30 days from hospital discharge? Q2) Does nutritional therapy reduce the risk of readmission within 30 days from hospital discharge? Q3) Is nutritional therapy cost-effective/does it reduce costs in hospitalized patients? and Q4) Is nutritional therapy cost effective/does it reduce costs in outpatients?

Results: For Q1 six of 15 identified observational studies indicated that malnutrition was predictive of re-admissions, whereas the remainder did not. For Q2 nine randomized controlled trials and two meta-analyses gave non-conclusive results whether re-admissions could be reduced by nutritional therapy. Economic benefit and cost-effectiveness of nutritional therapy was consistently reported in 16 identified studies for hospitalized patients (Q3), whereas the heterogeneous and limited corresponding data on out-patients (Q4) indicated cost-benefits in some selected sub-groups.

Conclusions: This result of this review supports the use of nutritional therapy to reduce healthcare costs, most evident from large, homogeneous studies. In general, reports are too heterogeneous and overall of limited quality for conclusions on impact of malnutrition and its treatment on readmissions.

1. Introduction

Disease-related malnutrition has deleterious consequences on patients' outcomes and healthcare costs. Evidence indicates that

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postoperative complications [1], risk of falls [2], hospital-acquired infections [3,4], risk of death [5] and costs of care [6] are significantly higher in malnourished than in well-nourished patients. The evolving recognition of the importance of malnutrition as a consequence, complication and cause of deterioration of many illnesses has emphasized the need for a scientific evaluation of the effectiveness of nutritional therapy. An appropriate nutritional therapy is able to improve outcome through preventing or correcting malnutrition-related disorders. However, the demonstration of improved outcome attributable to appropriate nutritional management is sometimes difficult, primarily due to the lack of standardized procedures regarding the definition of malnutrition, diversity of population studied, endpoints and proposed nutritional interventions [7,8].

For these reasons, the European Society of Clinical Nutrition and Metabolism (ESPEN) established the Nutrition Education Study Group (ESPEN-NESG). The aims of the ESPEN-NESG are to promote recognition of the need for nutritional knowledge and nutritional support in health services, to identify the barriers preventing implementation of nutritional screening and nutritional interventions in clinical practice, and to identify potential strategies to address these issues. During the first group meeting held in Rome in late 2012, four topics were highlighted in order to provide evidence-based recommendations on the impact of malnutrition, its prevention and correction on outcomes and healthcare costs. These topics comprised: the effect of malnutrition on morbidity, mortality and hospital stay; the cost of malnutrition; the effect of nutritional treatment on outcome parameters and the pharmacoeconomics of nutritional therapy. Readmission to the hospital has been recently recognized by the medical community and by administrators as a significant burden for healthcare systems. To obtain the best available evidence on these topics, the NESG approached the Croatian Cochrane Branch to perform a literature search.

The Croatian Cochrane Branch authors performed a systematic review of the literature to answer the following four key questions related to these four topics: 1) Is malnutrition an independent predictive factor for readmission within 30 days from hospital discharge? 2) Does nutritional therapy reduce the risk of readmission within 30 days from hospital discharge? 3) Is nutritional therapy cost-effective, does it reduce costs in hospital inpatient care?; and 4) Is nutritional therapy cost effective, does it reduce costs in outpatient care?

2. Methods

2.1. Inclusion and exclusion criteria

A systematic literature review was conducted and the relevant prospective cohort studies included for question 1; randomized controlled trials (RCT) or systematic reviews of RCTs were included for question 2; studies including economic analyses were included for questions 3 and 4. For the first three questions, participants were adult hospital patients with any disease, during their hospital stay or during follow-up after discharge. For the fourth question, participants were adult outpatients, i.e. patients who are not hospitalized for 24 h or more but who visit a hospital, clinic, or associated facility for diagnosis or treatment. For the purposes of summarizing the evidence, malnutrition was defined as disease-related malnutrition (secondary to a chronic or acute disease). Primary interventions of interest were oral/enteral/parenteral nutrition therapy, and the comparison intervention was no treatment or standard care. Studies with nutritional advice/counseling as the sole intervention of interest were excluded. Interventions aimed at improving nutritional status of infants (e.g. breastfeeding, fortified human milk, formulae) were excluded. The primary outcome measures for the first two questions were hospital readmission rates at 30 days or at any other time after index discharge. However, a considerable number of studies looked at the readmission outcome at other time-points and the application of the strict criteria of 30-days readmission would result in very few included studies; consequently all studies assessing the readmission at any time-point were included in the summary of evidence. For the last two questions, the primary outcome measure was cost-effectiveness of the intervention.

2.2. Data collection and analysis

For the first two questions, the following electronic databases were searched: The Cochrane Central Register of Controlled Trials (CENTRAL), The Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), MEDLINE (1946 onwards), and ClinicalTrials.gov. The titles and abstracts of every record retrieved by the searching process were independently screened for eligibility by two reviewers (DS and LP, Croatian Cochrane Branch, Split, Croatia). The search was not limited by language or publication status. When relevant studies were identified in non-English language, an effort was made to translate the key elements and include them in the summary of evidence if relevant. Flow diagram of study selection for Q1 and Q2 is shown in Fig. 1. Included systematic reviews were assessed for their methodological quality, using the AMSTAR tool [9]. Assessment of risk of bias in the included RCTs was done by using The Cochrane Collaboration's Risk of bias tool, which addresses the following domains: sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting and other issues. A modified Cochrane Risk of Bias tool, using three out of six original domains (blinding, selective data reporting, selective outcome reporting) and two additional domains (comparability of groups and confounding factors) were used to assess the risk of bias in the included non-randomized studies. Risk of bias was tabulated for each included study, along with a judgment of low, high or unclear risk of bias, as described in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions [10].

The following electronic databases were searched for the last two questions: NHS Economic Evaluation Database (NHS EED), Health Economic Evaluation Database (HEED), Health Technology Assessment (HTA, The Cochrane Library). Flow diagram of study selection for Q3 and Q4 is shown in Fig. 2. The retrieved citations were independently screened by two reviewers (DS and LP), data from included studies was extracted and presented in tabular form, risk of bias was assessed and a GRADE approach for evaluating the quality of evidence was applied where appropriate.

3. Results

Q1: Is malnutrition an independent predictive factor for readmission within 30 days from hospital discharge?

There were 15 studies identified from the literature searches and included in the final analyses: 12 prospective cohort studies (Agarwal et al., 2013, Aziz et al., 2011, Benedik et al., 2011, Chima et al., 1997, Koren-Hakim et al., 2012, Lim et al., 2012, Lobo Tamer et al., 2009, Mudge et al., 2011, Planas et al., 2004, Steer et al., 2010, Thomas et al., 2002, Vecchiarino et al., 2004; [11–22]), and three database studies (Hamaguchi et al., 2010, Zapatero et al., 2012, Zapatero et al., 2013; [23–25]). The main characteristics of the studies included in the systematic review are presented in Table 1. The regression analyses in four prospective cohort studies [12,13,18,22] as well as in two large database studies [24,25] showed a significant positive predictive value of malnutrition on

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