Nutritional Support in Respiratory Diseases

Module 38.2

Objectives, implementation and results of nutritional support in patients with COPD. What have we learnt?

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Learning Objectives

- To understand the importance of weight loss and nutritional depletion in Chronic Obstructive Pulmonary Disease;
- To develop an overview of the results of clinical trials of nutritional support in COPD;
- To understand the aims of nutritional support in COPD and how support programmes might integrate with other therapies;
- To understand the reasons why nutritional support programmes might be unsuccessful.

Contents

1. Background
2. Nutritional Intervention to increase weight in COPD
3. Nutritional support to improve performance in COPD
4. Current Guidance on Nutritional Support in COPD
5. Future Research
6. Conclusion

Key Messages

- Weight loss and nutritional depletion have important clinical consequences in COPD;
- Trials of nutritional supplementation have failed to demonstrate clear clinical benefits in COPD but adequately powered trials in appropriately selected “at risk” patients have not been performed;
- Nutritional support is likely to be more effective when combined with other treatment modalities such as pulmonary rehabilitation;
- Nutritional support may have a role in optimum substrate provision for exercise training in COPD.
1. Background

Chronic Obstructive Pulmonary Disease (COPD) is a common condition with a growing impact on global health services(1). In the UK it affects up to two million people and is one of the commonest causes of unplanned hospital admissions. COPD is a longterm condition characterised by progressive airflow obstruction leading to breathlessness, wheeze and sputum production. The early stages of the disease may go unnoticed but once established, the later stages are characterised by worsening disability due to exercise limitation and are punctuated by acute exacerbations that frequently require hospital admission. The more advanced stages of COPD are also characterised by a number of systemic features that have an important influence on the morbidity and morbidity of the disease. These include skeletal muscle dysfunction, osteoporosis, anaemia and depression. An association with low grade systemic inflammation has been observed for many of these systemic manifestations of COPD.

One of the earliest extra-pulmonary features of advanced COPD to be observed was progressive weight loss. This is associated with poor health status and prognosis independent of the severity of lung function impairment (2-6). Loss of both fat and lean mass (predominantly muscle) is frequently observed and in addition lean mass may be depleted in the presence of normal or increased fat mass (7). This means that muscle wasting may be underestimated by simple measurements of body mass index. More recent data has suggested that it is the loss of muscle mass which exerts the most influence on prognosis and symptoms (8).

The clinical importance of weight loss, particularly muscle wasting has lead to numerous attempts at improving body composition in COPD using a nutritional intervention and a number of controlled trials have been published. These various nutritional intervention trials have been summarised in a meta-analysis, a systematic review and more recently a Cochrane Library systematic review (9-11). All of these concluded that there was no overall effect of nutritional support on nutritional status, health status or functional performance. In the light of these findings, the role of nutritional support in the management of advanced COPD has been questioned. In the following sections I will outline possible reasons for the lack of efficacy of previous nutritional intervention trials, set out current best practice as advised by disease management guidelines and highlight areas of importance for future research.

2. Nutritional intervention to increase weight in COPD

Twelve RCTs of nutritional support in COPD were included in the recent Cochrane Review (11). The effects on body weight were inconsistent with the effect size small and the confidence intervals around the pooled standardised differences included zero (Fig. 1). Fewer studies measured body composition, exercise performance or health status and again effect sizes were small and confidence intervals included zero. There may be several reasons for the collective failure of nutritional support trials in COPD to date. Trials to date have varied widely in the duration and setting of the nutritional intervention and entry criteria were poorly standardised. Early studies provided fat rich supplements whereas later studies have provided more carbohydrate. This is probably because of concerns that the extra carbon dioxide resulting from the oxidation of carbohydrate would load ventilation and further compromise the respiratory system in COPD patients. Whilst an increase in minute ventilation has been demonstrated after a high carbohydrate meal (12), more recent data suggests that the clinical impact may have been overstated (13) and subsequent carbohydrate rich supplementation regimes have not caused adverse effects on breathlessness. There is some evidence that patients in a chronic inflammatory state may respond poorly to nutritional support (14). The inclusion of these patients in supplementation trials may have obscured benefits to other participants. However, it is likely that patients in an inflammatory state have greater nutritional depletion than others highlighting the difficulties with treating this subgroup of COPD patients. A proportion of patients may offset supplementation with a drop in normal dietary calorie intake (15). This and the gastro-intestinal side effects of supplementation may limit the size of supplementation that can be readily tolerated. Perhaps most crucially, most intervention trials have involved small sample sizes that probably lacked statistical power to detect clinically meaningful benefits.

Only three studies involved more than 50 patients, of which two have been published to date (16, 17). Both these studies attempted to boost the efficacy of calorie supplementation by combining the intervention with the anabolic stimulus of exercise training in the form of pulmonary rehabilitation. These studies also aimed to augment the performance benefits of pulmonary rehabilitation and therefore did not exclusively focus on underweight or weight losing patients.

In the study by Schols et al patients undergoing in patients pulmonary rehabilitation were randomised to receive a calorie supplement for the duration of rehabilitation or rehabilitation alone (16). An additional group also received anabolic steroids. The supplement contained 420Kcal but was fat rich (fat 51%, CHO 35%, protein 14%). Patients in the supplemented group gained weight (principally fat mass) compared with those receiving rehabilitation alone but there was no significant difference between the groups in 12-minute walk distance and respiratory muscle strength. Fat mass gains occurred in both the depleted and non-depleted groups.

In the study by Steiner et al a carbohydrate rich supplement was provided daily throughout an outpatient pulmonary rehabilitation programme (17). Weight gain, predominantly in the fat mass compartment, was observed in the intervention group whereas the control group lost weight. However this trial was principally aimed at augmenting exercise performance and included only a minority of underweight patients. Moreover, when severely undernourished patients were excluded from the analysis, gains in weight were of greater magnitude.

In summary, evidence to support the short term provision of nutritional support across the board in COPD is lacking. Adequately powered studies of nutritional supplementation in underweight or at
risk (weight losing) patients are lacking. Trials of long term nutritional support have not been performed raising the possibility that previous studies were of insufficient duration to provide clinical benefits. A retrospective study of patients receiving nutritional support suggested that the adverse prognostic effect of poor nutritional status may be overcome by nutritional support but this observation requires confirmation in prospective studies (18).

3. Nutritional support to improve performance in COPD

The importance of nutrition to performance in sport is now well recognised (19). Emphasis is placed on maximising carbohydrate intake prior to and during exercise. Carbohydrate supplementation during heavy exercise can prolong endurance performance and feeding with a high carbohydrate diet for several days before exercise can increase muscle glycogen content and enhance performance (20). Carbohydrate feeding may enhance the outcome of exercise training in healthy individuals (21, 22). Untrained individuals are particularly reliant on carbohydrate sources for exercise and an important training adaptation in the skeletal muscles is the ability to use fat as a fuel for energy metabolism (23). Although overall energy requirements decline with age, similar proportions of carbohydrate in the diet are recommended for exercise in the elderly (24). Meredith et al found that increases in strength and thigh muscle mass following resistance training were greater in subjects who received an additional calorie supplement (25). A similar study of frail nursing home residents showed impressive increases in strength from resistance training but no additional effect from nutritional supplementation (26).

Patients with advanced COPD may be very inactive because of exercise intolerance. Exercise reconditioning through pulmonary rehabilitation is of established benefit in the management of COPD (27). The benefits are largely mediated through improvements in fitness as a result of exercise training. Given that substrate availability is important for exercise and training in healthy subjects, there may be a role for nutritional support during rehabilitation in COPD. Two studies to date have explored this question. In the study of Schols et al supplementation provided during an inpatient rehabilitation programme did not improve field walking performance (16). However, this was a fat rich supplement and may not have been ideally suited to enhancing the effects of physical training, particularly in COPD where individuals who are extremely deconditioned may be very reliant on carbohydrate as a substrate for exercise (23). In the study by Steiner et al a carbohydrate rich supplement provided during an outpatient rehabilitation programme did not enhance the outcome of the programme across the board (17).

However in a subgroup of betternourished patients, supplementation resulted in greater gains in shuttle walk performance and these gains were correlated with the increase in overall carbohydrate intake (Fig 2).
Figure 2 Effects of CHO rich supplementation on exercise performance after rehabilitation. ISWT = incremental shuttle walk test, ESWT = endurance shuttle walk test. From Steiner et al 2003 (17).

Both of these studies involved predominantly endurance training. The role of protein and/or calorie supplementation in improving muscle strength or the outcome of resistance training has not been studied.

In summary, nutritional support may have a role during exercise training in patients with COPD but insufficient evidence exists to support its provision across the board during rehabilitation programmes.

4. Current guidance on nutritional support in COPD

COPD Disease management and pulmonary rehabilitation guidelines highlight the prognostic and functional importance of nutritional depletion in COPD (28-31). Assessment of nutritional status is recommended in the monitoring of such patients in most guidelines. The lack of evidence to support the widespread administration of nutritional support is highlighted. Uncertainty about the benefits of nutritional intervention in underweight patients is also acknowledged but recommendations are given to consider support in at risk patients (those with a BMI < 21Kg/m2, involuntary weight loss of > 5% in six months or 10% in 12 months or those with evidence of fat free mass depletion). No clear preference of nutritional supplementation over adaptation of dietary behaviour is given. Specific advice about supplement composition is not generally given but high carbohydrate supplements do not appear to cause significant problems.

5. Future research

Major questions remain about the mechanisms of weight loss, particularly muscle wasting in this disease. Recent evidence has implicated a low grade inflammatory state in muscle wasting and in these individuals weight loss may not be a “nutritional” problem and therefore not amenable to manipulation of nutrient intake. Future research is needed to identify those at risk of nutritional depletion and those who might respond to a nutritional support programme. Nutritional intervention may need to be more closely integrated to exercise rehabilitation such that the timing and composition of nutritional supplements are tailored to the mode of training. The long term benefits of nutritional support also remain uncertain and the impact of nutritional interventions on long term dietary behaviour requires evaluation. Nutritional support may be of particular benefit if provided
at times of greatest risk of weight loss. Exacerbations of COPD, particularly if these result in hospitalisation may have detrimental effects on energy expenditure and skeletal muscle function which could be ameliorated by nutritional support. Adequately powered controlled trials in this setting are required.

6. Conclusion

Weight loss is an important feature of advanced COPD. However, despite the intuitive appeal of nutrient supplementation for individuals with depleted body cell mass, trials of nutritional support have been disappointing. Although the negative findings of recent systematic reviews suggest that nutritional support may be of limited clinical benefit when prescribed across the board, it is likely that nutritional intervention will be of benefit if selected patients and circumstances. Further clinical trials are needed to advance the role of nutritional therapy in this important chronic disease.

References