

Rassegna - Review

COPD, when and how to feed

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ABSTRACT: *The association between weight loss and Chronic Obstructive Pulmonary Disease (COPD) has been recognized since the late 19th century. Nevertheless therapeutic management of weight loss and muscle wasting in patients with COPD has gained interest only recently since it was generally considered as a terminal progression in the disease process and, therefore, inevitable and irreversible.*

The renewed interest in nutritional support as therapy in COPD runs parallel to changing concepts in the disease management, which are not only predominantly aimed at the primary organ failure but also at the systemic consequences of the disease including nutritional depletion.

Despite the optimal implementation of nutritional therapy, as part of an integrated treatment approach of COPD, one should recognize that even then a sub group of patients may not reach the intended effect due to underlying mechanisms of weight loss, which cannot be simply reversed by caloric supplementation. Potential reversibility by means of specific nutrients (nutriceuticals) or pharmaceuticals is a major focus of future research in this field. Based on current understanding of the relationship between nutritional depletion and outcome in COPD, we describe in this review article a flow chart for nutritional screening and therapy. (RINPE 2002; 20: 113-23)

KEY WORDS: *COPD, Nutritional Support, Artificial Nutrition, Nutritional Counseling*

PAROLE CHIAVE: *BPCO, Supporto Nutrizionale, Nutrizione Artificiale, Counseling Nutrizionale*

INTRODUCTION

The association between weight loss and chronic obstructive pulmonary disease (COPD) has been recognized since the late 19th century. In the 1960s several studies already reported that a low body weight and weight loss are negatively associated with survival in COPD (1). Nevertheless, therapeutic management of weight loss and muscle wasting in patients with COPD has gained interest only recently since it was generally considered as a terminal progression in the disease process and, therefore, inevitable and irreversible. Furthermore, weight loss has even been suggested as an adaptive mechanism to decrease oxygen consumption. Recent studies have challenged this attitude and showed that weight loss and a low body weight are associated with poor prognosis independent of, or at least not closely correlated with the degree of lung function impairment (2, 3). Moreover, weight gain after nutritional support was associated with, decreased mortality (4).

The renewed interest in nutritional support as therapy in COPD runs parallel to changing concepts in the disease management not only predominantly aiming at the primary organ failure, but also at the systemic consequences of the disease including nutritional depletion.

RATIONALE FOR NUTRITIONAL SUPPORT

The most prominent symptoms of COPD are dyspnea and an impaired exercise capacity. During the past 10 years research has shown that besides airflow obstruction and loss of alveolar structure, skeletal muscle weakness is an important determinant of these symptoms (5). Recent studies have shown that peripheral skeletal muscle dysfunction is predominantly determined by skeletal muscle mass in COPD (6, 7).

Besides effects on peripheral skeletal muscle strength, several studies have also shown that body weight and particularly fat-free mass (FFM) as induced

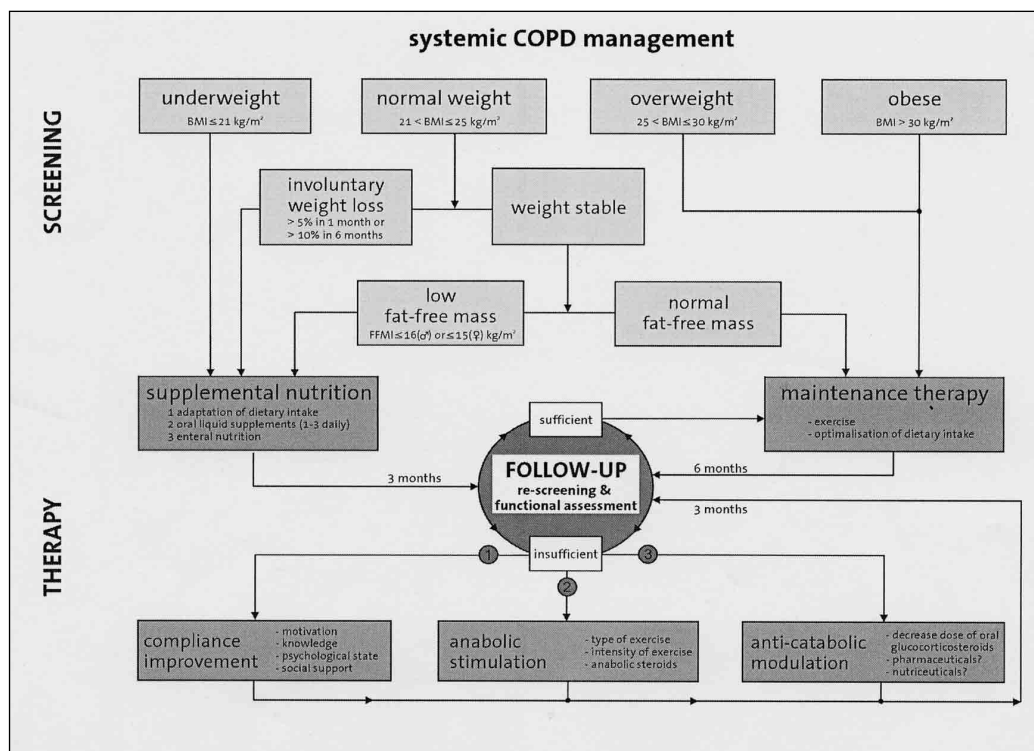


Fig. 1 - Flow-chart for nutritional screening and therapy.

measure of muscle mass are significant determinants of exercise capacity and exercise response (8-10). Patients with a depleted FFM were characterised by a lower peak oxygen consumption, peak work rate and early onset of lactic acid compared to non-depleted patients. These findings suggest that the functional consequences of nutritional depletion not only relate to muscle wasting per se, but also to alterations in muscle morphology and metabolism. Indeed experimental studies and studies in other wasting conditions have shown that nutritional depletion causes generalized fibre atrophy, but specifically decreases muscle fibre type II cross sectional area (11). Furthermore, altered levels of glycolytic and oxidative enzymes (11, 12) and depletion of energy rich substrates such as phosphocreatine and glycogen (13, 14) have been described after nutritional depletion. Furthermore, it is clearly shown that nutritional depletion not only decreases peripheral muscle function, but also affects respiratory muscle mass and strength (15).

The functional consequences of underweight and particularly of depletion of FFM are also reflected in a decreased health status as measured by the disease-specific St Georges Respiratory Questionnaire (16). Depletion of FFM is not only associated with weight loss, but may also occur in normal weight patients with a relatively increased fat mass (17). Patients with depletion of FFM irrespective of body weight, showed greater im-

pairment in health status and quality of life, in comparison with depleted patients with a relative preservation of FFM (18).

Several studies using different COPD populations have now convincingly shown that a low body mass index and weight loss are associated with an increased mortality risk (2, 4). Remarkably overweight patients with moderate to severe COPD even have a lower mortality risk than normal weight patients (2, 4). After adjustment for the effect of age, gender, lung function, smoking and resting lung function, the increased mortality risk was found in patients with a body mass index <25 kg/m² (Fig. 1) (4). This could be related to the functional consequences of selective depletion of FFM in part of the patients but also to adverse effects of recent weight loss on other outcome measures. In this context it is of interest to note that recent weight loss is an important factor for outcome of acute exacerbations as indicated by non-elective hospital readmission (19) and the need for and the outcome of mechanical ventilation (20).

NUTRITIONAL ASSESSMENT

Based on the relationship between nutritional status and outcome, the following screening measures of nutritional status are recommended (Fig. 1).

Weight indices

Based on the body mass index (BMI), patients can be characterised as underweight, normal weight and overweight. Underweight is normally defined as a body mass index less than 21 kg/m². In Caucasian people this value is comparable to 90% of ideal body weight, based on the Metropolitan Life Insurance Tables. However this value is rather arbitrary and according to recent recommendations this cut-off point in elderly hospitalised patients should be extended to 24 kg/m² (21). Interestingly this value strikingly corresponds to the increased mortality risk that was reported in patients with COPD and a BMI less than 25 kg/m².

Weight loss

There are limitations to weight for height indices. Underweight patients are not necessarily in a poor nutritional status. This was illustrated by the fact that underweight patients with a relative preservation of FFM had a comparable muscle strength and exercise performance as normal weight subjects with a normal FFM (17). The adverse effects of involuntary weight loss, however, are well described and progressive weight loss will ultimately lead to underweight and depletion of FFM. Therefore, recent involuntary weight loss should be considered in nutritional screening and follow-up. Commonly used criteria are weight loss >10% of usual body weight in the past 6 months or > 5% in the past month.

Body composition

Weight is a rather global measure of nutritional depletion since it does not take body composition into consideration. Weight can be simply divided into fat mass and FFM. The FFM consists of water (approximately 73%), proteins and minerals. Water is distributed intracellularly in the body cell mass and extracellularly. The largest single tissue of the body cell mass is muscle mass. In the absence of shifts between the water compartments, FFM is a useful measure of the body cell mass and thus of muscle mass. Depletion of FFM in COPD is defined as a FFM less than 16 kg/m² (males) and 15 kg/m² (females). This value is based on a linear gender specific relationship between FFM and body weight (in the absence of obesity) using a cut-off point for the BMI of 21 kg/m². Based on measurement of body weight and FFM, 4 groups of patients can be distinguished: 1) underweight and depletion of FFM; 2) underweight and relative preservation of FFM; 3) normal weight and depletion of FFM; 4) normal weight and normal FFM.

Deuterium dilution and bioelectrical impedance analysis are relatively easy, non-invasive methods to assess FFM and have been used and validated extensively in COPD (22, 23). Dual energy X-ray absorptiometry allows measurement of lean tissue mass, bone and fat mass not only at the whole body level, but also at the various regions (trunk, arm, leg) (24). Biochemically, depletion of FFM is reflected in a decreased creatinine height index as calculated by the 24h urinary creatinine excretion of the patient divided by a reference value based on ideal body weight (17).

In clinically stable patients with moderate to severe COPD, depletion of FFM has been reported in 20% of COPD out-patients (25) and in 35% of those eligible for pulmonary rehabilitation (17). Limited data are available regarding the prevalence of nutritional depletion in representative groups of mild COPD as well as in patients suffering from acute respiratory failure although in the latter values up to 70% have been reported (26). There is no clear relationship between measures of nutritional status and airflow obstruction, but weight loss and underweight are associated with decreased diffusing capacity and observed more frequently in emphysematous patients compared to chronic bronchitis (6). The difference in body weight between the two COPD subtypes is merely a difference in fat mass. Depletion of FFM, even despite a relative preservation of fat mass, also occurs in chronic bronchitis (6).

CAUSES OF WEIGHT LOSS AND MUSCLE WASTING

To be able to judge the need for and the effectiveness of nutritional therapy as well as the optimal nutritional support strategy, insight is needed into the underlying mechanisms and contributing factors of overall weight loss and specific tissue wasting in COPD. Weight loss and particular loss of fat mass, occurs if energy expenditure exceeds dietary intake. More specifically muscle wasting is a consequence of an imbalance between protein synthesis and protein breakdown. Alterations in both parts of the energy balance have been reported in COPD. Besides, increasing evidence points towards altered anabolic and catabolic mediators involved in the regulation of either protein synthesis or protein breakdown or both.

Energy expenditure

Total energy expenditure can be divided into different components. Basal metabolic rate is usually the largest component of total energy expenditure. Physical

activity-induced thermogenesis can vary substantially between different individuals. Other components of total energy expenditure are the diet-induced thermogenesis and components as drug-induced thermogenesis and the thermoregular component. By gas exchange measurement of patients in awake relaxed conditions after an overnight fast, it is now possible to conveniently measure so called resting energy expenditure (REE). REE comprises the sleeping basal metabolic rate and the energy cost of arousal.

Based on the assumption that REE is the major component of total energy expenditure in sedentary persons, several studies have measured REE in COPD. After adjustment for the metabolically active FFM, REE was found elevated in COPD (27). While in healthy control subjects FFM could explain up to 84% of the individual variation in REE, this was only 43% in COPD patients (28). Other factors, therefore, have been considered like work of breathing, hormone levels, drug therapy and inflammation. A likely cause of the increased metabolic rate in COPD patients is an increasing respiratory muscle work, since the energy cost of increasing ventilation is higher in patients with advanced disease than in healthy controls of comparable age and gender. REE however correlates only weakly if not at all to individual or combinations of detailed lung function tests and blood gas values (28). Thus patients with the worst lung function, and in whom the work of breathing should be the highest, are not necessarily hypermetabolic. Nasal intermittent positive pressure ventilation, which eliminates diaphragmatic and intercostal activity, did not reduce REE to normal in a group of hypermetabolic patients (29). Furthermore, in COPD and in chest wall disease, airflow obstruction and oxygen cost of breathing (OCB) were mutually related, but no correlation was found between OCB and REE (30).

Maintenance bronchodilating treatment for many patients consists of inhaled beta-agonists. Two weeks of salbutamol increased REE by less than 8% in healthy males (31). Acute inhalations of clinical doses of salbutamol, on the other hand, have been shown to increase REE in healthy subjects in a dose-dependent way up to 20% (32). High doses of nebulised salbutamol are commonly administered during acute disease exacerbations. Nevertheless, no significant acute metabolic effects of this treatment were shown in elderly COPD patients in comparison with an age-matched control group (33).

Another contributing factor to hypermetabolism may be related to inflammation. The polypeptide cytokine, tumour necrosis factor (TNF), is a proinflammatory mediator produced by different cell types. TNF inhibits lipoprotein lipase activity and is pyrogenic. It also triggers the release of other cytokines, which themselves

mediate an increase in energy expenditure, as well as mobilization of amino acids and muscle protein catabolism. Using different markers, several studies provided clear evidence for involvement of TNF-related systemic inflammation in the pathogenesis of tissue depletion. Elevated levels of TNF in (stimulated) plasma and of soluble TNF-receptors were found in patients with COPD (34-36), particularly those suffering from weight loss. Furthermore, several studies have shown a relationship between TNF-related inflammation and resting metabolic rate (37). Since diet-induced thermogenesis (DIT) accounts only for 10% of total daily energy expenditure, the influence of a possibly increased DIT on total daily energy expenditure will be small. Normal as well as increased DIT has been described in COPD patients (38). Despite the methodological difficulties in measuring total daily energy expenditure, recent studies focused attention on the activity - related energy expenditure in COPD patients. Using the doubly labelled water ($^2\text{H}_2\text{O}^{18}$) technique to measure total energy expenditure (TDE) it was demonstrated that COPD patients had a significantly higher TDE than healthy subjects (39). Remarkably, the non-resting component of total daily energy expenditure was significantly higher in the COPD patients than in the healthy subjects, resulting in a ratio between TDE and REE of 1.7 in COPD patients and 1.4 in normal subjects. Otherwise, when TDE was measured in patients with COPD and healthy persons in a respiration chamber, no differences in TDE were found between COPD patients and healthy persons, possibly by limitations of activities in the respiration chamber (40). No difference in TDE between hypermetabolic and normometabolic COPD patients was found and REE did not correlate significantly with total daily energy expenditure, when FFM was taken into account (41). The cause of an increased activity-related TDE is yet unclear. It could be related to the observed decreased mechanical efficiency during leg exercise (42). Part of this increased oxygen consumption during exercise can be explained by an inefficient ventilation in case of increased ventilatory demand especially under conditions of dynamic hyperinflation. Furthermore, studies indicate a severely impaired oxidative phosphorylation during exercise in COPD, accompanied by an increased and highly anaerobic metabolism involving both the energy release from high energy phosphate compounds as well as an enhanced glycolysis (43). Anaerobic metabolism is less efficient than aerobic metabolism.

Cellular energy metabolism

Besides an impaired oxidative phosphorylation during exercise, recent studies have shown alterations in

resting cellular energy metabolism in peripheral muscle. A decrease in the activity of citrate synthase (44), an increase in the glycolytic enzyme phosphofructokinase (45) and (in hypoxemic patients) an increase in the activity and expression of cytochrome oxidase have been reported (46). These enzymatic adaptations could indicate a shift towards a more glycolytic metabolism. The functional consequences of these changes were reflected in alterations in adenosine nucleotide metabolism as reflected by a decreased PCr/Cr and detectable levels of inosine monophosphate, indicative of an imbalance between the utilization and resynthesis of ATP in resting muscle of patients with COPD (47). It could be speculated that the observed changes in intracellular metabolites result in an increased overall energy metabolism.

Dietary intake

Hypermetabolism can explain why some COPD patients lose weight despite an apparent normal to even high dietary intake (48). Nevertheless, it has been shown that dietary intake in weight-losing patients is lower than in weight-stable patients both in absolute terms as well as in relation to measured REE (49). This is quite remarkable because the normal adaptation to an increase in energy requirements in healthy men is an increase in dietary intake. The reasons for a relatively low dietary intake in COPD are not completely understood. It has been suggested that patients with COPD eat sub-optimally because chewing and swallowing change breathing pattern and decrease arterial oxygen saturation. Furthermore, gastric filling in these patients may reduce the functional residual capacity and lead to an increase in dyspnea. Very intriguing is the role of leptin in energy homeostasis. This adipocyte-derived hormone represents the afferent hormonal signal to the brain in a feedback mechanism regulating fat mass. Besides, leptin has a regulating role in lipid metabolism and glucose homeostasis and increases thermogenesis. Furthermore, leptin has effects on T-cell mediated immunity. Few data are reported on leptin metabolism in COPD. Circulating leptin correlates well with BMI and fat percentage as expected, but significantly lower values were observed compared to healthy subjects (36). In experimental studies administration of endotoxins or cytokines produced a prompt increase in serum leptin levels (50). In COPD, one study also observed a relationship between leptin and soluble TNF-receptor 55, in particular in the emphysematous sub-type. Leptin as well as sTNF-receptor 55 were in turn inversely related to dietary intake in absolute terms as well as adjusted for REE (51). The exact regulation of leptin in COPD needs further exploration. Another factor of interest in evaluating dietary intake is the influence of

psychological dysfunctioning such as anxiety, depression and appetite. Although no systematic studies are available, limited physical abilities, financial constraints and lack of supportive care should also be considered as factors that may interfere with dietary intake.

OUTCOME OF NUTRITIONAL INTERVENTION

Oral nutritional supplements

The first clinical trials to investigate the effectiveness of nutritional intervention consisted of nutritional supplementation by means of oral liquid supplements. All short-term studies (2-3 weeks) (52, 53) showed a significant increase in body weight and respiratory muscle function. This short term effectiveness is probably related partly to repletion of muscle water and potassium besides constitution of muscle protein nitrogen (54). Only one study addressed the immune response to short-term nutritional intervention in 9 patients with advanced COPD (55). Refeeding and weight gain were associated with a significant increase in absolute lymphocyte count and with an increase in reactivity to skin test antigens after 21 days of refeeding.

Significant improvements (56, 57) in respiratory and peripheral skeletal muscle function but also in exercise capacity and health-related quality of life were observed in one in-patient and one out-patient study after 3 months oral supplementation by about 1000 kcal daily. Other out-patients studies, however, despite a similar nutritional supplementing regimen, the average weight gain was less than 1.5 kg in 8 weeks (58, 60). Besides non-compliance and biological characteristics, the poor treatment response may be attributed to at least partly to inadequate assessment of energy requirements and to the observation that the patients were taking supplements instead of their regular meals.

Nutrition and exercise

From a functional point of view it is obvious to combine nutritional support with exercise if possible. The effects of a daily nutritional supplement as an integrated part of a pulmonary rehabilitation program indeed resulted in significant weight gain (0.4 kg/week), despite a daily supplementation, which was, much less than in most previous out-patient studies (61). The combined treatment of nutritional support and exercise not only increased body weight but also resulted in a significant improvement of FFM and respiratory muscle strength. The clinical relevance of treatment response was shown in a post-hoc survival analysis of this study

demonstrating that weight gain and increase in respiratory muscle strength were associated with significantly increased survival rates (4). On Cox regression analysis weight gain during the rehabilitation period remained a significant predictor of mortality independent of baseline lung function and other risk factors including age, sex, smoking and resting arterial blood gases. In view of the ventilatory limitation and the experienced symptoms, exercise in most rehabilitation settings consists of general physical training, with emphasis on endurance exercise. Nutritional depletion, however, specifically impairs muscle strength. Studies in elderly subjects without pulmonary disease have shown that in particular strength training with nutritional support is superior to nutritional support alone in reaching an increase in FFM. No data are yet available regarding the effects of nutritional support and strength training in depleted patients with chronic respiratory disease.

TIMING OF NUTRITIONAL SUPPORT

Most studies have investigated the effects of nutritional supplementation in clinically stable patients. Anamnestic data, however, indicate that in some patients weight loss follows a stepwise pattern, associated with acute (infectious) exacerbations. During an acute exacerbation the energy balance is often temporarily negative due to a further increase in REE, but particularly due to a temporarily dramatic decrease in dietary intake (62). Furthermore, these patients may have an increased risk for protein breakdown which may limit the effectiveness of nutritional supplementation (62). Factors contributing to weight loss and muscle wasting during an acute exacerbation include an increase in symptoms, more pronounced systemic inflammation, alterations in leptin metabolism and the use of high doses of glucocorticoids. One study showed a positive effect of nutritional support during hospitalisation for an acute exacerbation, but clearly more research is needed to evaluate the relative effectiveness of nutritional support during or immediately after an acute exacerbation (63).

MACRONUTRIENT COMPOSITION OF NUTRITIONAL SUPPLEMENT

Carbohydrate/fat

After optimization of meals and dietary habits, nutritional supplements are added to balance energy expenditure or enhance weight gain. Meal related dyspnea and limited ventilatory reserves, however, may restrict

the quantity and composition of nutritional supplements in patients with respiratory disease. Nutrient administration is associated with an obligate increase in ventilation and metabolic rate. The composition of the caloric intake can influence carbon dioxide production and, therefore, ventilatory demand. The respiratory quotient (RQ or carbon dioxide production/oxygen consumption ratio) of glucose oxidation equals 1. The RQ of fat oxidation is 0.71 indicating a lower ventilatory load by reduced carbon dioxide production. Excessive carbon dioxide production by carbohydrate administration was observed in mechanically ventilated patients (64, 65). However, these effects only occurred in case of caloric overload. Under these circumstances triglyceride biosynthesis can be expected. Several studies in clinically stable COPD patients have studied the effects of nutritional supplements on functional capacity in the immediate postprandial period. They reported adverse effects of a high caloric, carbohydrate-rich supplement (920 kcal, 53% C) relative to a fat-rich supplement. These included a significantly greater increases in minute ventilation, carbon dioxide elimination, oxygen consumption, respiratory quotient, arterial carbon dioxide tension and fatigue score, together with a greater fall in the distance walked (66, 67). After a more physiologic energy load (250-500 kcal) no difference in post-prandial exercise capacity was shown between a high-versus a low-fat supplement (68) and even positive effects were reported of a carbohydrate-rich supplement on lung function and dyspnea sensation (69).

There are also contra-indications for a high-fat supplement related to the significant delay in gastric emptying even compared to moderate fat supplements (68). Due to the disease process itself, such patients already suffer from hyperinflation, a flattened diaphragm, and a reduction in abdominal volume, which results in feelings of bloating, abdominal discomfort, and early satiety. A significant delay in gastric emptying may lead to an extended time of abdominal distension, impacting on diaphragmatic mobility and thoracic expansion. High fat diets may also cause bloating, loose stools, or diarrhoea and may thus create tolerance problems. This finding is in line with a preferential use of carbohydrates in COPD patients during the acute phase of hospitalisation for an exacerbation (62). Furthermore, meal-related oxyhaemoglobin desaturation may limit caloric intake and contribute to meal-related dyspnea in some patients, primarily in those that are hypoxemic at rest (70). The degree of desaturation appeared to depend on meal type, being significantly higher after a fat-rich warm meal compared to a carbohydrate-rich "cold" meal (70).

Protein

The effects of wasting disease on protein metabolism is characterised by net protein catabolism owing to differences between protein synthesis and breakdown rates. This is seen in a negative nitrogen balance. The emphasis with respect to protein requirements in disease must be on optimal rather than minimal amounts of dietary proteins. Unfortunately, a clear clinical or physiological endpoint for the determination of optimal protein requirements is not available. Only studies documenting the effects of dietary protein content on nitrogen balance or on protein kinetics have been published in various conditions. The available data suggest that in healthy subjects and in stable disease, protein synthesis is optimally stimulated during administration of 1.5 g protein/kg/day. Similarly, although the catabolic effects of acute disease cannot be manipulated merely by nutrition, net protein catabolic rates in these conditions are lowest by administration of 1.5-2.0 g protein/day (71). Administration of proteins exceeding this quantity results only in increased protein catabolism.

Anabolic nutritional modulation

The observed alterations in cellular energy metabolism, towards a decreased oxidative metabolism, have increased the interest in nutritional modulation to enhance physical performance. Specific attention has been given to the potential benefit of amino acid modulation, in particular the branched chain amino acids and glutamate (GLU). Most consistent results have yet been reported for GLU. Intracellular GLU has various important functions, as it plays an important role in preserving high-energy phosphates in muscle through different metabolic mechanisms. GLU concentration is high in the free amino acid pool of human skeletal muscle. Intracellular GLU is known as an important precursor for the antioxidant glutathione (GSH) and glutamine synthesis in muscle. Muscle GLU is indeed highly associated with muscle GSH, and patients with emphysema suffer from decreased muscular GLU and GSH levels in lower limb muscle (72). Studies have shown that in healthy human muscle, the GLU pool functions to generate tricarboxylic acid (TCA) intermediates during the first minutes of exercise, which is achieved via the alanine aminotransferase reaction (pyruvate + GLU \rightarrow alanine + α -ketoglutarate) at the cost of GLU. Moreover, this reaction can shunt the pyruvate accumulated during exercise towards alanine instead of lactate, suggesting a possible role of the intracellular GLU level in the lactate response to exercise. In line with this hypothesis early lactic acidosis during exercise in patients with COPD

was indeed associated with a reduction in muscle GLU (73). Not only at rest, but also during twenty minutes of sub maximal constant cycle exercise a different response in amino acid status was found in skeletal muscle and plasma of COPD patients as compared with healthy age-matched controls (74). A significant reduction of most muscle amino acids was present post-exercise, whereas several plasma amino acids were increased, suggesting an enhanced amino acid release from muscle in COPD during exercise. The increase in plasma alanine and glutamine was even higher post-exercise, suggesting enhanced nitrogen efflux. No intervention results are yet available for COPD patients. However, in frail elderly subjects it has indeed been observed that oral amino acid intake stimulates the transport of amino acids into muscle, and that there is a direct link between amino acid transport and protein synthesis when ingested before exercise or some time after exercise.

Anti-catabolic nutritional modulation

Even in a controlled setting like an in-patient rehabilitation centre, part of the patients does not respond to nutritional therapy. Besides non-compliance to therapy, an inadequate energy intake relative to energy requirements, the inability of the patients to ingest the extra calories and inadequate metabolic handling may contribute. The interaction between nutritional depletion and systemic inflammation has drawn attention to the potential beneficial effects of anti-catabolic agents, in particular modulation of the inflammatory response. n-3 fatty acids have been investigated in other wasting conditions such as HIV, cancer and sepsis. This may be an interesting therapeutic alternative for part of the patients with COPD. Those exhibiting insignificant weight gain after nutritional support and anabolic stimulation (exercise, anabolic steroids) were characterised by an elevated systemic inflammatory response as reflected by enhanced levels of soluble TNF-receptors, circulating leptin and acute phase proteins (51, 75). A clinical trial is currently under investigation.

PRACTICAL IMPLEMENTATION OF NUTRITIONAL SUPPORT

Based on current insights in the relationship between nutritional depletion and outcome in COPD, a flow chart for nutritional screening and therapy is presented. Simple screening can be performed based on repeated measurements of body weight. Patients are characterised in terms of body mass index (BMI =

weight/height squared) and the presence or absence of involuntary weight loss. Nutritional supplementation is indicated for underweight patients (BMI < 21 kg/m²). Involuntary weight loss in patients with a BMI < 25kg/m² should be treated to prevent further deterioration; involuntary weight loss in patients with a BMI > 25kg/m² should be monitored to assess whether it is progressive. If possible, measurement of FFM as an indirect measure of muscle mass may provide a more detailed screening of patients, since this allows identification of normal weight patients with a depleted FFM, that even despite a normal body weight should be considered for diet therapy.

Depending on the underlying cause of energy imbalance (decreased dietary intake or increased nutritional requirements) initial nutritional therapy may range from adaptations of the dietary behaviour and food pattern followed by implementation of nutritional supplements. Nutritional support should be given as energy-dense supplements well divided during the day to avoid loss of appetite and adverse metabolic and ventilatory effects resulting from a high caloric load. When feasible, the patients should be stimulated to follow an exercise program. For the severely disabled cachectic patients unable to perform exercise training, even simple strength manoeuvres combined with ADL training and energy conservation techniques may be effective. Exercise not only improves the effectiveness of nutritional therapy, but also stimulates appetite. After 4-8 weeks, therapy response can be determined. If weight gain and functional improvement are noted, the caregiver and the patient have to decide whether more improvement by a similar strategy is feasible or whether maintenance is the aim. It may then also be worthwhile to add or alter the exercise

training program. If the desired response is not noted, it may be necessary to identify compliance issues. If compliance is not the problem, more calories may be needed by supplements or by enteral routes. Screening of nutritional status in relation to functional status can be done by the chest physician during hospitalisation for an acute exacerbation or during out-patient follow-up. The chest physician can consult the dietician for some insight into the cause and treatment of an impaired energy balance in weight losing subjects and the physiotherapist for the type and intensity of an exercise program. The respiratory nurse or a nutrition therapist can play a valuable role in hospital and home care of patients with chronic lung disease during regular visits or phone calls. They can monitor compliance and the weight course during diet therapy, give advice on meals and nutritional symptoms in the home setting to patient and family and feedback to the other caregivers. Despite an optimal implementation of nutritional therapy as part of an integrated treatment approach of COPD, one should recognize that even then a sub-group of patients may not reach the intended effect due to underlying mechanisms of weight loss that are yet unable to reverse by merely caloric supplementation. Potential reversibility by means of specific nutrients (nutriceuticals) or pharmaceuticals is a major focus of future research in this field.

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