REVIEW ARTICLE

Nutritional Status In COPD

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Changes in nutritional status, such as weight loss and malnutrition, are a very common complication in patients with chronic obstructive pulmonary disease (COPD). These changes primarily affect the patients' quality of life and functional capacity and they are also independent prognostic indicators of both morbidity and mortality. Malnutrition in these patients is due to multiple factors including increases in resting energy expenditure, decreased food intake, the effects of certain drugs, and, perhaps most importantly, a high systemic inflammatory response.

The present review covers the most important facets of the prevalence, etiology, pathogenesis, and consequences of malnutrition in COPD and considers which parameters for nutritional assessment are the most satisfactory for use in routine clinical practice. The strategy used to ensure correct nutritional status in these patients is also discussed.

Key words: *Chronic bronchitis. COPD. Malnutrition. Nutritional assessment.*

EPOC y estado nutricional

Las alteraciones nutricionales, entendidas como pérdida de peso o desnutrición, son una complicación muy frecuente en los pacientes con enfermedad pulmonar obstructiva crónica (EPOC) y afectan principalmente a su capacidad funcional y calidad de vida, además de constituir un indicador pronóstico de morbilidad y mortalidad independientes. Los factores que contribuyen a la desnutrición son múltiples; entre ellos cabe mencionar el aumento del gasto energético en reposo, el descenso de la ingesta, el efecto de determinados fármacos y, quizá el más importante, una elevada respuesta inflamatoria sistémica.

En este artículo se pretende revisar los aspectos más importantes sobre la prevalencia, etiopatogenia y efectos de la desnutrición en la EPOC, además de discutir los parámetros de valoración nutricional más adecuados en la práctica clínica diaria y la estrategia para que estos pacientes mantengan un correcto estado nutricional.

Palabras clave: *Bronquitis crónica. EPOC. Desnutrición. Valoración nutricional.*

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that is not fully reversible. The airflow obstruction is progressive and is associated with an anomalous inflammatory response of the lungs to harmful gases or particles, primarily tobacco smoke. As a result of important advances in our understanding of the systemic implications of COPD over the last 10 years, the traditional view that this disease affects only the lungs has been superseded, and COPD is now seen as a systemic disease affecting multiple organs and systems.[1]

Furthermore, the maintenance of optimum nutritional status in patients with respiratory diseases is vital because overall malnutrition has direct repercussions on the lung's function as a respiratory "pump" and because malnutrition directly affects both the respiratory muscles and the lung parenchyma, thereby contributing to worsening of the underlying disease. Weight loss, which is a common complication in patients with COPD, has been reported since the nineteenth century, primarily in patients with emphysema and those receiving long-term corticosteroid treatment. In these patients it is attributed to a series of factors including increased energy expenditure, decreased dietary intake, an imbalance between protein synthesis and breakdown, and other factors that have been less studied.[2]

Malnutrition is present in at least one third of moderate or severe cases of COPD, is a determining factor in the functional performance and quality of life of these patients, and is also a prognostic indicator of both morbidity and mortality, independent of other aspects of the disease, such as the deterioration of lung function.[3]

Epidemiology

Very few studies in the literature have analyzed the relationship between COPD and nutritional abnormalities and most have involved patients with emphysema, the paradigm context for malnutrition in COPD. In a study carried out by Wilson and colleagues,[4] approximately 43% of the patients with emphysema weighed under 90% of

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their ideal weight, while this figure was only 3% among patients with chronic bronchitis. Similarly, a decline in fat-free mass of 20% was observed among patients with moderate to severe COPD, and of 35% in patients taking part in pulmonary rehabilitation programs.[5]

In Spain, Pascual et al[6] reported obvious nutritional abnormalities in 53% of patients (overweight in 46.6% and malnutrition in 6.6%) and observed that the body-mass index (BMI) was the nutritional parameter that best predicted forced expiratory volume in 1 second (FEV_1). In another Spanish study, Soler et al[7] reported low body weight in 19.1% of the patients studied, muscle wasting in 47.2%, visceral protein depletion in 17.4%, and fat depletion in 19.1%. Of the patients with normal weight, 62.9% had muscle wasting

The earliest reference in the literature to an association between low weight and mortality was in 1967, when Vandenberg demonstrated a 50% mortality at 5 years of patients with COPD and weight loss, compared to 20% among weight-stable patients. More recently, in a study of data from 2130 patients who took part in a prospective population-based study (the Copenhagen City Heart Study), Landbo et al[8] found that BMI was an independent predictor of mortality in patients with COPD and that this association was stronger in the more advanced stages of the disease.

On the basis that COPD has systemic manifestations that are not reflected by FEV_1, Celli and coworkers[9] proposed a new multidimensional index for assessing severity in these patients. This index takes into consideration the BMI, the degree of airflow obstruction, severity of dyspnea, and exercise capacity measured by the 6-minute walk test. They concluded that this index was a better predictor of mortality than FEV_1, and that the BMI (included as a main variable) had independent prognostic value in COPD. These findings highlight the need for nutritional assessment in addition to functional evaluation in these patients.

Etiology and Pathogenesis

As a general rule, it can be said that weight loss occurs when there is a negative energy balance, that is, when expenditure exceeds intake. Similarly, muscle wasting occurs when protein catabolism exceeds protein synthesis.

The components of total energy expenditure in COPD patients have been analyzed by numerous authors, who have observed a relative state of hypercatabolism caused by an increase in one of the components: resting energy expenditure.[10] The increase in this variable in patients with COPD is multifactorial in origin, and the causes include an increase in the work of breathing, the presence of a systemic inflammatory response, and the use of β_2-agonists.

It is very tempting to attribute this increase in resting energy expenditure to the greater respiratory effort these patients must exert owing to hyperinflation, which makes contraction of their respiratory musculature more difficult and reduces the pressures they can generate. The theory is that this contraction involves a high consumption of oxygen and nutrients and leads to greater fatigability, thereby explaining the elevated resting energy expenditure and consequent weight loss found in patients with COPD and emphysema. However, resting energy expenditure remained high in several studies using nasal intermittent positive pressure ventilation—a technique that should theoretically reduce the inspiratory muscle effort—indicating that other factors must be involved. In short, it is difficult to quantify the impact of respiratory effort, and the results obtained vary depending on the measurement method used. The weakness of the correlation between the increase in resting energy expenditure and severity of pulmonary function impairment would suggest that the contribution of respiratory effort to this increase is slight.[11]

Currently, the more generally accepted theory is that the elevated resting energy expenditure found in these patients is related to cytokine activity. Several studies report increased concentrations of tumor necrosis factor-α, a proinflammatory mediator that intervenes in the pathogenesis of malnutrition in 2 ways: firstly by reducing energy intake and secondly by increasing the release of the cytokines that promote the mobilization of amino acids, thereby stimulating protein catabolism and, consequently, increasing resting energy expenditure.[12]

The possible impact of medication on resting energy expenditure has also been studied, and it has been observed that administering β_2-agonists to healthy individuals increases resting metabolic rate by 8% and that this increase is dose dependent.[13]

There is no consensus about whether the other 2 components of total energy expenditure (diet-induced thermogenesis and energy expenditure related to physical activity) are determining factors in total energy expenditure.

The second component in the energy balance is the reduction in intake. Studies have shown, in general, that the absolute dietary intake of most COPD patients is adequate for and may even exceed their requirements. However, dietary intake is relatively lower among the weight-losing patients, a phenomenon attributed to multiple causes including the reduction in oxygen saturation on swallowing and chewing, the presence of a flattened diaphragm compressing the stomach and giving rise to early satiety or, inversely, a distended stomach that compresses the lung and reduces functional residual capacity.[14] While it does not appear that lower dietary intake is the determining factor in the malnutrition of COPD patients, this possibility should, nonetheless, be taken into consideration.

The following are some other factors that could lead to malnutrition in COPD patients: reduced absorption, which, although not very marked, is observed to a certain degree in patients with α_1-antitrypsin deficiency; hemodynamic and hormonal abnormalities; and increases in concentrations of leptin secreted in response to various inflammatory cytokines released by alveolar macrophages in the presence of hypoxia.[15]

Nutritional Assessment in Patients With COPD

In general, insufficient attention is paid to the nutritional assessment of patients with COPD in routine practice. It should, like spirometry and arterial blood gas analysis, be included in the initial clinical evaluation of these patients. Regular follow-up of nutritional status is also essential

TABLE 1
Parameters for Assessing Nutritional Status in COPD*

Parameters	Comments
Weight and height	Cheap and simple. Isolated measurements not very useful
Ideal body weight	Value under 90% indicates malnutrition
Percentage weight loss	Useful in the initial assessment
Body mass index	Correlates with lung function
Skin folds	Measurement of body fat
Muscle circumference	Measurement of lean body mass
Bioelectrical impedance	Measurement of fat-free mass
Biochemical parameters: albumin, prealbumin, and transferrin	Not generally useful in COPD
Immunological parameters: lymphocyte count and CD3/CD4	Of little use
Prognostic indexes: nitrogen and albumin balance	Of little use

*COPD indicates chronic obstructive pulmonary disease.

because this variable has been shown to have independent prognostic value, a more than sufficient reason for its assessment.[16] Consequently, simple, easy-to-use, cheap, and reproducible procedures for the assessment of nutritional status are needed.

There is no single ideal nutritional marker, but a combination of several simple parameters can facilitate the diagnosis of malnutrition in these patients.[17] Several parameters are used to assess nutritional status and they can be basically categorized as either anthropometric or biochemical (Table 1).

– Body weight, which is very easy to measure. A record of weight over time is more useful than a single isolated measurement.

– Comparison with the predicted weight for height and sex in a specific population expressed as ideal body weight, or calculation of BMI. These variables are easily calculated. The BMI has been shown to correlate well with lung function parameters, such as the diffusing capacity of the lung for carbon monoxide, FEV_1, and the ratio of FEV_1 to forced vital capacity.

– Assessment of the muscle compartment using anthropometric data or densitometry.

– Evaluation of body composition by measurement of skin folds or, even better, bioelectrical impedance analysis. Body composition, and in particular the fat-free mass index, has been shown to be an independent predictor of mortality in COPD.[18]

– Biochemical markers, such as albumin, prealbumin and transferrin, have not been shown to be useful for assessing nutritional status in patients with COPD because they may be influenced by non-nutritional factors, such as infections and renal or hepatic disease.[17]

The parameters used to assess nutritional status in COPD patients will depend on the availability of resources but they should at least include weight, height, percentage of ideal body weight, and BMI. If possible these variables should be complemented by assessment of lean body mass and muscle mass, using either skin fold measurement or bioelectrical impedance analysis.[19] The malnutrition criteria for each parameter are shown in Table 2.

Several subjective measures for assessing nutritional status have recently been developed. These include the Subjective Global Assessment questionnaire and the Mini

TABLE 2
Diagnostic Criteria for Malnutrition

Parameter	Malnutrition Criteria
Involuntary weight loss: (usual weight–current weight) × 100/usual weight	5% in 1 month 10% in 3 months
Body mass index: weight (kg)/height $(m)^2$	Normal: 18.5-25 Mild: 17-18.4 Moderate: 16-16.9 Severe <16
Body fat measured by way of the tricipital or subscapular folds	Mild: percentiles 15-25 Moderate: percentiles 5-14 Severe <5
Lean body mass measured by way of arm muscle circumference: arm circumference – (3.14 × tricipital fold)	Mild: percentiles 15-25 Moderate: percentiles 5-14 Severe <5
Albumin	Mild: 2.8-3.4 g/dL Moderate: 2.1-2.7g/dL Severe <2.1 g/dL
Prealbumin	Mild: 10-15 mg/dL Moderate: 5-10 mg/dL Severe <5 mg/dL
Transferrin	Mild: 150-200 mg/dL Moderate: 100-150 mg/dL Severe <100 mg/dL

Nutritional Assessment scale, both of which are useful for identifying patients at high risk for developing complications associated with malnutrition and have a predictive value similar to the set of objective data considered as a whole and a level of agreement of more than 80%.[20] The advantage of these methods is their simplicity, reliability, and reproducibility, qualities that may recommend their routine use for the nutritional assessment of patients with COPD.

The Effects of Malnutrition on the Respiratory Apparatus

– *Changes in the respiratory musculature*. Abnormalities in skeletal muscle are common in COPD patients; contractility, strength, and resistance are reduced, while fatigability increases.[21] The etiology of muscular dysfunction in COPD is multifactorial and includes electrolyte abnormalities, atrophy due to lack of exercise, prolonged use of drugs such as corticosteroids,[22] changes in the geometry of the thoracic cage, hypoxia, and malnutrition. Malnutrition decreases muscular strength and resistance, and reduces glycolytic and oxidative capacity in both type I and type II fibers. A weak respiratory musculature contributes to dyspnea and has a negative impact on exercise tolerance.[23,24]

– *Morphological changes*. In various animal models, the lungs have been shown to lose mass as a result of malnutrition, although to a lesser extent than the body as a whole. This loss primarily affects protein content but fat content also diminishes. From a morphological standpoint this leads to a greater tendency of the lung to collapse, elongation of the airspaces, destruction of septa, and thinning of the interalveolar walls. These changes are due to an increase in proteolytic activity and a decrease in collagen content and may be partially reversible if the patient is adequately renourished.[3,25,26]

– *Biochemical changes*. Biochemical changes affect the alveolar surfactant provoking a decrease in total phospholipids, phosphatidylglycerol, and phosphatidylcholine. This triggers a rise in surface tension and a corresponding decrease in the protective effectiveness of the surfactant. These changes are due to a reduction in the enzyme activity that regulates its synthesis, to a reduced availability of energy substrates, and to characteristics of the local oxidative metabolism. These abnormalities may be reversible on renourishment, and a normal state is recovered more rapidly than in the case of connective tissue.[27]

In summary (although much remains to be clarified and most of the studies in the literature have used animal models), malnutrition appears to cause a series of alterations in muscles, especially the diaphragm, and also affects the lung parenchyma. The lungs become emphysematous in appearance and this changes respiratory dynamics.

Nutritional Strategy in COPD

It is essential to ensure that patients being treated for COPD maintain correct nutritional status and appropriate therapy should be implemented when necessary.

Nutritional support is indicated when the patient is malnourished and it has been established that his or her oral intake is inadequate or inappropriate for the recovery and or maintenance of an acceptable nutritional status. Nutrition should therefore be seen as another weapon in the arsenal of treatments for COPD together with drugs, exercise, and rehabilitation.[28] The objective of nutritional treatment is to remedy, as far as possible, the nutritional deficiencies detected and to minimize the damaging effect of such deficiencies on respiratory function.[29] This is not an easy objective to achieve in patients with COPD. Most of the studies that have investigated the impact of nutritional support in these patients have failed to obtain positive results with respect to improvements in functional performance or nutritional status. This does not mean, however, that appropriate nutritional treatment is not necessary because only very few randomized trials have been undertaken and, in general, the population samples analyzed were very small or treatment was administered for only a very short time.[30]

Energy Requirements of Patients With COPD

The main problem when prescribing nutritional support for a patient with COPD is to avoid an excess of nonprotein calories, an even more important question than macronutrient composition and/or distribution.

The energy supplement, in calories, should not exceed resting energy expenditure multiplied by a factor of 1.2. The carbohydrate content should not exceed 25% to 30% of the calories supplied. Glucose should be limited to 5 mg/kg/min to prevent lipogenesis and respiratory quotients above 1.[31] Fat content should be between 50% and 55% of the total energy supplied. Mixtures of oils should be used in order to prevent an overload of linoleic acid known to stimulate excessive synthesis of proinflammatory eicosanoids. This kind of diet ensures reduced production of carbon dioxide, but good clinical results are less easily obtained.[31]

Protein supplementation leads to an increase in the respiratory response to hypercapnia, not always a beneficial outcome in these patients. However, several studies have demonstrated that they may benefit from diets rich in branched-chain amino acids.[32]

Potassium, phosphates, and magnesium should always be included since a deficit of these micronutrients will considerably reduce the capacity of the patients' respiratory musculature and hypomagnesemia favors bronchial hyperreactivity. The antioxidants vitamins C and E and β-carotene also play an important role in improving the clinical and functional status of these patients.[33] Selenium improves respiratory function, particularly in smokers. In the presence of cor pulmonale, water and sodium restriction are recommended.[30]

Nutritional Supplements

Studies analyzing the benefits of using nutritional support in the treatment of patients with COPD have yielded conflicting results. Some authors report an increase in body weight in patients taking commercial liquid

supplements and a corresponding improvement in the effectiveness of the respiratory musculature related to the recuperation of muscle mass, water, potassium, and muscle protein nitrogen,[34] but others report a complete lack of effect.[30,35,36] While this lack of response is attributable to many factors (advanced age, anorexia, inadequate dietary intake despite the effort made), the principal cause is an elevated systemic inflammatory response evidenced by increases in acute-phase reactant proteins and tumor necrosis factor. Moreover, the small increases in weight that have been observed are the result of an increase in total body water and body fat in general.[37]

In general, better outcomes are obtained when nutritional support is complemented by exercise taking the form of a regular program of both respiratory and muscular rehabilitation.[38] For this reason, nutritional support should form part of any rehabilitation program in order to improve the patient's weight, muscle mass, and the strength of their respiratory musculature.[39,40] In such cases, weight gain is a predictor of survival, independently of the baseline lung function values and other risk factors, such as age, sex, smoking status, and values from arterial blood gas analysis.

Formula composition varies on a case-by-case basis. It is accepted that in patients with stable COPD any of the standard preparations used in the treatment of a variety of diseases may be prescribed, and that there is a margin of variability in caloric density, fiber content, flavors, and consistency. However, in unstable patients or patients at risk for exacerbation, formulas high in fats and somewhat low in carbohydrates have been proposed with the object of reducing carbon dioxide production.[41-44]

Although high-fat supplements may be beneficial in patients whose condition is unstable, it should be borne in mind that such formulas can delay gastric emptying and may cause flatulence or even diarrhea.[45] Moreover, hemoglobin desaturation has been reported on eating and this effect is more pronounced with hot meals and high-fat foods than with cold meals and low-fat foods.

Delivery of Nutritional Supplements

Parenteral administration is normally reserved for cases in which the digestive route is not an option. In such cases, the nutritional supplements should be the same as those indicated above.

Enteral delivery of nutrition can be nasoenteric or enterostomal. Nasoenteric feeding is indicated when it is estimated that enteral nutrition will be required for a period of less than 4 to 6 weeks. An enterostomal tube inserted surgically or placed using fluoroscopic or endoscopic methods (percutaneous endoscopic gastrostomy) is indicated when enteral nutrition is required for more than 6 weeks.[44]

A comparison of the results obtained with nasoenteric delivery and gastrostomy in patients with COPD reveals that there is insufficient evidence in the literature to establish which method is preferable. In some cases, an increase in mortality at 30 days has been reported after implantation of a percutaneous endoscopic gastrostomy in patients with COPD.[46] However, differences were found between the results obtained with enteral feeding through a nasoenteric tube and outcomes in patients taking supplements orally, with a greater improvement in nutritional status in the former group.[47]

Other Options

The other options that have been studied include the combined use of anabolizing agents—such as steroids—and nutritional supplements,[48] and the use of recombinant human growth hormone to stimulate lipolysis, protein anabolism, and muscle growth.[49] The results are not, however, conclusive because in cases in which an increase in muscle mass has been observed, it has been accompanied by increased energy expenditure but no improvement in the patient's functional performance or exercise capacity.[50]

Conclusions

From the available evidence, it appears that patients with COPD are at high risk for malnutrition, making it essential that these patients undergo careful assessment and screening to identify those who require dietary treatment. Moreover, despite the numerous studies undertaken to prove the efficacy of various nutritional formulas, the reality is that there is no scientific evidence that demonstrates any significant benefit to patients receiving nutritional support. Dietary treatment has not been shown to improve anthropometric parameters, lung function or exercise capacity. Consequently dietary recommendations for these patients should always be made bearing in mind the harmful effect of excessive intake, and dietary treatment should not be prescribed routinely.

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