

Review

Alteration in nutritional status and diaphragm muscle function

Bertrand Dureuil*, Yves Matuszczak

Département d'anesthésie-réanimation, Hôpital Charles Nicolle, 1, rue de Germont,
76031 Rouen cedex, France

(Received 3 February 1998; accepted 2 March 1998)

Abstract – Diet-induced undernutrition causes deleterious changes in the structure and function of the diaphragm muscle. Diseases associated with somatic wasting cause atrophy of the respiratory muscles. In cachectic subjects, the diaphragm muscle mass and thickness are reduced in proportion to the reduction in body weight. In addition, respiratory muscle strength and endurance are reduced more dramatically than the weight loss. This finding suggests that malnutrition induces a reduction in muscular mass which is associated with a decrease in contractility. Diaphragmatic weakness may increase the risk of respiratory failure in patients with chronic obstructive pulmonary disease (COPD). The primary goal of a successful nutritional programme is to improve the diaphragm strength by correcting the mineral, electrolyte and energetic disturbances at the muscular level, the latter being responsible for the decreased contractability associated with malnutrition. © Inra/Elsevier, Paris

diaphragm muscle / strength / endurance / contractility / malnutrition

Résumé – **Altérations du statut nutritionnel et fonction diaphragmatique.** L'état de malnutrition est associé à des altérations de la structure et de la fonction du diaphragme. Les pathologies conduisant à une perte de poids produisent une atrophie des muscles respiratoires. Chez les sujets cachectiques, la masse et l'épaisseur du diaphragme sont réduits de manière proportionnelle à la perte de poids. De plus, la réduction de force et d'endurance des muscles respiratoires est considérablement supérieure à la perte de poids. Ces données indiquent que la malnutrition induit une perte de masse musculaire associée à une baisse de contractilité. La faiblesse du diaphragme peut majorer le risque de décompensation respiratoire chez les patients insuffisants respiratoires chroniques. L'objectif premier d'un programme de renutrition est d'améliorer la force diaphragmatique en corrigeant les désordres électrolytiques, minéraux et énergétiques aboutissant à la réduction de la contractilité musculaire chez le patient malnutri. © Inra/Elsevier, Paris

muscle diaphragmatique / force / endurance / contractilité / malnutrition

* Correspondence and reprints

1. INTRODUCTION

The respiratory muscles, like the heart, must function competently for life. Malnutrition is a leading cause of impaired respiratory muscle contractility, affecting both its strength and endurance. The objectives of this review were first to define the role of the diaphragm as the main respiratory muscle, second to describe the consequences of malnutrition on the diaphragm muscle, and third to evaluate the effects of nutritional repletion on diaphragm muscle function.

2. DIAPHRAGM MUSCLE

The respiratory muscles constitute a vital pump that is just as important as the cardiac pump. Breathing is an endurance activity, and the muscle fibre composition of the diaphragm is well suited to the task [15]. In the human diaphragm, 75 % or more of diaphragm muscle fibres have good to excellent endurance characteristics. It is extremely useful to determine the pump performance in terms of those affecting energy supply and demand. Since an appropriate energy supply/demand ratio is necessary to sustain indefinitely the work of breathing and to adapt to the changes in ventilation caused by an increased ventilatory demand, causes of pump failure or dysfunction can be classified and understood, leading to appropriate therapeutic intervention. Factors that determine the energy supply and demand on the respiratory muscles are shown in *table I*. Nutrition is a common factor to both energy supply and demand. Since the diaphragm is the most important muscle of the respiratory pump, reduction in diaphragm muscle strength is of clinical importance in patients because it brings them close to the threshold of diaphragm fatigue in the case of increased respiratory load [15]. The major determinants of fatigue are the force and duration

of diaphragmatic contraction. Force is expressed as the ratio of pressure developed by the diaphragm in one breath (transdiaphragmatic pressure: P_{di}) to the maximum pressure the diaphragm is able to generate ($P_{di\ max}$). If malnutrition decreases $P_{di\ max}$, then the ratio $P_{di}/P_{di\ max}$ increases and the patient is more prone to develop diaphragm fatigue which may in turn lead to respiratory failure.

3. EFFECTS OF UNDERNUTRITION ON DIAPHRAGM MUSCLE

Animals subject to chronic starvation undergo similar and substantial decrements of body and respiratory muscle weight (*table II*). Diaphragm muscle bundles from undernourished animals have their maximal tetanic force reduced to the same extent as diaphragm muscle mass, so that the contractile force normalized to muscle mass remains normal [8]. This means that in the undernourished animals the cause of muscle weakness is loss of contractile elements, since the remaining muscle can develop normal force per unit of muscle in response to maximal stimulation. The same results are also reported after only 4 days of total acute starvation in rats [6].

Starvation causes atrophy of some but not all the muscle fibres. Kelsen et al. [8] found that the diaphragm of undernourished hamsters, like other skeletal muscle, underwent atrophy of type II but not type I fibres. That is, there was no change in the diameter of the slow-twitch oxidative fibers, but there was a 25 % reduction in the diameter of the fast-twitch glycolytic and fast-twitch oxidative glycolytic fibres.

Two to three days of starvation cause the rate of protein synthesis in isolated rat diaphragm strips to fall by half, and more

Table I. Factors determining energy supply and demands of the respiratory muscles.

Energy demands	Energy supply
Work of breathing minute ventilation frequency and tidal volume compliance and resistance	Oxygen transport oxygen saturation hemoglobin concentration cardiac output
Strength lung volume muscle mass muscle contractility nutritional status neuromuscular disease	Respiratory muscle blood flow cardiac output mean blood pressure force and duration of contraction
Efficiency VD/VT ratio pattern of breathing oxygen cost per liter of minute ventilation	Blood substrate available energy store ability to extract energy sources

VD: physiological dead space volume; VT: tidal volume.

Table II. Body weight and diaphragm muscle dimensions in humans.

Variable	Patients	
	Normal weight	Under weight
Body weight (kg)	64	40*
Body weight (% of ideal)	99	71*
Diaphragm muscle mass (g)	218	150*
Diaphragm muscle thickness (cm)	0.32	0.26*
Heart weight (g)	313	281*

From reference [1]; * significantly different from normal weight ($P < 0.005$).

than doubles the rate of protein degradation [7].

In humans, malnutrition reduces skeletal muscle mass. It was believed that perhaps the respiratory muscles in humans were privileged sites that were spared any loss of muscle protein during starvation because of their constant activity. In a necropsy study designed to assess the diaphragm in health and disease, it was

found that alterations in body weight and muscularity profoundly affect the diaphragm muscle mass [1]. In poorly nourished patients, the body weight and diaphragm muscle mass were reduced to 70 and 60 % of normal, respectively. It was observed that both diaphragm muscle mass and heart weight varied with body mass but that changes in diaphragm muscle mass were far more extensive than those of the heart. Both the area and the

thickness of diaphragm muscle changed as well as the muscle mass. There is a significant relationship between either the diaphragm muscle mass or thickness and body weight [1].

In patients with chronic obstructive pulmonary disease (COPD), diaphragm muscle mass and thickness vary with body weight in a fashion similar to that of patients without chronic pulmonary disease [16]. In addition, patients with greater degrees of emphysema had more severe reduction of body and diaphragm weight.

In living patients with a mean body weight 71 % of ideal, respiratory muscle strength was only 37 % of normal [2]. Both inspiratory and expiratory muscles were weakened to the same extent. The 60 % reduction in respiratory muscle strength is out of proportion to the 40 % loss of diaphragm muscle mass in patients with equal weight loss studied at necropsy [2]. This suggests that the respiratory muscles of these underweight patients are myopathic. Indeed, in underweight patients, diaphragm contractile force appears to fall to a far greater extent than can be explained by loss of muscle mass alone.

Alterations in intracellular electrolytes as well as mineral disturbances may account for the decreased diaphragm contractility. Hypophosphatemia reduces diaphragm contractile strength in mechanically ventilated patients during acute respiratory failure [3]. Hypocalcemia is associated with decreased diaphragm function in dogs [4]. Low serum Mg levels can also cause decreases in respiratory muscle strength in humans [11]. Chronic hypocaloric dieting produces changes in diaphragm muscle that may be important to the onset of muscle dysfunction. In addition to protein catabolism, these changes include depletion of glycolytic and oxidative enzymes, reduction in high energy phosphate stores, and increases in intracellular calcium. Severe malnutrition

depresses muscle glycolytic energy activity, thus reducing the availability of energy from glycolysis during contraction [9]. Energy stores are also decreased in severe malnutrition. Creatine phosphate level drop in association with a loss of total muscle creatinine [14]. Thus the reserves of energy phosphorus were decreased and the calculated free ADP rose, suggesting deficient oxidative phosphorylation activity. The electrophysiological properties of the muscle can also be altered by modifications of the cell membrane properties, which decrease the sodium-potassium pump activity, alter the ionic permeability, and thus unbalance the intracellular electrolyte composition [14]. These alterations could account for the diaphragm myopathic disturbances observed in chronic malnutrition.

The effect of alterations in respiratory muscle function in undernourished patients clinically free of lung disease has been correlated with changes in pulmonary function [2]. The alteration in muscle mass influenced both strength and endurance and reduced vital capacity. Both inspiratory and expiratory muscle strength is reduced. In addition diaphragm muscle weakness reduces vital capacity, and expiratory muscle weakness increases residual volume and alters the diaphragm optimum length, thus reducing its efficiency.

4. THERAPEUTIC INTERVENTIONS

In patients with anorexia nervosa, renutrition was associated with a marked improvement of diaphragmatic function. Since alterations in muscle contractile and endurance properties are not simply or solely due to changes in lean tissue, renutrition produces an improvement in muscle performance at a time when significant changes in body composition could not be detected [12]. This may be related

to the rapid correction of the mineral, electrolyte and energetic disturbances following an increase in nutrition and electrolyte intake as stated above.

In severe COPD patients with a high degree of malnutrition, several studies failed to show the benefit of nutritional intervention in terms of weight gain and respiratory muscle improvement [10, 13]. Others [17] reported that when given sufficient calories in excess of their needs, the patients gain weight. In six patients with emphysema, Wilson et al. [17] reported that they were able to appropriately increase food intake for a 2-week period, without evidence of malabsorption, and an improvement in respiratory muscle function and diaphragmatic strength was observed. However, the short period of this study strongly suggests that the major factor responsible for these findings was an increase in muscular contractility rather than in lean mass. Recent reports failed to demonstrate any beneficial effect of recombinant human growth hormone treatment on muscle strength or exercise tolerance in underweight patients with COPD [5].

5. CONCLUSIONS

Severe malnutrition can cause diaphragm weakness. Clinicians should recognize that even mild forms of malnutrition could be expected to complicate an already compromised respiratory muscle function. Clinically, this could be manifested as an increased predisposition to respiratory failure in patients with COPD or an increased difficulty in weaning patients with acute respiratory failure from mechanical ventilation. Nutritional support in malnourished patients can be expected to improve respiratory muscle function compromised by malnutrition, although the response of patients with COPD to nutritional support may be less

than that in patients suffering from other diseases such as anorexia nervosa.

REFERENCES

- [1] Arora N.S., Rochester D.F., Effects of body weight and muscularity on human diaphragm muscle mass, thickness and area, *J. Appl. Physiol.* 52 (1982) 64–70.
- [2] Arora N.S., Rochester D.F., Respiratory muscle strength and maximal voluntary ventilation in undernourished patients, *Am. Rev. Resp. Dis.* 126 (1982) 5–8.
- [3] Aubier J.M., Murciano D., Lecogucic Y., Viirés N., Squara P., Pariente R., Effects of hypophosphatemia on diaphragmatic contractility in patients with acute respiratory failure, *N. Engl. J. Med.* 313 (1985) 420–424.
- [4] Aubier M., Viirés N., Piquet J., Murciano D., Blanchet F., Marty C., Gherardi R., Pariente R., Effects of hypocalcemia on diaphragmatic strength generation, *J. Appl. Physiol.* 58 (1985) 2054–2061.
- [5] Burdet L., de Mural B., Schutz Y., Pichard C., Fitting J.W., Administration of growth hormone to under weight patients with chronic obstructive pulmonary disease, *Am. J. Respir. Crit. Care Med.* 156 (1997) 1800–1806.
- [6] Dureuil B., Viirés N., Veber B., Pavlovic D., Pariente R., Desmots J.M., Aubier M., Acute diaphragmatic changes induced by starvation in rats, *Am. J. Clin. Nutr.* 49 (1989) 738–744.
- [7] Goldberg A.L., Odessey R., Oxidation of amino acids by diaphragm from fed and fasted rats, *Am. J. Physiol.* 223 (1972) 1384–1391.
- [8] Kelsen S.G., Ference M., Kapoor S., The effects of prolonged undernutrition on the structure and function of the diaphragm, *J. Appl. Physiol.* 58 (1985) 1354–1359.
- [9] Layman D.K.M., Merdian-Bender M., Hegarty P.V.J., Swan P.B., Changes in aerobic and anaerobic metabolism in rat cardiac and skeletal muscles after total or partial dietary restrictions, *J. Nutr.* 111 (1981) 994–1000.
- [10] Lewis M.I., Belman M.J., Dorr-Uyemura L., Nutritional supplementation in ambulatory patients with chronic obstructive pulmonary disease, *Am. Rev. Resp. Dis.* 135 (1987) 1062–1068.
- [11] Molloy D.W., Dhingra S., Solven F., Wilson A., Mc Carthy D.S., Hypomagnesemia and respiratory muscle power, *Am. Rev. Resp. Dis.* 129 (1984) 497–498.

- [12] Murciano D., Rigaud D., Pingleton S., Armengaud M.H., Melchior J.C., Aubier M., Diaphragmatic function in severely malnourished patients with anorexia nervosa, *Am. J. Resp. Crit. Care Med.* 150 (1994) 1569–1574.
- [13] Otte K.E., Ahlburg P., D'Amore F., Stellfeld M., Nutritional repletion in malnourished patients with emphysema, *Am. J. Parent Ent. Nutr.* 13 (1989) 152–156.
- [14] Pichard C., Vaughan C., Struk R., Armstrong R.L., Jeejeebhoy K.N., Effect of dietary manipulation (fasting, hypocaloric feeding and subsequent refeeding) on rat muscles energetics as assessed by nuclear magnetic resonance spectroscopy, *J. Clin. Invest.* 82 (1988) 895–901.
- [15] Rochester D.F., The diaphragm: contractile properties and fatigue, *J. Clin. Invest.* 75 (1985) 1397–1402.
- [16] Thurlbeck W.M., Diaphragm and body weight in emphysema, *Thorax* 33 (1978) 483–487.
- [17] Wilson D.O., Rogers R.M., Sanders M.H., Pennock B.E., Reilly J.J., Nutritional intervention in malnourished patients with emphysema, *Am. Rev. Resp. Dis.* 134 (1986) 672–677.