DOI: 10.1590/0004-282X20150132

Current issues in the respiratory care of patients with amyotrophic lateral sclerosis

Tópicos atuais no tratamento respiratório de pacientes com esclerose lateral amiotrófica

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ABSTRACT

Amyotrophic lateral sclerosis is a progressive neuromuscular disease, resulting in respiratory muscle weakness, reduced pulmonary volumes, ineffective cough, secretion retention, and respiratory failure. Measures as vital capacity, maximal inspiratory and expiratory pressures, sniff nasal inspiratory pressure, cough peak flow and pulse oximetry are recommended to monitor the respiratory function. The patients should be followed up by a multidisciplinary team, focused in improving the quality of life and deal with the respiratory symptoms. The respiratory care approach includes airway clearance techniques, mechanically assisted cough and noninvasive mechanical ventilation. Vaccination and respiratory pharmacological support are also recommended. To date, there is no enough evidence supporting the inspiratory muscle training and diaphragmatic pacing.

Keywords: amyotrophic lateral sclerosis, respiratory function, rehabilitation.

RESUMO

Esclerose lateral amiotrófica é uma doença neuromuscular progressiva que resulta em fraqueza muscular, redução dos volumes pulmonares, tosse ineficaz, retenção de secreção e insuficiência respiratória. Medidas como a capacidade vital, pressão inspiratória e pressão expiratória máximas, pressão inspiratória máxima nasal, pico de fluxo de tosse e oximetria de pulso são recomendados para monitorar a função respiratória. Os pacientes devem ser acompanhados por uma equipe multidisciplinar, buscando melhorias na qualidade de vida e melhores estratégias para lidar com os sintomas respiratórios. A abordagem de cuidados respiratórios inclui técnicas de desobstrução das vias respiratórias, tosse assistida mecanicamente e ventilação mecânica não invasiva. Vacinação e suporte farmacológico também são recomendados. Até o momento, não existem provas suficientes que suportam o treinamento muscular inspiratório e a estimulação diafragmática.

Palavras-chave: esclerose lateral amiotrófica, função respiratória, reabilitação.

SHORT OVERVIEW OF ALS

Amyotrophic lateral sclerosis (ALS) is characterized by progressive degeneration of both cortical and alpha motor neurons of the final common pathway. Despite being a progressive degenerative process which primarily affects motor systems, ALS is now recognized to involve several non-motor systems and in long survivors affects many subcortical structures. Many hypotheses have been formulated about what causes ALS, including chemical exposures, occupational exposure, military service, infectious agents, nutritional intake, physical activity, and trauma. Worldwide, ALS affects white males aged > 60 years more often than any other group[1]. In the past three decades new practice parameters to the clinical care in ALS were developed and several clinical trials were performed[2]. As ALS remains as an incurable, progressive and fatal condition, the treatment strategies are focused in improving the quality of life[3]. The only effective pharmacological treatment is Riluzole, a putative glutamate release blocker linked to modestly prolonged survival[2]. Other therapeutic measures concerning respiratory support are outlined in this paper.

PULMONARY FUNCTION IN ALS

Respiratory muscle strength

Progressive weakness remains the foremost characteristic of ALS. However, while some ALS patients progress rapidly, others have slow progression of muscle weakness;

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Conflict of interest: There is no conflict of interest to declare.
Received 19 March 2015; Received in final form 22 May 2015; Received in final form 10 June 2015.

furthermore, some ALS patients have significant upper motor neuron dysfunction, while others have little[4]. Severe weakness leads to breathlessness and ventilatory failure. The clinical significance of respiratory muscle weakness depends not only on the weakness severity, but also on the mechanical load imposed to the ventilatory system. Patients with ALS are likely to have severe respiratory muscle weakness, affecting in most cases both the inspiratory and expiratory muscles. The tests most widely used to assess respiratory muscle strength are the maximal inspiratory (MIP), expiratory (MEP), and sniff nasal inspiratory pressure (SNIP). The measurement of MIP and MEP is quick, non-invasive, and normal values have been established[5]. A recent study showed higher MEP values in comparison to MIP in patients with neuromuscular diseases; in this work, the MEP/MIP ratio was 1.33 ± 0.62 in patients with ALS and differed from those observed in other neuromuscular conditions[4].

Spirometry

Spirometry measures how an individual inhales and exhales air volumes in a given unit of time. It provides flow and volume measurements, and a very useful tool in clinical practice to suggest and even set diagnostics[6]. The characteristic abnormality of inspiratory muscles weakness is a low vital capacity (VC)[7]. The simplicity of the VC maneuver makes it ideal for repeated measurements. In patients with ALS, repeated measurement of the CV has been shown to be a simple and efficient way to detect the loss of lung function[8]. With substantial diaphragm weakness, the VC is reduced and falls further when the patient is supine; in normal subjects, the supine fall is < 10% of the sitting values[9]. In longstanding conditions, VC in the supine position decreases between 30-50% compared with upright value[10]. This finding is almost pathognomonic of respiratory muscle paralysis.

In chronic respiratory muscle weakness, reductions in the compliance of the lung and chest wall and microatelectasis result in great reductions in VC for a given level of weakness[11]. Through ROC curve analysis, Kwon et al.[12] showed that the phrenic latency (AUC = 0.7655) and FVC (%) (AUC = 0.8239) discriminated ALS patients from healthy controls. In patients with ALS, however, Fregonezi et al.[13] showed that 57% had decreased VC, 75% had reduced SNIP, and 81% had decreased MEP. Interestingly, Javad Mousavi et al.[14] demonstrated that FVC and FEV_1 are useful non-invasive parameters in the prediction of survival in ALS patients, even after controlling for relevant non-pulmonary characteristics.

Gas exchange

The ability to conduct gas exchange depends basically on the 'respiratory pump', which moves air in and out of the lungs. The respiratory muscles, an integral and vital component of the respiratory process, serve as a vital link between the different components of the pump, which consist of the respiratory centers, the conducting nerves, and the lung itself[15]. In simple terms, failure of the pump may lead to respiratory decompensation and development of hypercapnia[16]. This condition is associated to hypoxemia, which results from failure of the gas exchange portion of the system. In patients with ALS, respiratory muscle weakness leads to hypoxemia, mainly due to ventilation/perfusion mismatch, and eventually ventilator failure (global hypoventilation) which leads to hypoxemia and hypercapnia. When the pulmonary function is relatively normal, hypercapnia does not occur until there is profound weakness, with strength reduced to approximately one quarter of normal[17].

The diffusing capacity for carbon monoxide (DLco) is a measure of gas exchange and, therefore, tends to change early in the course of certain diseases that affect the respiratory system. It examines the gas transfer from the alveoli into the interior of red blood cells. DLco is reduced but normal or rose when adjusted for volume, and this distinguishes respiratory muscle weakness in ALS patients from alveolar disorders such as pulmonary fibrosis[18].

PULMONARY REHABILITATION AND RESPIRATORY SUPPORT

The respiratory muscle weakness is associated to a reduction in pulmonary volumes, secretion retention and, in the most advanced stages of the disease, respiratory failure. Moreover, the aspiration and infection episodes contribute to progressive pulmonary function deterioration, making the respiratory complications the main cause of death in ALS[19]. Additionally, such patients can present with sleep disordered breathing (because of the loss of swallowing and airway protection determined by glottic muscles) and chronic hypoventilation, requiring specific diagnostic strategies and the use of non-invasive ventilation. Therefore, the respiratory care approach to ALS patients has to take in consideration the secretion retention and the ventilatory impairment, which may require the use of airway clearance techniques, mechanically-assisted cough and invasive or noninvasive mechanical ventilation[20]. Management is optimized in a multidisciplinary team setting; observational studies suggest that this improves survival by around 8 months[3].

Nonpharmacologic airway clearance techniques

Among the nonpharmacologic airway clearance techniques, chest physical therapy (postural drainage, vibration and/or percussion), positive expiratory pressure, intrapulmonary percussive ventilation, and high-frequency chest wall compression were assessed in previous studies, but cannot be recommended for routine use due to insufficient evidence[21,22]. Conversely, as the main underlining mechanisms of secretion retention are the impaired ventilation and ineffective cough, most of the currently used

techniques aim to improve the cough efficiency by increasing the inspiratory volume, the expiratory drive pressure or both. Patients who have weak expiratory muscle strength but relatively well-preserved inspiratory strength can benefit from "manually assisted cough," which replace or augment abdominal muscle contraction[22]. In turn, patients with weak inspiratory muscles can improve their cough efforts with breath-stacking technique, manual (using a resuscitator bag) or mechanical insufflation therapy. The breath-stacking therapy consists in performing multiple and short inspiratory efforts without expiration. The sum of these inspirations results in a larger volume which can be used with a subsequent spontaneous or manually assisted cough. Since the glottis closure between the subsequent inspirations may be difficult for ALS patients, a one-way valve can be used to prevent loss of inspired volume[22]. When a resuscitator bag is available, it can be used along with a one-way valve and a mouthpiece in a series of breath-stacking maneuvers, until the patient is maximally insufflated. Manually assisted cough (MAC) is inferior to spontaneous cough when MEP is > 34 cm H_2O, and the additional benefit of breath stacking may be reduced when MEP > 34 cm H_2O or VC > 1.9 liters[23]. When VC is < 340 ml, MEP < 14 cm H_2O or unassisted PCF is < 90 L/min these manual methods are not likely to provide adequate cough assistance, and mechanically assisted cough (M-IE) should be considered[23]. Moreover, M-IE resulted in a significantly higher mean PCF (7.47 L/s) than the combination of breath-stacking and manually assisted cough (4.27 L/s). Mechanically assisted cough is provided by a device which applies, through mask or tracheostomy, a relatively high inspiratory pressure (about 40-45 cm H_2O) aiming at hyperinflate the lungs. Then the pressure is switched to negative values (usually -40 to -45 cm H_2O), promoting suction that mimics the physiological cough effort. MI-E has proven efficacy in augmenting the cough peak flow in patients with and without bulbar impairment and is recommended as routine treatment for asymptomatic ALS patients with PF < 160 L/min and symptomatic patients with PF < 255-270 L/min[23].

Noninvasive ventilation and tracheotomy

The noninvasive ventilation (NIV) is an alternative to tracheotomy in patients with clinical signs (tachypnea, use of accessory muscles, paradoxical movement of the abdomen, decreased chest wall movement, weak cough, sweating, tachycardia, morning confusion, hallucinations, weight loss, mouth dryness) and symptoms (dyspnea on minor exertion or talking, orthopnea, frequent nocturnal awakenings, excessive daytime sleepiness, daytime fatigue, morning headache, difficulty clearing secretions, apathy, poor appetite, poor concentration or memory) of respiratory failure and hypoventilation[19,20,24]. Tracheostomy prevention facilitates the use of glossopharyngeal breathing for patients who can master the noninvasive ventilation technique[24]. Soudon et al.[25] compared the clinical complications of tracheostomized patients with neuromuscular disease with those who were entirely NIV supported and found tracheal injury, chronic hypersecretion and pulmonary infection to be more frequent, with a greater requirement for institutional care in individuals with tracheostomy. NIV offers the patient and family effective management without surgical risk, long-term complexity and the additional nursing care required with tracheostomy[19,25]. A sniff nasal inspiratory pressure < 40 cm H_2O, nocturnal oxygen desaturation of 90% for at least one cumulative minute, vital capacity < 50% and elevated arterial partial pressure of CO_2 (PCO_2) are useful criteria for initiation of NIV[19]. The NIV regimen usually starts with nighttime use and during the day as needed. Bilevel positive airway pressure machines are considered the best devices to provide NIV, in combination with many kinds of interfaces (oronasal or nasal masks, nasal prongs, and mouthpieces). A special mouthpiece with a lip seal may prevent air leakage in patients whose lips are weak, but nasal prongs can be necessary[26].

Oxygen therapy is not needed and should be avoided in nearly all patients with ALS, since it can exacerbate carbon dioxide retention, resulting in hypercapnic coma or respiratory arrest[23].

A recent consensus recommended the indication of tracheostomy only for patients who cannot maintain a SpO_2 or greater than or equal to 95% despite continuous noninvasive ventilatory support and mechanically assisted cough, a common condition among patients with ALS[26].

Vaccination, drugs and other therapies

There are great advances in public health resulting from immunizations; however, there are still deaths and sequelae caused by diseases that can be prevented through vaccination. The American Association of Neurology recommends performing vaccination with both pneumovax and influenza for ALS patients[27].

As the respiratory mucosa contributes a constant flow of serous and mucoid fluids, mucolitics like guaifenesin or N-acetilcysteine and/or an anticholinergic bronchodilator like ipratropium and/or theophylline, or even furosemide, may add some benefit in clearing secretions, but there are no controlled studies on ALS patients[20].

Although inspiratory muscle training and diaphragmatic pacing have demonstrated some benefit, more studies are necessary until these therapies can be considered safe and reliable treatment options for patients with ALS[3,28].

In conclusion, patients with ALS need a comprehensive approach, which can be provided by a multidisciplinary team. Muscle weakness is the hallmark of the disease, resulting in respiratory impairment. Since ALS is incurable and progressive, an appropriate follow up including the respiratory function assessment is essential to guide the supportive therapy.

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