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Bulbar impairment score predicts noninvasive volume-cycled ventilation failure during an acute lower respiratory tract infection in ALS☆

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) patients can suffer episodes of lower respiratory tract infections (LRTI) leading to an acute respiratory failure (ARF) requiring noninvasive ventilation (NIV).
Aim: To determine whether clinical or functional parameters can predict noninvasive management failure during LRTI causing ARF in ALS.
Material and method: A prospective study involving all ALS patients with ARF requiring NIV in a Respiratory Care Unit. NIV was provided with volume-cycled ventilators.
Results: 63 ALS patients were included (APACHE II: 14.93 ± 3.56, Norris bulbar subscore (NBS): 18.78 ± 9.68, ALSFRS-R: 19.90 ± 6.98, %FVC: 40.01 ± 18.07%, MIC: 1.62 ± 0.74 L, PCF 2.51 ± 1.15 L/s, PImax −34.90 ± 19.44 cm H_2O, PEmax 51.20 ± 28.84 cm H_2O). In 73.0% of patients NIV was successful in averting death or endotracheal intubation. Differences were found between the success and failure in the NBS (22.08 ± 6.15 vs 8.66 ± 3.39, $p < 0.001$), ALSFRS (22.08 ± 6.11 vs 12.71 ± 4.39, $p < 0.001$), PCF_{MI-E} (3.85 ± 0.77 vs 2.81 ± 0.91 L/s, $p = 0.007$) and ALS onset (spinal/bulbar 33/13 vs 7/10, $p = 0.03$). The predictor of NIV failure was the NBS (OR 0.53, 95% CI 0.31–0.92, p 0.002) with a cut-off point of 12 (S 0.93; E 0.97; PPV 0.76; NPV 0.97).
Conclusions: NBS can predict noninvasive management failure during LRTI in ALS.

1. Introduction

Respiratory failure associated with progressive respiratory muscle weakness is the main cause of hospitalization and mortality in amyotrophic lateral sclerosis (ALS) patients [1]. The use of respiratory muscle aids at home, namely noninvasive ventilation (NIV) and mechanically assisted coughing (MAC), prolongs survival [2,3], relieves symptoms [2], averts hospitalizations [3] and improves quality of life for ALS patients [2,3]. Nevertheless, despite careful patient management, lower respiratory tract infections (LRTI) can occur [4], which can lead to a rapid decline in respiratory muscle function and, in some cases, to a life threatening situation [5].

NIV is currently a standard practice for the management of both acute hypercapnic respiratory failure in chronic obstructive pulmonary disease (COPD) patients and hypoxemic respiratory failure in cardiogenic pulmonary edema patients [6], and reliable guidelines regarding NIV application for such patients are available [7]. However, although pulmonologists can also find recommendations on the use of NIV for clinically stable ALS patients [2], data regarding the usefulness of NIV in avoiding endotracheal intubation (ETI) and preventing mortality during acute episodes in patients suffering neuromuscular diseases (NMD) are scarce [6–8]. Although some published results do point to the potential usefulness of both volume-cycled and pressure-cycled NIV in such situations, they are based on heterogeneous populations of NMD patients [9–11], few of whom were ALS sufferers.

This important lacuna in scientific knowledge concerning NIV in ALS needs to be addressed. For those ALS patients who refuse tracheotomy

Abbreviations: AB, acute bronchitis; ALS, amyotrophic lateral sclerosis; ALSFRS-R, revised amyotrophic lateral sclerosis functional rating scale; APACHE II, Acute Physiology and Chronic Health Evaluation; ARF, acute respiratory failure; AUC, area under the curve; CAP, community acquired pneumonia; COPD, chronic obstructive pulmonary disease; BMI, body mass index; ETI, endotracheal intubation; FVC, forced vital capacity; %FVC, predicted FVC; ICU, intensive care unit; LRTI, lower respiratory tract infection; MAC, mechanically assisted cough; MIC, maximum insufflation capacity; NBS, Norris bulbar subscore; NIV, noninvasive ventilation; NMD, neuromuscular disease; PCF, peak cough flow; PCF_{MIC}, manually assisted PCF; PCF_{MI-E}, mechanically assisted PCF; PEmax, maximum expiratory pressure; PImax, maximum inspiratory pressure; RCU, respiratory care unit; ROC, receiver operating characteristic; RR, respiratory rate; SBI, severe bulbar impairment; TMV, tracheotomy mechanical ventilation.

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mechanical ventilation (TMV), NIV could be the only procedure available for the prolongation of their lives, but maintaining NIV when ineffective may be futile and increase patient suffering. There is known to be a possible association between bulbar impairment and poor NIV and MAC outcomes in ALS patients during LRTI [9,12], but the data available are insufficient to provide accurate information with which to guide the decision-making process in clinical practice. The aim of this study is to determine whether a clinical or functional parameter can predict the failure of noninvasive provided by volume-cycled ventilators in ALS patients during an LRTI.

2. Material and methods

2.1. Study design and patients selection

This prospective study was performed in a referral ALS unit from March 2005 to September 2014, and included, after informed consent, all the ALS patients suffering an LRTI episode who had been admitted to our respiratory care unit (RCU) requiring NIV. The hospital's ethics committee approved the protocol. Patients with previous pulmonary disease were not included in this study.

The criteria for eligibility were: 1) a diagnosis of probable or definitive ALS; [13] 2) an LRTI episode, as defined by the guidelines of the European Society of Clinical Microbiology and Infectious Diseases [14], which could consist of acute bronchitis (AB) or definite community-acquired pneumonia (CAP); 3) Indication of the use of NIV de novo, due to the presence of any of the following criteria adapted from the current guidelines: [7] severe respiratory distress, respiratory rate >30 breaths/min, use of accessory respiratory muscles or paradoxical abdominal motion, PaO_2 < 60 mm Hg despite oxygen therapy, PaCO2 > 45 mm Hg or impaired consciousness 4) In the case of those patients who were already using NIV at home before the LRTI episode, they were eligible for inclusion when NIV and MAC failed [2] to relieve the above mentioned clinical criteria or to maintain SpO2 ≥ 90%.

Since scheduled clinical and functional assessments are made every three months for our ALS patients [15], pulmonary function and cough capacity had been assessed in the three month period prior to the LRTI, when the patients were in a medically stable condition. Patients were also evaluated with the Revised Amyotrophic Lateral Sclerosis Rating Scale (ALSFRS-R) [16], and with the Norris scale bulbar subscore (NBS) upon admission [17].

On admission to the RCU, patients were evaluated [18], monitored, and received full medical and psychological support.

NIV was delivered via a volume-cycled ventilator using the assist/control mode, through an oronasal mask at night and through a simple mouthpiece or a lipseal mouthpiece or a nasal mask during the day when necessary. For all interfaces used, ventilator settings were adjusted and patient-ventilator interaction was evaluated on the basis of clinical observation, continuous pulsioximetry, the visual inspection of waveforms and data on the ventilator screen, and periodic blood gas measurements. When the ventilator did not provide the information required, a respiratory monitor (Easy View. Puritan Bennet, Carlsbad, Ca) was added to the circuit. During the first few hours of NIV (until satisfactory adaptation to NIV was achieved), the attending physician would remain at the bedside in order to monitor the clinical response and adjust the ventilator settings the mask, straps, etc. Afterwards, the physician would be called by the nursing staff whenever SpO_2 fell, the ventilator alarm sounded (settings: 10 cm H_2O for low pressure and 35 cm H_2O para high pressure) or the patient complained of respiratory distress. Supplementary oxygen was delivered when SpO_2 < 95% despite adequate NIV ($PaCO_2$ ≤ 45 mm Hg, with peak inspiratory pressure around 20 cm H_2O and respiratory thoracoabdominal excursions synchronic with the ventilator).

Respiratory secretions were managed with MAC (Cough-Assist, JH Emerson, Cambridge, MA).

2.2. End points and definitions

The primary outcome variables were: 1) treatment success, defined as the successful management of the acute respiratory episode by means of NIV and MAC without resorting to ETI; 2) treatment failure, defined as transfer to ETI or death at any time during the study.

NIV and MAC were considered effective (*initial improvement*) if, after two hours, the pH was 7.35–7.45, $PaCO_2$ 35–45 mm Hg, the respiratory rate was 12–20 bpm, SpO_2 was stable, the patient was comfortable with the ventilator and the use of the accessory muscles had ceased. If, after the initial 2 h, the pH was greater than 7.45 or lower than 7.35, and $PaCO_2$ was greater than 45 mm Hg or lower than 35 mm Hg, but the pH had improved by 0.1 and $PaCO_2$ by 10 mm Hg, in comparison with the figures recorded upon admission to hospital, then NIV and MAC were also considered effective. *Sustained improvement* in gas exchange was defined as the ability of NIV and MAC to maintain the above defined improvement in pH, $PaCO_2$ and PaO_2 during the period of hospitalization. If this sustained improvement enabled the patient to be discharged, *treatment success* was achieved. Patients whose clinical or physiological situation deteriorated once more after removal of NIV, and so had no ventilator-free time, were said to require *continuous NIV*.

Treatment failure occurred – making an ETI necessary – when an experienced clinician in consultation with critical care staff observed one or more of the following circumstances: [7] failure to improve or deterioration of arterial blood gas tensions (mainly rapidly decreasing SpO_2), failure to alleviate symptoms, deteriorating level of consciousness, intolerance of or failure of coordination with the ventilator, emergence of complications making an ETI necessary, or the stated wish of the patient to withdraw treatment. Treatment failure also occurred if MAC (or repeated bronchoscopies) was unable to remove airway secretions and/or patients felt continuously encumbered or dyspnoeic. The Intensive Care Unit (ICU) protocol of our hospital only permits the substitution of ETI with a tracheostomy in intubated ALS patients, and thus for these patients no attempt was made to extubate and use non-invasive management [19].

For those patients who refused ETI, appropriate palliative care was provided.

For additional information on methods and equipment, see the online supplement.

2.2.1. Statistical analysis

Data were expressed as mean ± SD and data comparisons were performed using Student's t-test. Categorical data were compared using the chi-square test. Univariate and multivariate logistic regression analyses were performed to determine those variables that were independently associated with noninvasive management failure. Receiver operating characteristic (ROC) curves were used to identify a cut-off point in those variables that best predicted the patients for whom noninvasive management would be ineffective during an acute respiratory failure (ARF) secondary to an LRTI. Statistical significance was taken as $p < 0.05$.

3. Results

During the period of study, 63 ALS patients were admitted to our RCU due to an ARF secondary to an LRTI, requiring NIV. All patients agreed to NIV instead of ETI as the first management procedure and none were excluded from the study. Data on demographics, respiratory function and cough capacity assessment are shown in Table 1. Forty-nine patients (77.8%) used home NIV prior to the LRTI with a mean of 10.27 ± 4.69 h/day (range 8–24 h/day) and all of them used a volume-cycled ventilator with an oronasal mask during sleep and a mouthpiece when awake if necessary. Forty-two patients (66.7%) used MAC at home and 32% of patients received enteral feeding through gastrostomy tubes. The causes of ARF were: AB (58.7%), CAP (36.5%), respiratory tract infection with atelectasis (3.2%) and aspiration