Editorial: Respiratory Management of Patients with Amyotrophic Lateral Sclerosis

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The article by Drs. Bédard and McKim entitled “Respiratory Management of Patients with Amyotrophic Lateral Sclerosis” in the current edition of the Ontario Thoracic Reviews serves as a pertinent reminder of the importance of active respiratory management of the patient with amyotrophic lateral sclerosis (ALS). While ALS is the focus of the article, the reader will appreciate that many of the management principles outlined in the article can be applied to patients with other forms of neuromuscular disease affecting the respiratory muscles, also - in particular, the use of lung volume recruitment (LVR or “breath stacking”), assisted coughing, and non-invasive ventilation (NIV). The crucially important thematic management issue, appropriately emphasized by Drs. Bédard and McKim, is active respiratory monitoring and timely intervention with therapeutic maneuvers to prevent development of respiratory complications and to optimize the quality of life in patients with ALS (again, the principle applies to other forms of neuromuscular disease affecting the respiratory system).

There are some helpful practical gems that the reader can extract from this article – what pressures to start bilevel positive pressure

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treatment in patients with ALS, for example, and what symptoms and physiological variables to monitor in patients with neuromuscular disease affecting the respiratory system. In particular, the authors emphasize keeping it simple—there is often no need for a sleep study to initiate bilevel treatment in patients with neuromuscular disease—select pressures and a back-up rate that are comfortable for the patient and that achieve reasonable tidal volumes; fine-tuning of the settings can be managed later, if needed. The authors point out that overnight oximetry, which is readily available in most communities, can provide valuable information to assist the physician and respiratory therapist as to the adequacy of nocturnal ventilation, and whether bilevel settings and/or mask fitting requires adjustment, particularly if sleep studies are not readily available or practical (because of the patient’s immobility). Overnight oximetry is particularly valuable in patients with bulbar disease, who are unable to perform lung function testing, to supplement the clinical assessment of respiratory muscle weakness and alert the respirologist to evidence of nocturnal hypoventilation.

Physicians who are not familiar with the use of LVR, assisted coughing and mechanical insufflation may enjoy supplementing this article with a visit to the web site of the Institute for Rehabilitation Research and Development, where Dr. McKim and his colleagues have prepared video demonstrations of these techniques (www.irrd.ca). Knowledge of these simple techniques is empowering for the respirologist managing neuromuscular disease and critical for the morbidity and mortality of the patient with ALS. The authors are to be commended for promoting a simple, practical approach to respiratory management of the patient with ALS; this is an approach that we can readily understand and adopt.

**Respiratory Management of Patients with Amyotrophic Lateral Sclerosis**

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**Introduction**

The care of patients with amyotrophic lateral sclerosis (ALS) is a very challenging but truly rewarding role for respiratory specialists. ALS is an incurable neurodegenerative disease affecting both upper and lower motor neurons, resulting in progressive skeletal muscle weakness. At onset, it generally affects predominantly either limb or bulbar muscles. Rarely, its first presentation can be respiratory failure secondary to early respiratory muscle involvement.

The median survival after onset of symptoms is 3 years.
Respiratory failure, usually associated with pneumonia, is the most common cause of death\textsuperscript{i}. Progressive inspiratory and expiratory respiratory muscle weakness results in reduction of ventilatory efficiency and cough effectiveness. Bulbar muscle involvement can also cause dysphagia and aspiration.

The only licensed drug, Riluzole, improves survival by 2-3 months\textsuperscript{ii}. In absence of significant disease-modifying therapy, the main emphasis of care is on management of symptoms and complications of the disease. In this regard, respiratory management is of primary importance, especially since non-invasive ventilation (NIV) appears to improve both quality of life and survival\textsuperscript{iv}. The goal of this article is to review the state of the art in respiratory management of ALS patients and to provide practical information, consistent with the recent Canadian Thoracic Society Home Mechanical Ventilation guideline\textsuperscript{v}, to clinicians caring for this population.

**Respiratory assessment and follow-up**

Patients should have a respiratory assessment at diagnosis and every two to six months depending on disease progression\textsuperscript{vi}. This evaluation should include review of relevant symptoms and performance of pulmonary function testing (PFT) (Table 1).

### ANNOTING The 2013-2014 Electronic Grant-in-Aid Competition

The OTS/CLA will be accepting applications for studies relating to lung health. With this electronic system, you will be able to open an account, upload your registration and application and add team members to your account. Some useful features will be available such as posting reader feedback for editing working documents and sharing with other team members.

To qualify for funding, candidates are asked to complete two (2) steps:

1. **Registration Deadline:** November 16, 2012
   
   Please register at [www.ngr.myreviewroom.com](http://www.ngr.myreviewroom.com) by November 16, 2012. You are required to provide your name, institution, identify the type of research (clinical or basic science), the project title, and a maximum one page abstract.

2. **Submit Application by December 7, 2012 by 4:30 p.m. Pacific Time.** The original hardcopy application must be sent to your Provincial Lung Association, the Post-Mark must be no later than December 7, 2012. ONE (1) electronic copy of the application form and the appendices, in Word or PDF must be submitted to the Canadian Lung Association via [www.ngr.myreviewroom.com](http://www.ngr.myreviewroom.com) by December 7, 2012 4:30 p.m. Pacific Time.

**Tutorials for navigating the registration and application website:** Click here

**National Grant Review/Provincial Guidelines:** Click here

**Note:** be sure to read and follow the additional Ontario guidelines (At-a-glance section on page 8).

Grant-In-Aid Application Form visit the OTS research awards section: [http://www.on.lung.ca/page.aspx?pid=567](http://www.on.lung.ca/page.aspx?pid=567)

Pulmonary function measurements have important prognostic value\textsuperscript{iii} and some are better predictors of survival than ALS functional rating scales\textsuperscript{iv}. Evolution of the disease varies significantly between individuals. Regular PFT performance demonstrates the rate of decline and identifies when significant pulmonary impairment is reached since this may be difficult to assess on clinical basis\textsuperscript{viii}. Timing of some interventions, such as cough-assisting techniques, NIV and gastrostomy feeding tube, relies on knowledge of PFT values. Also, efficiency of airway clearance aids can be evaluated objectively by measuring peak cough flow (PCF).

**Airway clearance**

Invariably, the ability to adequately cough and clear secretions from airways becomes impaired with disease progression. The cough reflex involves a near-maximal inspiration followed by closure of the glottis, contraction of expiratory muscles to further increase intrathoracic pressure and finally sudden glottic opening resulting in forceful expiration. In ALS, reduced cough efficacy is related to inspiratory and expiratory muscle weakness as well as glottic impairment. Retained secretions in the airways reduce ventilation and predispose to pneumonia and respiratory failure.

Cough effectiveness can be easily measured using a peak flow meter with the patient forcibly coughing into a mouth piece or a face mask. A minimal PCF of 160 L/min has been demonstrated necessary to prevent reintubation of patients with neuromuscular disease, irrespective of their breathing capacity\textsuperscript{vii}. However, a PCF < 270 L/min identifies individuals with neuromuscular diseases, including ALS, at risk of respiratory complications and who benefit from preventive airway clearance techniques \textsuperscript{x-vii}. This is the accepted target value for introducing airway clearance management both by the Canadian and American Thoracic Societies\textsuperscript{x,xi}.

When PCF is < 270 L/min and in the absence of risk for barotrauma, lung volume recruitment (LVR, a.k.a. “breath stacking”) should be introduced with measurement of assisted PCF and maximum insufflation capacity (MIC). This is usually done with a hand-held resuscitation bag via a mouthpiece or a face mask. By closing the glottis between each inspiratory volume, the patient will stack multiple breaths, reaching maximal lung volume closer to normal predicted (Figure 1 and 2). This volume is referred to as the MIC and is proportional to respiratory system compliance and bulbar function\textsuperscript{xii}. LVR improves PCF and dyspnea in neuromuscular disease patients and, in the context of an airway clearance protocol, has reduced the number of hospitalizations and hospital days per year in an observational study\textsuperscript{xi}. LVR significantly slows pulmonary function decline in Duchenne muscular dystrophy\textsuperscript{xiv}, presumably by maintaining chest wall range of motion and lung compliance.

With sufficient strength in upper extremities, patients are able to perform LVR with a hand-held resuscitation bag. When needed it can be administered by a caregiver. It is generally recommended 3 to 4 times daily, but there are no data informing the optimal frequency of sessions and number of full lung inflations during each of them.

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LVR can also be done with glossoaryngeal breathing (GPB), using pharynx and tongue muscles to force boluses of air into the lungs\(^{xv}\). GPB can be taught but some patients instinctively develop this ability. Patients using noninvasive mouthpiece or invasive ventilation can use ventilator breaths to do LVR.

In all cases, manually assisted cough (MAC) can be added to LVR to further improve cough effectiveness\(^{xvii}\) (Figure 1). While the patient is seated or semi-recumbent, with a full lung inflation, a rapid one or two-hand abdominal thrust is applied by a caregiver below the xiphoid process just prior to glottic opening.

If, despite using LVR and MAC, the patient's assisted PCF remains < 270 L/min or the technique cannot be performed by the patient, a trial of mechanical in-exsufflation (MI-E) is indicated. Through a face mask, a positive pressure is applied to the airway and is rapidly shifted to a negative pressure, simulating the effect of a cough. It can also be used through an artificial airway. The CoughAssist\(^{TM}\) (Philips Respironics) is the only device available in Canada. Several case reports and observational studies have shown its utility in improving PCF, managing respiratory infection, reversing atelectasis and avoiding hospitalization\(^{xvii-xviii}\). It may however be of little assistance with significant bulbar impairment and insufficient upper airway stability to maintain patency during the exsufflation phase\(^{xix}\). Its cost is approximately $5000 versus $75 for LVR with a resuscitation bag.

There are insufficient data to recommend the use of other devices such as high frequency chest wall oscillation or intrapulmonary percussive ventilation for airway clearance.

**Immunization**

Pneumococcal and annual seasonal influenza vaccination should be provided to ALS patients in accordance to the Canadian Immunization Guide\(^{xx}\).

**Dysphagia and nutrition**

Progressive bulbar impairment leads to dysphagia which often results in inadequate caloric and fluid intake and secondary worsening of weakness and fatigue. It also increases the risk of aspiration, choking and recurrent chest infection.

Initial management of dysphagia includes evaluation by a speech therapist and modification of food and fluid consistency as well as postural changes. Simultaneous care by a dietician is important to ensure adequate nutritional intake.

Percutaneous endoscopic gastrostomy (PEG) may be ultimately needed in order to provide a safe alternative route for delivering nutrition and may prolong survival, but the degree of evidence is low\(^{xxi}\). Optimal timing of PEG placement is not defined, but the risk of the procedure is higher when the FVC is < 50% of predicted, which is generally considered as a relative contraindication\(^{xxii}\). PEG insertion should be discussed with the patient and family members in presence of symptomatic dysphagia, weight loss or preventively, in face of declining pulmonary function.

**Sialorrhea**

Sialorrhea is a frequent symptom in ALS and is caused by oropharyngeal muscle weakness and reduced ability to swallow. It can be extremely bothersome to the patient and socially embarrassing. It can also prevent successful NIV.

Although few data are available in ALS, pharmacologic therapy is the first approach, based on information from other neurologic conditions associated with sialorrhea\(^{xxiii}\). Different anticholinergic medications can be used (Table 2). Suction machines are also frequently employed for symptom control, although there is no evidence supporting their value in ALS.

When refractory to medical therapy, salivary gland injection with botulinum toxin is an option that appears to be safe and useful for treating sialorrhea in ALS patients\(^{xxiv-xxv}\). Another possibility is low dose radiation therapy to the salivary glands\(^{xxvi}\).

Patients can also complain of thick tenacious mucus, which is difficult to clear. In that case, trial of either propanalol or metoprolol may relieve symptoms\(^{xxvi}\). Nebulized saline or N-acetylcysteine may also be useful but no controlled studies are available.

**Noninvasive ventilation**

Noninvasive ventilation (NIV) has been shown in one randomized controlled trial to improve survival (205 days (p=0.006)) and quality of life in ALS patients without severe bulbar dysfunction. In patients with poor bulbar function, NIV improved different aspects of quality of life but did not confer a survival benefit\(^5\). Four prospective and three retrospective studies also reported improved survival in ALS patients using NIV, but of modest magnitude. All studies looking at health-related quality of life showed improvement of some domains that persisted despite disease progression. Other benefits reported by different studies included improved gas exchange, reduced rate of decline in VC and enhanced cognition\(^5\).

Indications for NIV varied among the different studies which demonstrated benefit. However, some criteria are well accepted given their ability to predict hypoventilation and/or their prognostic value. These are: orthopnea, daytime hypercapnia, symptomatic sleep disordered breathing, FVC < 50% of predicted and SNP or MIP < 40 cm H\(_2\)O\(^6\) (Table 3).

NIV should be offered to ALS patients in the presence of any of these criteria. There is no evidence for suggesting where the NIV should be initiated and how to select ventilator settings. However, based on literature and CTS guidelines, ventilator parameters should be adjusted for optimal patient comfort and improvement of symptoms\(^5\). All studies that reported details of NIV used the S/T mode in which a backup rate (BUR) can be provided. There are three rationale supporting this mode over S mode: sleep disordered breathing in ALS consists mainly of REM-related non-obstructive hypopneas and central apneas\(^{xxvii}\).

Patients with respiratory muscle weakness may fail to reliably
trigger breaths from the bilevel device, and the BUR ensures respiratory muscle rest\textsuperscript{xviii}. Arterial blood gas, nocturnal oximetry and/or polysomnography are not required but can be useful in some specific cases. Due to limited mobility and care requirements, an in-laboratory sleep study is difficult to perform for most ALS patients.

At The Ottawa Hospital CANVent Unit the first trial of NIV is made in clinic with a respiratory therapist. Bilevel ventilation in S/T with sustained inspiratory time (Ti) or PC mode, is used with the BUR set one or two breaths less than the patient’s spontaneous respiratory rate and no less than 12 breaths per minute. EPAP is generally set at 4 or 5 cmH\textsubscript{2}O unless obstructive sleep apnea is known or suspected. IPAP is set to achieve an estimated tidal volume of 8 to 10 ml/kg of ideal body weight and Ti is adjusted for an I:E ratio as close as possible to 1:1, considering patient comfort. Triggering, cycling and rise time are daytime support and eventually continuous, 24-hour ventilation. The ability to maintain a significant MIC-VC difference and an assisted PCF > 160 L/min predicts successful use of 24-hour NIV, independently of VC or extent of need for ventilatory support\textsuperscript{xix}. Moreover, patients with sufficiently preserved bulbar function can benefit from daytime, volume-targeted mouthpiece ventilation (MPV). By making a seal around the mouthpiece and creating a negative pressure using cheek muscles, as many breaths can be triggered as needed in order to relieve dyspnea, maintain ventilation and perform LVR. Day MPV allows for more flexibility for feeding, speech and mobility than conventional NIV. The ventilator and mouthpiece are mounted on the patient’s wheelchair (Figure 3).

**Table 1. Respiratory assessment at each visit**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Pulmonary function testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>Sitting FVC</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>One or more of: Supine VC</td>
</tr>
<tr>
<td>Poor sleep</td>
<td>SNP</td>
</tr>
<tr>
<td>Excessive daytime sleepiness</td>
<td>MIP</td>
</tr>
<tr>
<td>Morning headache</td>
<td>PCF spontaneously and/or assisted</td>
</tr>
<tr>
<td>Poor concentration and/or memory</td>
<td>ABG or EtCO\textsubscript{2} when hypercapnia suspected</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Nocturnal oximetry ± tCO\textsubscript{2} when symptomatic</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>SDB suspected</td>
</tr>
<tr>
<td>Aspiration</td>
<td></td>
</tr>
<tr>
<td>Recurrent chest infection</td>
<td></td>
</tr>
</tbody>
</table>

FVC: forced vital capacity, VC: vital capacity, SNP: sniff nasal pressure, MIP: maximal inspiratory pressure, PCF: peak cough flow, ABG: arterial blood gas, EtCO\textsubscript{2}: end-tidal carbon dioxide, tCO\textsubscript{2}: transcutaneous carbon dioxide, SDB: sleep-disordered breathing.
Table 2. Anticholinergic medications for sialorrhea treatment

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage/Method</th>
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<tbody>
<tr>
<td>Atropine</td>
<td>0.4 mg s/c every four to six hours</td>
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<td></td>
<td>1% ophthalmic drops, 1-4 drops sublingual two to four times daily</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>10 to 50 mg per os once daily at bedtime</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>0.2 mg s/c three times daily</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>1.5 mg transdermal patch, 1 or 2 patches applied behind ear, change every 3 days</td>
</tr>
</tbody>
</table>

Table 3. Indications for noninvasive ventilation in ALS

- Orthopnea
- Daytime hypercapnia
- Symptomatic sleep disordered breathing
- FVC < 50% predicted
- SNP < 40 cmH$_2$O or MIP < 40 cmH$_2$O

FVC: Forced vital capacity, SNP: sniff nasal pressure, MIP: maximal inspiratory pressure

Figure 1. Lung volume recruitment (LVR) with breath stacking and effect of manually assisted cough. Adapted from ACI Respiratory Network, Domiciliary Non-Invasive Ventilation in Adult Patients (www.aci.health.nsw.gov.au)

Figure 2. Flow volume loops with and without lung volume recruitment (LVR). Red: spontaneous vital capacity. Blue: maximum insufflation capacity (MIC) with LVR.

Figure 3. ALS mouthpiece ventilation
References


