Continuous Mouthpiece Daytime Amyotrophic Lateral Sclerosis in Noninvasive Ventilation: Definitive Solid Therapy?

To the Editor:

Treatment options for amyotrophic lateral sclerosis (ALS) are very limited.[1] In some cases, noninvasive ventilation (NIV) by mouthpiece ventilation is a technique that is useful in the treatment of chronic ventilatory failure, particularly in neuromuscular patients.[2] The literature on mouthpiece ventilation in ALS is limited, and there are no published evidence-based guidelines concerning mouthpiece ventilation. Its application is mainly based on the experience of a few centers. Mouthpiece ventilation is particularly useful when there are problems with conventional masks. Patient selection for adequate bulbar muscle function is of paramount importance, and in these patients, mouthpiece ventilation was shown to be an effective alternative to tracheostomy, optimizing convenience and communication.

We have read with great interest the study by Bédard and McKim[3] that concludes that mouthpiece ventilation is a safe, convenient, and effective way to provide NIV in ALS with adequate bulbar function requiring continuous ventilatory support. Although this study shows an original contribution for NIV in severe ALS, we believe that there are some key issues that require evaluation.

First, the addition of mouthpiece ventilation was based primarily on the objective of improving quality of life related to prolonged hours of inconvenient and uncomfortable mask use (>12 h daily) (24 of 37 subjects) and symptoms of dyspnea (9 of 37 subjects).[3] We believe other aspects need to be considered.

Second, the evaluation of bulbar function remains subjective as a clinical assessment, where some clinical tests (swallowing and speech) and patient recall define the level of bulbar involvement. This is in contrast to the evaluation of ventilation, where several objective functional markers are followed through time. Of all of the routine respiratory tests ordered, cough peak flow is the only test that reflects bulbar function in addition to inspiratory and expiratory muscle function. The difference between cough peak flow and peak expiratory flow has thus been proposed to measure bulbar involvement.[4]

Third, the bulbar subscores of the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale discriminated between those subjects having sufficient bulbar function to succeed with mouthpiece ventilation and those who did not. It seems to be a simple and useful tool to assess candidacy for mouthpiece ventilation. In this study, the scores' cutoff points are arbitrary, and no study has defined a cutoff that accurately reflects an objectively measured clinical impairment. We need a more accurate way to detect and quantify the level of bulbar involvement.[4] For example, a specific test of bulbar function may help to recognize the group of patients at higher risk of NIV failure or in need of early initiation of mechanical cough assistance, or it may simply help to better classify/quantify bulbar involvement[4] Further prospective clinical trials to confirm the efficacy of mouthpiece ventilation should be offered as a rational alternative to tracheostomy for individuals able to hold a mouthpiece, particularly in individuals with non-bulbar ALS needing continuous ventilatory support.

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Continuous Mouthpiece Daytime Amyotrophic Lateral Sclerosis in Noninvasive Ventilation: Definitive Solid Therapy?—Reply

In reply:

We appreciate very much the opportunity to respond to the letter from Drs Fiorentino and Esquinas with regard to our publication on mouthpiece ventilation in amyotrophic lateral sclerosis (ALS).[1] We are pleased that it was read with great interest, and we sincerely thank our subjects for allowing us the opportunity to document the effectiveness of mouthpiece ventilation. Providing ventilator support and airway clearance to individuals with ALS is often challenging; therefore, developing more accurate means of assessment and novel techniques of support, such as mouthpiece ventilation, is critical, particularly in avoiding unnecessary tracheostomy placement.

We are in full agreement with many of the statements expressed in this letter and recognize the importance of mutual effort in establishing evidence-based and best practices in the respiratory care of those with ALS. Sadly, even in the Canadian Thoracic Society clinical practice guideline on home mechanical ventilation,[2] there are no specific recommendations for mouthpiece ventilation for patients with ALS, although there are for patients with Duchenne muscular dystrophy. The recommendations for up to 24-h noninvasive ventilation (NIV), rather than tracheostomy, although not explicit, could be interpreted to include mouthpiece ventilation, clearly a form of NIV. We also agree that the paper demonstrates that mouthpiece ventilation is safe, convenient, and effective and that, indeed, key issues are still in need of further evaluation.

In particular, we agree entirely that a more objective assessment of bulbar function and its potentially predictive relationship to success with mouthpiece ventilation would be helpful rather than relying on the first 3 questions of the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale score, referred to as the bulbar subscore (b-ALSFRS-R). Within individuals, this score may vary from time to time, and in our experience, it may differ significantly from a more objective clinician assessment. However, we do not have consistent access to more objective measures of bulbar function and must rely on this value as a subjective estimate. It may also be of greater utility in studying populations of ALS patients as opposed to single individuals. Not even we, however, would rely entirely upon

a single threshold in the b-ALSFRS-R score (<6/12) to exclude a patient from mouthpiece ventilation, but we would rely on an adequate clinical trial, particularly in the absence of prospective studies establishing a more discriminative threshold in a larger population of individuals with ALS. Hence, a small number of subjects were included whose b-ALSFRS-R score was low but who seemed at least initially to be capable and motivated enough to grip the mouthpiece. Even prospective trials may not be able to adequately address the question of sufficient bulbar function for mouthpiece ventilation in given individuals. In the same way that clinically, individuals with severe bulbar ALS with low cough peak flows may not be expected to tolerate NIV or mechanical in-exsufflation based on objective evaluation and published experience,[3-6] much to our surprise, many do. As a result, we suspect that even prospectively established, objective cutoffs will not replace adequate clinical trials of mask NIV, mechanical in-exsufflation, or mouthpiece ventilation.

While we also agree that cough peak flow is an excellent assessment of bulbar function, we would not suggest that it "is the only test that reflects bulbar function." Although glottic function is clearly necessary to enhance expiratory flows above those observed with forced exhalation alone, in our experience, the difference between the maximum insufflation capacity and vital capacity is an equally robust measure of glottic and bulbar function. In fact, the difference between the maximum insufflation capacity and vital capacity has been demonstrated to correlate highly with cough peak flow in a population with Duchenne muscular dystrophy.[7] Clinically, some individuals may fail to demonstrate an enhanced cough peak flow greater than the peak expiratory flow but may still demonstrate a considerable difference between maximum insufflation capacity and vital capacity. As such, we would prefer to rely on either measure or both to help define those who are more likely to manage mouthpiece ventilation effectively.

Further discussion would also be appropriate with regard to the suggestion that mouthpiece ventilation is "particularly useful when there are problems with conventional masks." Rather, mouthpiece ventilation is introduced precisely to replace even perfectly comfortable and effective masks and expressly to provide independence from them. Indeed, mouthpiece ventilation facilitates speech, swallowing, and, perhaps most importantly, the ability to autonomously perform regular lung volume recruitment to increase cough peak flow, maintain airway clearance, and possibly improve respiratory mechanics, all critical activities that cannot be performed with mask NIV. Furthermore, the suggestion that "other aspects [*besides quality of life*] need to be taken into account," if implying that the symptom of dyspnea and/or prolonged use of mask NIV is not a legitimate, sole indication for mouthpiece ventilation and that more objective measure are required, is to suggest that ALS patients experiencing daytime dyspnea need to remain on a confining mask and not be relieved or permitted the ability to perform autonomous lung volume recruitment until more objective signs, such as, presumably, daytime hypercapnia, are identified. To establish definitively the survival benefit of mouthpiece ventilation in ALS, hypercapnia might be necessary, but to provide independence and quality of life in breathing, communicating, and taking nutrition by mouth, it is not. We would continue to advocate that, in those capable of retaining and using a mouthpiece, the introduction of mouthpiece ventilation should occur as soon as the daily amount of mask ventilation exceeds 12 h or whatever time threshold will provide the patient with comfort, relief of dyspnea, and effective daytime ventilation as well as autonomous airway clearance.

We join you in the anticipation of future trials that will better define optimum candidates and the role of mouthpiece ventilation in the respiratory management of individuals with ALS.

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P_{aO_2}/F_{IO_2} Is Not a Guesstimation

To the Editor:

I read with great interest and with some concern the paper by Cao et al[1] that compared volume-controlled and pressure-limited noninvasive ventilation (NIV) in subjects with acute hypercapnic respiratory failure. The authors reported on P_{aO_2}/F_{IO_2} rather than P_{aO_2} as part of their baseline demographics in Table 1 and in their results in Figure 5. The methods for NIV described that supplemental oxygen was delivered through a port in the mask with flow adjusted to maintain oxygen saturation using a specific machine (FLEXO ST30, Curative Medical Technology, Suzhou, China). They used a formula to determine F_{IO_2} delivered to each subject and reported results as P_{aO_2}/F_{IO_2}, which causes me some concern. The authors did state that the conversion factor provided an approximation of F_{IO_2}, which was influenced by minute ventilation, breathing pattern, and gas leakage. I feel that an approximation of F_{IO_2} cannot accurately predict P_{aO_2}/F_{IO_2} where a completely closed system and accurate F_{IO_2} is not provided. I found one abstract[2] that used the formula to help rapidly predict correlation of S_{pO_2}/F_{IO_2} in non-intubated patients as a surrogate to arterial blood gas for determining P_{aO_2}/F_{IO_2} in emergency room patients, which may be a novel noninvasive way to assess respiratory failure.[3-5]

I could not find any reference to the formula to validate and verify an F_{IO_2} via a port for NIV. I have used REMstar NIV machines (Philips Respironics, Murrysville, Pennsylvania) for several decades, and the