Considerations About the Effect of Cough Assist on Laryngeal Function in Neurologic Disease

To the Editor:

We read with interest the work by Andersen et al1 about transnasal laryngoscopy during mechanical insufflation-exsufflation in amyotrophic lateral sclerosis (ALS). We believe the following should be considered.

First, the larynx is a complex structure that cannot simply be thought of as a passive valve through which one may insufflate and exsufflate the lungs with similar responses in all, particularly not in patients with intrinsic laryngeal weaknesses and reduced motor control. Given the nature of ALS, with its combination of upper and lower motor neuron signs, glottic narrowing in patients with ALS could be the infranuclear paralytic type, the supranuclear nonparalytic type, or a combination of the two. Vocal cord abductor paresis and laryngospasm in ALS are rarely described in the neurologic literature and autopsy studies.2

During exsufflation in all patients with neuromuscular disorders, including ALS, there was constriction of the hypopharynx, an exaggeration of the findings seen in patients without neuromuscular disorders to a varying degree. Constriction seemed very pronounced in subjects with hypotonic bulbar weakness. Clearly, airway closure on both insufflation and exsufflation is a major limitation in applying mechanical insufflation-exsufflation and is likely to be distressing in those patients most severely affected. Andersen et al1 showed that adduction of supraglottic structures limits insufflation in patients with bulbar neuromuscular disease, including ALS. They surmise that upper airway collapse and/or spasm may be generated. In particular, gradual development of bulbar dysfunction may influence the extent to which a successful use of mechanical insufflation-exsufflation is to be expected.4

Third, in patients with bulbar symptoms, noninvasive ventilation and mechanical insufflation-exsufflation should be managed individually, with the expectation that settings and interventions may need to be modified with disease progression. In patients with ALS, the clinical response to noninvasive use of mechanical insufflation-exsufflation is variable, which indicates a certain motor dysfunction of the upper airways. In some cases, the effect of mechanical insufflation-exsufflation seems to be reduced in parallel to disease progression and deteriorating bulbar dysfunction. It is difficult to predict beforehand which individuals will succeed because there are no evidence-based predictive factors.

Treatment failure with mechanical insufflation-exsufflation in patients with bulbar symptoms is likely to be caused primarily by laryngeal adduction during insufflation, predominantly at the supraglottic level. This response precludes air filling of the lungs during insufflation, which causes discomfort and subsequent inefficient exsufflation. A similar approach is appropriate in starting noninvasive ventilation; high inspiratory pressures may generate airway closure, and so pressure should be gently titrated upward.5

The main methodological problem in the study was the gradual increase in pressure during the intervention to familiarize the subjects to the feeling of mechanical insufflation-exsufflation. This could be a confounding factor; the subjects become familiarized with the feeling of mechanical insufflation-exsufflation through experience and modification of movements according to the theory of motor learning. Randomizing the intervention sequences could prevent this issue, but, in clinical settings, pressures are always increased gradually to be as gentle as possible for patients.

Individually customized settings for pressure and flow can improve and extend the use of noninvasive mechanical insufflation-exsufflation in ALS, and flexible laryngoscopy can be an efficient tool in selected patients who do not respond as expected. When we increase our understanding of these issues, we can, it is hoped, develop better clinical instructions, more fine-tuned settings, or even new functions for mechanical insufflation-exsufflation devices.

Antonio M Esquinas MD PhD
Intensive Care Unit
Hospital Morales Meseguer
Murcia, Spain

Giuseppe Fiorentino MD
UOC di Fisiopatologia e Riabilitazione
AO Ospedali dei Colli Napoli
Naples, Italy

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Laryngoscopy Can Be a Valuable Tool for Unexpected Therapeutic Response in Noninvasive Respiratory Interventions

In reply:

We thank Antonio M. Esquinas and Giuseppe Fiorentino for their acknowledgments and for their summary of some of the findings from our investigation on this under-
The studied topic of laryngeal response patterns to mechanical insufflation-exsufflation,\textsuperscript{2-4}

We certainly agree that the larynx must not be seen merely as an opening at the top of the airway tree. As we have described in our work, the larynx is a highly complex valve that needs to adjust, adapt, and actively respond to a wide range of physiological situations and stressors. Basic features such as structure, function, and innervation are not fully understood in health or in disease. We know that the application of positive airway pressures can lead to laryngeal adduction, even in healthy individuals.\textsuperscript{2} Moreover, laryngeal collapse due to high ventilatory volumes during ongoing exercise was recently defined and described as an independent disease entity labeled “exercise-induced laryngeal obstruction.”\textsuperscript{5,6}

Thus, it should not come as a surprise that complex motor neuron diseases like amyotrophic lateral sclerosis (ALS) influence laryngeal function and can compromise the laryngeal ability to accommodate intermittent increases in air flow applied by mechanical insufflation-exsufflation. Whether high or abruptly applied positive pressures can lead to laryngeal collapse in a noninvasive ventilation setting is an issue that remains to be studied systematically.

Concerning the concern of “type of ALS” versus “laryngeal responses to mechanical insufflation-exsufflation,” these aspects were discussed in detail in our previous cross-sectional study.\textsuperscript{3} We agree that these issues are important to understand in order to expand on the utilization of noninvasive therapeutic alternatives in this vulnerable group of patients. We acknowledge and certainly encourage that our findings should be systematically tested in larger ALS populations treated and followed at institutions larger than ours. Our studies have so far demonstrated that the larynx in these patients plays the role of the bottleneck of the airways by its nature, and that it functions as an important valve that regulates pressure and air-flow access to the airway tree below. This has obvious consequences for the use of all types of mechanical respiratory support that utilize noninvasive positive airway pressures in these patients. Importantly, it seems reasonable to assume that these findings are relevant, not only in patients with bulbar innervated muscle dysfunction, but also in other and larger patient groups; however, this remains to be studied.

Obviously, as Esquinas and Fiorentino note, we could have randomized the order of the pressure settings while performing the intervention study instead of increasing the pressures gradually, as we chose to do. We chose this approach to provide the participants with the necessary time to familiarize themselves with the protocol, similar to the mechanical insufflation-exsufflation pressure titration typically used with patients in clinical settings.\textsuperscript{7} For obvious reasons, clinical research performed in ALS patients must be extraordinarily well designed and should include elements that aim to also improve the daily care of the included patients.\textsuperscript{7} Considering the explorative context in which this study was performed, we felt it important that the use of the patients “end-of-life time” should be perceived as meaningful, that the treatments had a clinical benefit, and that we could provide clinical advice to improve their care during their disease progression. In our opinion, the approach chosen did not influence our results significantly, but this should be tested in further studies.

To conclude, this research field is still in a very early phase, and there is a range of unanswered questions. Transnasal fiberoptic laryngoscopy has previously been seen as a specialized examination that should be performed in an otolaryngology clinic. At present, transnasal fiberoptic laryngoscopy is a technique that can be used in several functional contexts, such as during swallowing, inspiratory muscle training, or during an exercise test\textsuperscript{8-11}, and it can be performed by a trained doctor, by a speech therapist, and by other allied health professionals. We believe that transnasal fiberoptic laryngoscopy performed during ongoing noninvasive respiratory therapies will improve the understanding of laryngeal responses and will help clinicians optimize the treatment for patients who need noninvasively delivered pressures. We encourage others to use this method, both in clinical work and in research projects. We believe that transnasal fiberoptic laryngoscopy will be a valuable tool for a variety of respiratory therapeutic interventions in selected patients who do not respond as expected.

\textbf{Tiina M Andersen PT PhD}  
Norwegian Advisory Unit on Home Mechanical Ventilation, Thoracic Department  
Haukeland University Hospital  
Bergen, Norway

\textbf{Astrid Sandnes MD}  
Department of Pediatrics  
Haukeland University Hospital  
Department of Clinical Science  
University of Bergen  
Bergen, Norway

\textbf{Hege Clemm MD PhD}  
Department of Clinical Medicine  
Haukeland University Hospital  
Bergen, Norway

\textbf{Ove Fondenes MD}  
Norwegian Advisory Unit on Home Mechanical Ventilation, Thoracic Department  
Haukeland University Hospital  
Bergen, Norway

\textbf{Roy M Nilsen PhD}  
The Faculty of Health and Social Sciences  
Western Norway University of Applied Sciences  
Bergen, Norway

\textbf{Ole-Bjørn Tysnes MD PhD}  
Department of Neurology  
Haukeland University Hospital  
Department of Clinical Medicine  
University of Bergen  
Bergen, Norway

\textbf{John-Helge Heimdal MD PhD}  
Department of Otolaryngology/Head and Neck Surgery  
Haukeland University Hospital  
Department of Clinical Medicine  
University of Bergen  
Bergen, Norway

\textbf{Maria Vollseter MD PhD}  
Norwegian Advisory Unit on Home Mechanical Ventilation, Thoracic Department  
Haukeland University Hospital  
Department of Clinical Science  
University of Bergen  
Bergen, Norway
Ola D Røksund PT PhD
Department of Pediatrics
Haukeland University Hospital
The Faculty of Health and Social Sciences
Western Norway University of Applied Sciences
Bergen, Norway

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