Non-invasive ventilation in neonates: the lungs don’t like it!

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Nasal intermittent positive pressure ventilation (nIPPV) is a non-invasive modality of ventilatory support that is frequently used for a number of clinical conditions. Suggested applications for nIPPV include the treatment of respiratory distress and apnea of prematurity, sleep apnea syndromes, COPD, and as a bridge between mechanical ventilation and unassisted breathing (1, 5). Its appeal derives largely from its non-invasive nature: portability, the avoidance of acute and chronic damage to the airways during intubation, and minimization of mechanical ventilation-induced lung injury (baro- and volotrauma). In the special case of premature infants, nIPPV prevents subglottic stenosis and is associated with a lower incidence of extubation failure and of bronchopulmonary dysplasia (2, 5). The benefits of nIPPV come with an unexpected problem: it causes reflexive inspiratory contraction of the thyroarytenoid muscle, a glottal constrictor, narrowing the glottis and increasing airway resistance (4). Since non-invasive ventilation requires low-resistance airways throughout the respiratory system, this reflex creates a limitation to airflow of sufficient magnitude to ultimately impair gas exchange (3). Moreover, it is not immediately clear where in the respiratory system such a reflex would be triggered. The paper by Roy et al. in this issue of the Journal presents a clever study that demonstrates that inspiratory activation of glottal constrictors during nIPPV is most likely mediated by bronchopulmonary receptors (6).

The authors’ premise is straightforward enough: reflexive glottal narrowing in response to nIPPV is triggered either by receptors in the upper or in the lower airways. Solving the problem of how to test the relative importance of these two receptor populations is the most novel contribution of this study. Using newborn lambs, Roy et al. designed an interesting two-way approach. First, a set of newborn lambs was implanted with wire electrodes around the intrathoracic vagus nerves using video-assisted surgery; simple electrocautery and traction on the wires at selected times during the study were sufficient to rapidly section the nerves, removing the sensory input from bronchopulmonary receptors. The effect of
nIPPV on laryngeal muscle EMG activity was then tested in the same animals before and after bilateral vagotomy. The results showed increased inspiratory EMG activity in the thyroarytenoid muscle (glottal constrictor) during nIPPV, a response completely abolished by bilateral vagotomy. nIPPV also inhibited inspiratory EMG activity in the cricoarytenoid muscle (glottal dilator); importantly, this effect was not affected by vagotomy. The surgical tour de force continued in a second set of animals in which the authors established chronic isolation of the upper airways: basically, they just divided the trachea directly below the larynx. The rostral (laryngeal) end was attached to an aortic prosthesis; airflow through the upper airways was diverted to the outside through a neck stoma. The caudal (tracheal) end was used to create a tracheostomy below the neck stoma, and a very short endotracheal tube was attached to the skin around it, in effect creating a bypass of the upper airways. This chronic awake animal preparation allowed the authors to demonstrate that inspiratory thyroarytenoid EMG activity increased and cricothyroid activity decreased only with nIPPV through the tracheostomy, and not during nasal ventilation. Roy et al. rightly concluded that the inspiratory increase in glottal constrictor activity during nIPPV originates from bronchopulmonary receptors. The origin of the simultaneous inspiratory decrease in EMG activity in the glottal dilator could not be identified.

Where do we go from here? The seemingly inappropriate activation of laryngeal muscles during nIPPV is not innocuous; it has been convincingly demonstrated that glottal narrowing during nIPPV increases airway resistance and results in significant variations in tidal volume (3, 4). Blunting this reflex should result in improved ventilatory support. A related question is whether the involvement of bronchopulmonary receptors in the inspiratory glottal constriction during nIPPV is different in the adult respiratory system or unique to the newborn animal. While the precise sensory pathway has not been tested in adults, it is clear that glottal constriction with nIPPV is not limited to neonatal lambs (3). Assuming that the origin of this response applies to all populations receiving nIPPV, a strategy to
modify it seems a logical next step. Roy et al. did not directly test which particular subset of bronchopulmonary receptors might be stimulated during nIPPV. Nevertheless, they do provide some evidence from this and other studies pointing to the rapidly adapting receptors as the most likely candidates. In the face of growing popularity of nIPPV, the sensory pathways of the glottal constrictive response should be elucidated in order to develop a pharmacological approach to improve the effectiveness of nIPPV. If we go past the immediate clinical relevance in terms of improvement of ventilation during nIPPV, a red flag comes up immediately: is inspiratory glottal constriction a significantly greater problem during nIPPV in patients with conditions such as sleep apnea where upper airway patency is already compromised? Furthermore, is this reflex affected by the disease processes that led to the need for nIPPV in the first place? These are just the most obvious questions whose answers are likely to change the clinical application of nIPPV.

Finally, the authors raise an intriguing issue by suggesting that inspiratory activation of the thyroarytenoid muscle during nIPPV (decreasing glottal size) protects the lungs from overinflation. What are the lungs telling us about our current approach to nIPPV? Is it possible that typical ventilatory settings are just too harsh, and the lungs are crying “uncle” via the bronchopulmonary receptors? In other words, is “inappropriate” glottal narrowing during the inspiratory phase of nIPPV a sign of lung overinflation? We should remember that nIPPV only decreases the incidence of airway and lung damage, it does not completely prevent it. Clinically, the fine-tuning of nIPPV for optimal ventilatory support with minimal pulmonary and cardiovascular consequences remains a complicated art. Roy et al. present the basic approach to turn it into a science.
REFERENCES


