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EDITORIAL

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Nasal CPAP in preterm infants – does it work and how?

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The application of continuous distending pressure to the upper airways has become an increasingly popular technique not only in adult but also in paediatric and neonatal respiratory medicine. In 1971, Gregory et al. were the first to report the application of CPAP to treat premature infants with respiratory distress syndrome (RDS) [1]. It was welcomed as the missing link in the hot-tempered debate whether minimal handling and oxygen supplementation or intubation and mechanical ventilation offers the best therapeutic approach to the very premature infant with RDS [2].

The conclusive randomised controlled trial to verify the benefit of early CPAP application in preterm infants is still missing. Previous studies suggest that nasal CPAP is associated with benefits in terms of reduced respiratory failure and reduced duration and invasiveness of respiratory support; without worsening other standard measures of neonatal outcome [3, 4, 5, 6]. Nasal CPAP seems effective in preventing failure of extubation [7, 8] and is used in the treatment of obstructive sleep apnoea in preterm infants [9].

A variety of different interfaces such as nasal prongs, nasopharyngeal tube, endotracheal tube or face mask are currently used to deliver CPAP via either continuous or variable gas flow systems. The few comparative studies of nasal CPAP modalities report conflicting results regarding whether one technique is superior to the other [10]. Non-invasive ventilatory modes such as synchronised nasal intermittent positive pressures ventilation add further options to support the respiration of preterm infants. This diversity in technology makes it nearly impossible to compare results from previous clinical trials. Future trials will have to delineate which technique offers the best non-invasive mode of ventilatory support in this age group.

The physiological mechanisms by which nasal CPAP improves respiration in neonates are not thoroughly understood. Prior to discussing possible effects of applying a positive distending pressure to the upper airways, the developmental changes that occur in chest wall and upper airway mechanics need to be understood. The very compliant chest wall places the preterm infant at a mechanical disadvantage during respiration. This explains the paradoxical inward rib cage motion caused by the negative pleural pressure necessary for inspiration, which is observed even in the absence of lung disease. The highly compliant chest wall also results in a static FRC that is decreased to a level at which airway closure, atelectasis, and ventilation/perfusion mismatch occur. In response, the infant employs several strategies to actively elevate FRC above the relaxation volume. All these mechanisms cause intrinsic PEEP and involve: a) tonic activity of the diaphragm throughout the respiratory cycle; b) a high respiratory rate and premature termination of the expiratory phase; and c) laryngeal breaking or glottic closure during expiration. It is evident that positive pressure applied at the mouth will help to support the infant's constant effort to actively elevate its FRC. Physiological studies suggest that CPAP, by increasing end-expiratory lung volume, stabilises the highly compliant chest wall thereby improving pulmonary mechanics and thoracoabdominal asynchrony [11, 12, 13].

Conversely, thoracoabdominal asynchrony is also a recognised breathing pattern of upper airway obstruction [14]. The benefit of nasal CPAP on upper airway re-

spiratory mechanics may not be overlooked. Increased flexibility of the epiglottis and the laryngeal cartilage together with decreased connective tissue support of the upper airway structures predispose the infant to partial and complete upper airway obstruction during tidal breathing [15, 16]. Anatomical differences such as the cephalad position of the larynx further increase the proportion of the upper airway resistance to total respiratory resistance in infants. Miller and colleagues demonstrated that CPAP produced a decrease in total supraglottic resistance during both inspiration and respiration in preterm infants[17]. They speculated that this decrease resulted from mechanical splinting of the upper airway. In support of this notion, it has also been shown that CPAP increases the width of the compliant laryngeal opening and decreases the collapsibility of the lateral pharyngeal wall by acting as a pneumatic strut [18, 19, 20].

By means of respiratory inductance plethysmography (RIP), Elgellab et al. report in this issue of *Intensive Care Medicine* [21], that nasal CPAP decreases thoracoabdominal asynchrony and increases tidal volume and FRC in preterm infants. The relative contribution of the decrease in upper airway resistance to the overall effect of CPAP on thoracoabdominal asynchrony remains unclear. The finding that CPAP increases the end-expiratory lung volume level is a logical consequence of applying constant pressure to the respiratory system. RIP can be used to trace changes that occur in the end-expiratory lung volume level. These values, however, do not equate to an absolute level of FRC and the validity of any changes in FRC hold only when the body posture is fixed during such measurements. Nevertheless, RIP offers a promising non-invasive tool to assess the benefit of CPAP treatment at the bedside.

One major goal of respiratory therapy is to restore the patients to normal FRC. It is unclear how much CPAP is necessary to restore premature infants to "normal" or "best" FRC. Interestingly, Elgallab et al. [21] found a continuous improvement of all respiratory parameters by increasing CPAP stepwise in a random order from 0 to 8 cmH_2O. The authors need to be congratulated for their attempt to titrate CPAP by means of a physiological respiratory measurement. They demonstrate that CPAP up to 8 cmH_2O is safe in preterm infants. This is higher than what many neonatologists would dare to apply. The clinical determination of an adequate level of CPAP is typically based upon blood gas values and physical examination. Excessive amount of CPAP may be deleterious by increasing the work of breathing and causing a fall in tidal volume, beside the negative cardiovascular effect and the risk of barotrauma. Further studies should aim to delineate the safety level of nasal CPAP in preterm infants and establish a non-invasive method that allows us to determine and monitor the individual best CPAP. Despite its clear limitation, RIP may provide the means for a continuous non-invasive assessment of CPAP treatment. Whether the technique is useful in detecting CPAP failure needs to be evaluated.

In conclusion, many questions with respect to nasal CPAP therapy in preterm infants remain unresolved. CPAP improves thoracoabdominal asynchrony by increasing FRC and chest wall stability, but also by decreasing upper airway collapsibility and decreasing upper airway resistance. The relative contribution of the various physiological mechanisms to the overall benefit of CPAP support is unclear. Further research is required to determine the best mode of administration and to define its role in the modern neonatal intensive care setting. Methods are desired that allow titration to the individual best CPAP and help to predict failure of CPAP treatment. The work presented in this issue [21] is a promising first step in the direction of non-invasive CPAP monitoring.

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