Respiratory medicine

Respiratory support of infants with bronchiolitis related apnoea: is there a role for negative pressure?

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Commentary on the paper by Al-balkhi *et al* (see page 288)

Negative pressure ventilation is not new. Indeed the first practical ventilator for human subjects was the iron lung designed in the late 1920s to provide ventilatory assistance to patients with poliomyelitis.[1] However, negative pressure ventilation has been largely superseded by developments of positive pressure ventilation equipment and techniques, including non-invasive positive pressure ventilation. In this issue of the journal, Al-balkhi and colleagues suggest a role for negative pressure ventilation in the treatment of infants with apnoea associated with bronchiolitis.[2] So is negative pressure ventilation on the brink of a comeback or should it be properly consigned to history?

Negative pressure ventilation (NPV) relies on the application of a subatmospheric pressure to the thorax, which is transmitted to a reduction of intrapleural pressure, leading to expansion of the lungs. By cycling the pressure and allowing passive deflation of the lungs as the negative intrapleural pressure rises, alveolar ventilation can occur. Advantages of negative pressure ventilation include avoidance of the adverse effects of endotracheal intubation and positive pressure ventilation. The patient's airway may be accessed readily during NPV for diagnostic or therapeutic procedures such as suctioning of secretions or fibreoptic bronchoscopy. There is also a beneficial effect on cardiac output, probably related to increased systemic venous return, although this effect may only apply when negative pressure is applied to the thorax alone using a cuirass or wrap rather than to the entire body surface as occurs with a tank ventilator.[3] Negative pressure ventilation has been successfully applied to the treatment of children after cardiac surgery, particularly total cavo-pulmonary connection (Fontan)[4] or correction of tetralogy of Fallot.[5] Potential problems associated with NPV include augmentation of upper airway obstruction in patients with abnormalities of the extrathoracic airway or bulbar dysfunction and the possibility of reflux and aspiration associated with dynamic effects on the lower oesophageal sphincter.[6]

Studies of the role of negative pressure ventilation in acute respiratory disorders in adult patients have focused on clinical outcomes in acute respiratory failure associated with chronic obstructive pulmonary disease (COPD) or neuromuscular disorders. These were recently reviewed by Corrado and Gorini.[7] In adults with COPD, a number of uncontrolled studies have reported short term improvements in gas exchange, but the significance of these physiological changes to clinical outcomes is uncertain. A controlled study of NPV compared with conventional ventilation in adults with COPD reported no significant differences in mortality but a reduction in duration of ventilation in patients treated with NPV.[8] A comparison of two different modalities of non-invasive ventilation (NPV and non-invasive positive pressure ventilation) reported similar proportions that needed rescue invasive ventilation and no significant difference in mortality between treatment groups. However, patients treated with NPV had significantly shorter duration of ventilation and length of hospital stay.[9] Therefore, there are data from the adult literature to suggest a beneficial effect of NPV on physiological and clinical outcomes in acute on chronic respiratory failure associated with COPD. However, this is a very different population from infants and young children with acute respiratory failure. In the paediatric population, negative pressure ventilation has been reported to be effective in the management of neonatal acute respiratory distress syndrome in uncontrolled[10 11] and controlled studies.[12 13] Samuels and Southall have previously reported short term reductions in oxygen requirements of infants and young children with respiratory failure due to a variety of causes who were treated with NPV[14] and, in a randomised controlled trial of treatment of neonatal respiratory distress syndrome, Samuels and colleagues reported that continuous negative extrathoracic pressure (CNEP) reduced the need for endotracheal intubation and its subsequent pathophysiological consequences of prolonged oxygen requirement and chronic lung disease compared with standard therapy.[15] Outside the neonatal age group, there are few published randomised controlled studies of the use of NPV in the treatment of acute respiratory failure. A recent Cochrane systematic review identified one study, published in abstract form only, that met adequate methodological criteria.[16 17] This study reported short term reduction in oxygen requirements in a proportion of infants with bronchiolitis treated with CNEP. However, the Cochrane systematic review concluded that there was insufficient evidence on which to judge the effectiveness of CNEP. The authors reached the same conclusion about non-invasive continuous positive airway pressure (CPAP) treatment of children with acute hypoxaemic respiratory failure. The apparent lack of a sound evidence base for this commonly applied treatment modality is perhaps surprising. A non-randomised study has reported short term improvements in physiological variables in infants with bronchiolitis and ''impending respiratory failure'' treated with CPAP,[18] but there has been no systematic evaluation of this treatment in the paediatric age group.

So what does the study by Al-balkhi and colleagues add? The entry criterion was bronchiolitis related apnoea, a common reason to consider ventilator assistance in infants but one about which relatively little is understood in terms of its mechanisms. It is suggested that respiratory syncytial virus (RSV) may augment laryngeal chemoreceptor responses[19] and similarities exist between reflex laryngeal apnoea, apnoea of prematurity, and that associated with RSV.[20] Alternatively the association of RSV related apnoeas with preterm infants or those of young postnatal age points to effects on immature respiratory control mechanisms.[21] Apnoeas tend to occur early in the course of RSV bronchiolitis and have been reported to be associated with a significant risk of mechanical ventilation, with the relative risk increasing from 2.4 for one apnoea to 6.5 for multiple apnoeas in one large study.[22] Therefore, the study population appears to be appropriate to the question posed. The retrospective design of this study and the relatively small number of subjects studied were limitations acknowledged by the authors, and the absence of key data, such as gas exchange at entry, makes true comparison of disease

severity between the study populations difficult. Although ''standard'' treatment was used in both study centres, there was a significant difference in the proportions of infants treated with methylxanthines. Methylxanthines have been reported to increase diaphragmatic contractility[23] and a combined effect of this with the inhibition of inspiratory muscle activity by NPV[24] on efficiency of ventilation cannot be discounted, in addition to the reported effects of caffeine on RSV related apnoea cited by the authors.[25] However, the authors have not been extravagant in their claims for negative pressure ventilation in this context and have produced some interesting, although preliminary findings. Their call for a prospective randomised controlled trial of respiratory support strategies in the treatment of bronchiolitis related apnoea is reasonable. The design of such a study should include clinically important as well as physiological outcomes.[26] However, given the well publicised curtailment of activities of one of the principal research active groups in this field, it may be some time before such a trial sees the light of day.

Where does this leave the clinician caring for an infant with bronchiolitis and clinically significant apnoeas? Despite the lack of evidence from randomised control trials, it would appear that non-invasive respiratory support offers the potential advantage of avoiding endotracheal intubation, at least for some infants. The majority of institutions caring for infants and young children with critical respiratory illnesses will have access to equipment and expertise for the delivery of non-invasive CPAP and/or bilevel positive airway pressure (BiPAP). Until further evidence becomes available, this modality is likely to remain the first choice therapeutic intervention for infants with bronchiolitis related apnoea.

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REFERENCES

1 **Drinker PA**, McKhann CF. Landmark perspective: The iron lung. First practical means of respiratory support. *JAMA* 1986;**255**:1476–80.
2 **Al-balkhi A**, Klonin H, Marinaki K, *et al*. Review of treatment of bronchiolitis related apnoea in two centres. *Arch Dis Child* 2005;**90**:288–91.
3 **Lockhat D**, Langleben D, Zidlka A. Hemodynamic differences between continuous positive and two types of negative pressure ventilation. *Am Rev Respir Dis* 1992;**146**:677–80.
4 **Shekerdemian LS**, Bush A, Shore DF, *et al*. Cardiorespiratory interaction after Fontan operations: augmentation of cardiac output using negative pressure ventilation. *Circulation* 1997;**96**:3934–42.
5 **Shekerdemian LS**, Bush A, Shore DF, *et al*. Cardiorespiratory responses to negative pressure ventilation after tetralogy of Fallot repair: a hemodynamic tool for patients with a low-output state. *J Am Coll Cardiol* 1999;**33**:549–55.
6 **Marino WD**, Pitchumoni CS. Reversal of negative pressure ventilation-induced lower esophageal sphincter dysfunction with metoclopramide. *J Gastroenterol* 1992;**87**:190–4.
7 **Corrado A**, Gorini M. Negative pressure ventilation: is there still a role? *Eur Respir J* 2002;**20**:187–97.
8 **Corrado A**, Gorini M, Ginanni R, *et al*. Negative pressure ventilation versus conventional mechanical ventilation in the treatment of acute respiratory failure. *Eur Respir J* 1998;**12**:519–25.
9 **Corrado A**, Confalonieri M, Marchese S, *et al*. Iron lung versus mask ventilation in the treatment of acute on chronic respiratory failure in COPD patients: a prospective randomised controlled study. *Chest* 2002;**121**:189–95.
10 **Outerbridge EW**, Roloff DW, Stern L. Continuous negative pressure in the management of severe respiratory distress syndrome. *J Pediatr* 1972;**81**:384–91.
11 **Alexander G**, Gerhardt T, Brancalari E. Hyaline membrane disease. Comparison of continuous negative pressure and nasal positive airway pressure in its treatment. *Am J Dis Chest* 1979;**133**:1156–9.
12 **Fanaroff AA**, Cha CC, Sosa R, *et al*. Controlled trial of continuous negative external pressure in the treatment of severe respiratory distress syndrome. *J Pediatr* 1973;**82**:921–8.
13 **Silverman WA**, Sinclair JC, Gandy GM, *et al*. A controlled trial of management of respiratory distress syndrome in a body-enclosing respirator. I. Evaluation of safety. *Pediatrics* 1967;**39**:740–8.
14 **Samuels MP**, Southall DP. Negative extrathoracic pressure in the treatment of respiratory failure in infants and young children. *BMJ* 1989;**299**:1253–7.
15 **Samules MP**, Raine J, Wright T. Continuous negative extrathoracic pressure in neonatal respiratory failure. *Pediatrics* 1996;**98**:1154–60.
16 **Shah PS**, Ohlsson A, Shah JP. Continuous negative extrathoracic pressure or continuous positive airway pressure for acute hypoxemic respiratory failure in children (Cochrane review). In: *The Cochrane Library*, Issue 1. Chichester: John Wiley & Sons, 2004.
17 **Hartman H**, Noyes JP, Wright T, *et al*. Continuous negative pressure ventilation in infants with bronchiolitis. *Eur Respir J* 1994;**S18**:379.
18 **Soong WJ**, Hwang B, Tang RB. Continuous positive pressure by nasal prongs in bronchiolitis. *Pediatr Pulmonol* 1993;**16**:163–6.
19 **Lindgren C**, Grogaard J. Reflex apnoea response and inflammatory mediators in infants with respiratory tract infection. *Acta Paediatr* 1996;**85**:798–803.
20 **Pickens DL**, Schefft GL, Storch GA, *et al*. Characterization of prolonged apneic episodes associated with respiratory syncytial virus infection. *Pediatr Pulmonol* 1989;**6**:195–201.
21 **Church NR**, Anas NG, Hall CB, *et al*. Respiratory syncytial virus-related apnea in infants. Demographics and outcome. *Am J Dis Child* 1994;**138**:247–50.
22 **Kneyber MCJ**, Brandenburg AH, de Groot R, *et al*. Risk factors for respiratory syncytial virus associated apnoea. *Eur J Paediatr* 1998;**157**:331–5.
23 **Aubier M**, Murciano D, Viires N, *et al*. Diaphragmatic contractility enhanced by aminophylline: role of extracellular calcium. *J Appl Physiol* 1983;**54**:460–4.
24 **Gleran J-C**, Jounieaux V, Parreira VF, *et al*. Effects of intermittent negative pressure ventilation on effective ventilation in normal awake subjects. *Chest* 2002;**122**:99–107.
25 **Tobias JD**. Caffeine in the treatment of apnea associated with respiratory syncytial virus infection in neonates and infants. *South Med J* 2000;**93**:294–6.
26 **Randolph AG**, Meert KL, O'Neil ME, *et al*. The feasibility of conducting clinical trials in infants and children with acute respiratory failure. *Am Rev Respir Crit Care Med* 2003;**167**:1334–40.