Role of automation in neonatal respiratory support

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Abstract
Premature infants frequently present with respiratory instability, which is associated with fluctuations in ventilation and gas exchange. Adjustment of respiratory support to the infant’s needs is limited by staff availability and workload. Hence, automation is being explored as a way to improve the care of the premature infants. New modes of automatic respiratory support are being developed and becoming available for clinical use in preterm infants. These modes are expected to compensate for some of the limitations that presently exist in the conventional forms of respiratory support. Available evidence and preliminary findings are promising, but further investigation is needed to determine the effects of these modalities on the long-term outcome of preterm infants.

Keywords: Automatic; closed loop; mechanical ventilation; premature; supplemental oxygen.

Introduction
Mechanical ventilation and oxygen supplementation are essential tools to maintain adequate gas exchange in newborn infants in respiratory failure. The need for these forms of respiratory support can be protracted, particularly in premature infants of shorter gestational ages. Unfortunately, because of their immaturity and fragility, many of these premature infants also experience the side effects of prolonged ventilatory support and oxygen supplementation. Premature infants frequently present with respiratory instability, which leads to variability in ventilation and gas exchange. In addition to the underlying lung disease, this is largely attributed to immaturity of the respiratory control mechanisms and low and unstable functional residual capacity due to their highly compliant chest wall and insufficient surfactant. Although clinical teams frequently adjust the support to match the infant’s needs, their workload limits time availability and makes continuous tailoring of the support to the infant’s needs difficult. Automation is being explored as a way to improve the care of the premature infant who requires respiratory support. This is a review and discussion of the currently available evidence and preliminary findings of automated modalities of neonatal respiratory support. The objectives of this review are to discuss the potential advantages and identify the areas where further investigation is needed to determine the effects of automation on the long-term outcome of preterm infants. The current and possible future applications of automation in neonatal respiratory support are discussed below.

Automation in mechanical ventilation
In conventional mechanical ventilation, ventilator settings are adjusted manually based on blood gas values and monitored parameters of ventilation. Because of the infant’s respiratory instability, ventilatory settings are often set to provide greater support than that actually needed by the infant to assure adequate ventilation at all times. This leads to periods of excessive support that delay weaning from the ventilator.

Automated modes of ventilatory support have been developed to maintain specific parameters of ventilation, such as tidal volume or minute ventilation at a target level by continuous adjustments of peak pressure, ventilator frequency, or both. The goal of these automated modes of ventilation is to achieve a balance between adequate ventilation and the risk of ventilator-associated lung injury due to excessive ventilatory support. Although maintaining a specific arterial blood gas status level is the ideal goal, unavailability of arterial blood gas data on a continuous basis requires the use of surrogates, such as tidal volume and minute ventilation targets.

Automatic adjustment of peak pressure with tidal volume as target
In volume-targeted ventilation, the peak inspiratory pressure applied to the airway is automatically adjusted to maintain a target tidal volume ($V_T$) selected by the clinician. These adjustments, which generally occur in response to changes in respiratory system mechanics and the infant’s own inspiratory effort, maintain more stable ventilation and hence gas exchange. There is evidence that volume-targeted ventilation can reduce $V_T$ variability, the occurrence of hypocapnia, and fluctuations in oxygenation when compared with conventional pressure-limited ventilation [4, 5, 18, 19, 23].

Automatic reduction of the ventilator peak inspiratory pressure can play an important role during the weaning process.
as the infant’s lung function and inspiratory effort improve. Volume-targeted ventilation has been shown to be effective in accelerating weaning in premature infants [12, 22, 26, 27]. Although this faster weaning and shorter course of ventilation has not consistently improved long-term respiratory outcome, a meta-analysis showed improvements in the combined outcome of death or bronchopulmonary dysplasia (BPD) as indicated by a reduction in the relative risk of 0.73 (0.57–0.93) compared with pressure-limited ventilation [31].

These potential advantages of volume-targeted ventilation in the care of the ventilated premature infant are important, and an increasing number of centers are adopting its use. The role of volume-targeted ventilation will be better defined when additional information on the most appropriate target $V_t$ for infants of different gestation and respiratory status is available as well as on the individual roles and/or differences between the various modalities of volume target ventilation (see Table 1).

### Automatic adjustment of ventilator frequency with minute ventilation as target

Automatic adjustment of the ventilator frequency to maintain a selected minute ventilation level is aimed at reducing the level of support during periods when the contribution of the infant’s spontaneous breathing to minute ventilation is sufficient or to increase the ventilator frequency when this is not sufficient to maintain the target ventilation level. Targeted minute ventilation was shown to be effective in reducing the average ventilator frequency by approximately 50% in preterm infants recovering from respiratory distress syndrome (RDS) [9] and in near-term infants without lung disease [15]. At times however, the ventilator frequency was automatically increased to maintain the target minute ventilation during periods of central apnea or when changes in respiratory mechanics resulted in reductions in $V_t$ and minute ventilation.

Methods consisting of a combined adjustment of peak pressure and frequency to simultaneously target tidal volume and minute ventilation [10] and the adjustment of the ventilator frequency in response to fluctuations in arterial oxygen saturation [17] are interesting future applications for automation of respiratory support. Although the current role of targeted minute ventilation in the care of preterm infants is not extensive and can be considered experimental, its use is likely to grow as new data become available (see Table 1).

#### Proportional assist ventilation and neurally adjusted ventilatory assist

Proportional assist ventilation (PAV) is a mode where the ventilator supplements the infant’s respiratory effort to overcome obstructive or restrictive loads associated with lung disease. In PAV, the pressure is automatically adjusted in proportion to the measured tidal volume, flow, or both. PAV has been shown to be effective in reducing inspiratory effort and improving ventilation with lower pressures compared with conventional modes in infants recovering from RDS or with evolving chronic lung disease [24, 25].

In neurally adjusted ventilatory assist (NAVA), the ventilator pressure is automatically adjusted in proportion to the electrical activity of diaphragm, which is used as indicator of the infant’s respiratory center output. This is being proposed as a way to boost the infant’s ability to generate $V_t$, reduce the diaphragm’s activity, or both, depending on the infant’s condition. NAVA was shown to maintain similar ventilation and gas exchange with lower pressures and better synchrony between the infant and the ventilator compared with conventional ventilation in preterm infants but without a significant reduction in diaphragmatic activity [1].

Currently, available data on PAV and NAVA indicate short-term benefits, but further research is needed to fully assess the effects of these modalities on long-term pulmonary outcomes (see Table 1).

#### Automated control of inspired oxygen: targeting arterial oxygen saturation

Preterm infants receiving supplemental oxygen spend considerable time with arterial oxygen saturation ($\text{SpO}_2$) above and below the clinically intended range [16]. This is largely influenced by the infant’s respiratory instability and limitations in staff availability to make frequent adjustments [11, 28]. Because of the increased risk of eye, lung, and central

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**Table 1** Effects of automatic modes of respiratory support.

<table>
<thead>
<tr>
<th></th>
<th>Volume-targeted ventilation</th>
<th>Targeted minute ventilation</th>
<th>PAV</th>
<th>NAVA</th>
<th>$\text{SpO}_2$ targeting by automatic control of $\text{FiO}_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td>$\downarrow V_t$ variability</td>
<td>$\downarrow$ Mandatory breaths</td>
<td>$\downarrow$ Breathing effort</td>
<td>$\uparrow$ Synchrony</td>
<td>$\uparrow$ Time in target $\text{SpO}_2$</td>
</tr>
<tr>
<td></td>
<td>$\downarrow$ Hypocapnia</td>
<td>$\downarrow$ Peak pressure</td>
<td>$\downarrow$ Oxygen exposure</td>
<td>$\downarrow$ Peak pressure</td>
<td>$\downarrow$ Severe hypocapnia and respiratory failure</td>
</tr>
<tr>
<td></td>
<td>$\downarrow$ Severity of hypoxia spells</td>
<td></td>
<td>$\downarrow$ Synchrony</td>
<td>$\downarrow$ Oxygen exposure</td>
<td>$\downarrow$ Severe hypoxia spells</td>
</tr>
<tr>
<td></td>
<td>$\downarrow$ Risk of death or BPD</td>
<td></td>
<td></td>
<td></td>
<td>$\downarrow$ Staff workload</td>
</tr>
<tr>
<td><strong>Areas requiring further exploration</strong></td>
<td>$\bullet$ Optimal target $V_t$</td>
<td>$\bullet$ Optimal minute ventilation target</td>
<td>$\bullet$ Effect on respiratory outcome</td>
<td>$\bullet$ Effect on respiratory outcome</td>
<td>$\bullet$ Effects on mortality and respiratory, ophthalmic and neurologic outcome</td>
</tr>
</tbody>
</table>
|                      | $\bullet$ Advantages of individual modalities | $\bullet$ Effect on respiratory outcome |                           |                           | $\bullet$ Optimal range of $\text{SpO}_2$ |}
nervous system injury, one of the most important concerns is the exposure to hyperoxemia, which, in preterm infants with lung disease, results from the administration of excessive inspired oxygen. Although maintenance of SpO₂ targets can be improved by increased attentiveness [14], uninterrupted attention and frequent manual adjustments are difficult to achieve without increases in workload.

Systems for automatic adjustment of the fraction of inspired oxygen (FiO₂) to maintain a target SpO₂ have been developed. Their goals are to improve the maintenance of a desired SpO₂ range and reduce oxygen exposure. This is achieved by timely adjustments of FiO₂ in response to fluctuations in SpO₂ out of a preset target range. This approach has been shown to be as effective or better than conventional care in maintaining SpO₂ within target in premature infants [2, 3, 7, 8, 13, 20, 21, 29, 30]. This was also true among infants with very frequent fluctuations in SpO₂ who represent the most challenging population for the clinical staff [6]. In these infants, the proportion of time within the target range of SpO₂ (87%–93%) increased from 32 to 40%. Because nursing staff often maintain a higher oxygenation in an attempt to prevent hypoxemia during manual control, automatic FiO₂ control was most effective in reducing hyperoxemia. This was demonstrated by a reduction in the proportion of time with SpO₂ above the range (>93%) from 37% to 21% and in the proportion of time in the highest range of SpO₂ (>98%) from 5.6 to 0.7%. This was accompanied by decreased exposure to oxygen as shown by a reduction in the median FiO₂ from 0.37 to 0.32.

An additional consequence of automatic FiO₂ control was a considerable reduction in staff workload that was a consistent finding in these studies. This was quite striking among infants who present with very frequent episodes of hypoxemia where the reduction in the number of manual adjustments of FiO₂ decreased from 112 to 10 per day [6]. This reduction may be an important benefit because it may allow redirection of staff effort to other aspects of care. However, automated control of FiO₂ could potentially lead to reduced attentiveness. Hence, the use of automatic control of FiO₂ still requires vigilance of the adequacy of ventilation to avoid situations where a higher FiO₂ masks a condition that could otherwise result in hypoxemia, e.g., hypoventilation or decreased lung volume. Although this limitation is at this time speculative, careful application of these systems is recommended along with the use of built-in warnings of increased baseline FiO₂ or decreased ventilation.

At present, an important consideration with manual or automatic FiO₂ control in preterm infants is the target range of SpO₂ to be used clinically. Caution is recommended because the optimal range of SpO₂ has not been clearly defined in preterm infants. It is possible that important beneficial or detrimental effects of different target ranges of SpO₂ may exist or become more apparent when such ranges are kept more effectively with automation than what is achieved under routine care.

Available data indicate the potential advantages for automatic control of FiO₂ resulting from an improved maintenance of the target SpO₂ range, reduced hyperoxemia, and less oxygen exposure. The benefits or disadvantages of SpO₂ targeting by automatic control of FiO₂ on mortality and long-term respiratory, ophthalmic, and neurologic outcome still need to be examined (see Table 1).

References

The system for automatic adjustment of inspired oxygen discussed here was developed and patented by Drs. Claure and Bancalari, who are Faculty of the University of Miami. The University of Miami, the assignee for this patent, has a licensing agreement with CareFusion. CareFusion provided research support for the studies with this system.

The authors stated that there are no conflicts of interest regarding the publication of this article.