Volume controlled ventilation in clinical practice: are the results comparable to those from a randomised controlled trial?

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Abstract

Objective: To determine if the advantages of Volume Controlled Ventilation (VCV) seen in randomised controlled trials (RCTs) are reproducible in daily clinical practice. Design: Hospital-based retrospective cohort study. Setting: James Cook University Hospital. Participants: Infants born between February 2008 and September 2009 with gestational age 24-31 weeks, weight 600-1500 g and diagnosis of respiratory distress syndrome for which they received VCV. Outcome measures: Total duration of mechanical ventilation, survival to discharge and frequency of bronchopulmonary dysplasia (BPD) were compared between the study cohort and the cohort treated with VCV in 2002-2004 RCT. Results: There was no statistically significant difference in the main outcome measures between the two cohorts (duration of ventilation: 171 hours versus 216 hours; p = 0.425, survival: 89.7% versus 91.2%; p = 1.00 and frequency of BPD 27.6% versus 28.1%; p = 1.00). Conclusion: The efficacy and safety of VCV in very preterm low birth weight babies can be maintained in routine clinical practice.

Key words: pre-term, neonate, ventilation

Introduction

Volume Controlled Ventilation (VCV) is a relatively new modality of ventilation in neonatal intensive care. In VCV the clinician selects a volume of gas to be delivered to the patient, while the ventilator pressure is automatically adjusted to deliver this volume [1]. Theoretically, this should result in a more consistent delivery of tidal volume and reduce the chances of “volutrauma” which is considered to be a major component of Ventilator Induced Lung Injury (VILI) [2, 3].

Indeed, a recently published meta-analysis of randomized controlled trials on volume targeted modes of ventilation confirmed the potential advantages of these modes over traditional Pressure Limited Ventilation in terms of reducing the duration of ventilation [Mean Difference 2.36] and its associated complications i.e. death or bronchopulmonary dysplasia (BPD), pneumothorax and periventricular leucomalacia (PVL) or grade 3-4 intraventricular haemorrhage (IVH) in very preterm and low birth weight babies [4].

Two trials included in this meta-analysis were conducted on our units and demonstrated significant reductions in weaning time and duration of intubation and ventilation in babies who weighed between 600 and 1000 g and had received VCV as a primary mode of ventilation compared to those treated with traditional Time Cycled Pressure Limited (TCPL) mode of ventilation [5, 6]. During these studies, the assigned mode of ventilation was conducted according to a strict ventilatory management protocol specifically designed for the study.

In light of this evidence our unit policy was changed and following a cross-over period for teaching and training of medical and nursing staff, VCV replaced PCV in January 2007 as the standard of care for babies who require mechanical ventilation for respiratory failure. The purpose of the present study was to assess generalisability of the findings of the published trials and determine if the results of VCV carried out in context of a rigorous protocol used in randomised controlled trials are reproducible in day to day clinical practice.

Patients and methods

The medical records of infants admitted to the Level 3 Neonatal Unit at James Cook University Hospital, Middlesbrough during an 18-month period between February 2008 and September 2009, were reviewed. Babies born between 24 and 31 weeks’ completed gestation and weighing between 600 and 1500 g with a clinical diagnosis of respiratory distress syndrome (RDS), who had re-
ceived volume controlled ventilation as a primary mode of respiratory support, were included in this study. Infants with severe congenital malformations that affect life expectancy or respiratory outcomes were excluded.

Outcome measures of interest were total duration of mechanical ventilation, survival to discharge from the unit and frequency of BPD (defined as oxygen dependency or receiving any form of mechanical respiratory support at 36 weeks’ postmenstrual age (PMA)). Data was also collected for common neonatal complications associated with prematurity such as IVH, PVL and patent ductus arteriosus (PDA) receiving treatment. All data gathered was pre-existing and recorded so that subjects could not be identified.

The equipment and ventilatory strategy used in clinical practice matched that used in the randomised controlled trial, i.e. VCV in assist/control mode as the initial mode of ventilation changed to Pressure Support Ventilation with Synchronised Intermittent Mandatory Ventilation (SIMV) for weaning. During both stages ventilator variables were set to target an exhaled tidal volume (VTe) of 4-6 ml/kg. This was monitored and adjusted on hourly basis. Target blood gas indices, including a pH 7.25 to 7.40, PaCO₂ 4.5 to 6.5 kPa, and PaO₂ 7 to 10 kPa (50-75 mmHg) were used for initial stage of ventilation. Subsequently PaCO₂ was allowed to rise to 8 kPa (60 mm Hg) if pH remained > 7.20. Once the infants were deemed to be recovering from their acute respiratory illness (PIP < 16 cm H₂O and FiO₂ < 3.0), the ventilatory mode was changed from assist/control to SIMV with pressure support. All babies received caffeine citrate 10 mg/kg prior to extubation and all babies were placed on nasal Continuous Positive Airway Pressure (using pressure of 4 to 6 cm H₂O) for as long as clinically indicated. The remainder of clinical care was according to our unit’s standard protocol.

During the current study period there were no other major changes in our unit management protocol for preterm babies admitted with respiratory failure and routine surfactant replacement therapy was given to all infants requiring ventilation. Data were analysed using SPSS 18.0 software (PASW statistics data editor) with Chi square test and Fishers exact test used for categorical variables and Student’s t-test for continuous data.

Results

Sixty-nine preterm infants meeting the gestational age and weight criteria, and requiring mechanical ventilation for RDS were identified. Eleven were excluded from the analysis, with six having received a combination of pressure and volume ventilation and another five having significant congenital abnormalities deemed to be affecting their respiratory outcome [total anomalous pulmonary venous drainage (TAPVD), tracheo-oesophageal fistula with oesophageal atresia, bilateral multicystic dysplastic kidneys with renal impairment, large ventriculo-septal defect, Downs syndrome]. Thus the study population consisted of fifty-eight infants with mean gestational age of 27 weeks (SD 3.8) and mean birth weight of 1083 g (SD 255). The population in the present cohort was comparable to that treated with VCV in the RCT (Table 1). There were differences however in birth weight, which was higher, and in the number of infants who had received a full course of antenatal steroids, which was lower, in the current study group. There was no difference in gestational age between the groups.

Table 1. Comparison of baseline characteristics of the two groups of infants

<table>
<thead>
<tr>
<th></th>
<th>RCT (n = 57)</th>
<th>Present study (n = 58)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender N (%)</td>
<td>38 (66.7%)</td>
<td>29 (50%)</td>
<td>0.089</td>
</tr>
<tr>
<td>Two doses Antenatal steroids N (%)</td>
<td>44 (77.2%)</td>
<td>33 (56.9%)</td>
<td>0.028</td>
</tr>
<tr>
<td>Ex-utero N (%)</td>
<td>6 (10.5%)</td>
<td>18 (31%)</td>
<td>0.011</td>
</tr>
<tr>
<td>Gestation Mean (SD) weeks</td>
<td>27.1 (2.0)</td>
<td>27.5 (3.8)</td>
<td>0.587</td>
</tr>
<tr>
<td>Birthweight Mean (SD) grams</td>
<td>985 (232)</td>
<td>1083 (255)</td>
<td>0.033</td>
</tr>
</tbody>
</table>

The clinical outcomes of interest i.e. total duration of ventilation and survival to discharge were also similar as was the presence of BPD (defined as oxygen dependency or requirement for respiratory support at 36 weeks’ PMA). There was no statistically significant difference in incidence of complications between the two cohorts, except PDA receiving treatment which was significantly lower in the present cohort (Table 2). Two infants developed pneumothorax, one of which was left-sided following PDA ligation and the other was bilateral but occurred whilst the infant was receiving CPAP prior to being intubated and mechanically ventilated. Four babies had grade III or IV IVH and two had PVL. Seven babies had...
haemodynamically significant PDA receiving medical and/or surgical treatment.

Table 2. Frequency of clinical outcomes in the two groups of babies

<table>
<thead>
<tr>
<th></th>
<th>RCT (n = 57)</th>
<th>Present study (n = 58)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of ventilation Mean (SD) hours</td>
<td>216 (300)</td>
<td>171 (299)</td>
<td>0.425</td>
</tr>
<tr>
<td>Any IVH N(%)</td>
<td>21 (36.8%)</td>
<td>17 (29.3%)</td>
<td>0.432</td>
</tr>
<tr>
<td>Severe IVH N(%)</td>
<td>5 (8.8%)</td>
<td>4 (6.9%)</td>
<td>0.743</td>
</tr>
<tr>
<td>PVL N(%)</td>
<td>2 (3.5%)</td>
<td>2 (3.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>CLD @ 36 weeks N(%)</td>
<td>16 (28.1%)</td>
<td>16 (27.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>PDA N(%)</td>
<td>17 (29.8%)</td>
<td>7 (12.1%)</td>
<td>0.023</td>
</tr>
<tr>
<td>Pneumothorax N(%)</td>
<td>1 (1.8%)</td>
<td>2 (3.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Survival N(%)</td>
<td>52 (91.2%)</td>
<td>52 (89.7%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

SD – standard deviation
IVH – intraventricular haemorrhage
PVL – periventricular leucomalacia
BPD – bronchopulmonary dysplasia
PDA – patent ductus arteriosus

**Discussion**

Randomised controlled trials (RCTs) and systematic reviews provide the most reliable evidence for safety and efficacy of new treatments and have implications for both clinical practice and future research. However, the full benefit of such scientific progress may not be realised if the results of RCTs cannot be generalised or reproduced in day to day clinical practice. This may happen for a variety of reasons; including individual’s own preference, lack of staff training and inability to deal with “trouble shooting” associated with specific mechanical devices. The purpose of our study was to determine if the efficacy and safety of VCV in daily clinical application is similar to that reported in clinical trials using rigorous study protocols.

Although our sample size was small, the data suggest that the efficacy and safety of VCV in very preterm low birth weight babies can be maintained in ongoing clinical practice to the same extent as observed in controlled clinical trials, with similar durations of ventilation and incidence of BPD in the two groups studied. The small difference between the two cohorts in incidence of PDA receiving treatment is unlikely to have significantly influenced our results. It may simply be explained on the basis of change in clinical practice over the time with evidence of treatment benefit being limited, but could also reflect the ability to wean and extubate infants earlier with tendency to treat being when we fail to do so. It is important to note that the trend towards more aggressive weaning from mechanical ventilation that has now become popular in many centres was not adopted in our unit during the study period.

We acknowledge that our study has two main limitations. Firstly, our unit had been using VCV as the primary mode of ventilation for one year at the time the data was collected, which may have given us some advantage in terms of understanding the mechanics of the equipment being used and an improved ability to deal with “trouble shooting”. However there is no good reason to believe that this cannot be done in other neonatal units with provision of appropriate staff training and indeed a recent survey has shown a significant increase in the number of units in the UK using volume target modes of ventilation [7]. Secondly, the retrospective nature of our study and use of historical controls may undermine its strength but there was no other way to answer the question we posed.

Providing data on reproducibility and generalisability of clinical trials can only help towards dissemination and utilisation of evidence-based practices as well as allowing the opportunity for collection of valuable and reliable information in a registry approach in order to generate hypotheses for further trials.

**References**


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