Volume guarantee ventilation in the weaning phase of preterm infants

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KEYWORDS
Volume guarantee; Respiratory distress syndrome; Mean airway pressure; Weaning phase

Abstract

Background: Weaning from mechanical ventilation is a dynamic process influenced by many factors. Volume guarantee is a new option within the patient-triggered modes of ventilation and it can be best described as pressure-limited, continuous flow ventilation with tidal volume guidance or tidal volume targeting.

Objectives: The aim was to assess whether volume guarantee (VG) added before presumed window time of 48 h pre-extubation can help to significantly shorten this window in infants with respiratory distress syndrome (RDS).

Patients and methods: This study was conducted at Al-Azhar University (Damietta, NICU of Pediatric Department) in collaboration with Mansoura Faculty of Medicine, Egypt, between January 2012 and January 2013. Forty ventilated babies were randomly assigned during weaning phase to either VG (group 1) (10 SIMV + VG & 10 PSV + VG); or no VG group 2 (10 SIMV & 10 PSV). All babies were ventilated by Drager Babylog 8000 ventilator due to respiratory distress syndrome (AC or SIMV as initial mode).

Results: Infants randomized to VG group achieved weaning success criteria faster than those randomized to no VG group. Adding VG at the weaning phase resulted in more stable TV, a significant decrease in the mean airway pressure (MAP), oxygenation index, weaning duration, post extubation NCPAP duration and extubation failure. No statistically significant differences were observed in the incidence of pneumothorax, patent ductus arteriosus (PDA), bronchopulmonary dysplasia (BPD), weight gain and neonatal sepsis.

Conclusion: Volume guarantee seems to be both safe and effective in this group of patients.

Introduction

Weaning from mechanical ventilation is a dynamic process and is influenced, particularly in newborns, by many factors such...
as different stages of lung development, changing status of the underlying lung disease, secondary complications, unique interaction of the neonatal heart and lungs, and the relation between central control of respiratory drive and respiratory muscles.1

Volume guarantee (VG) is a new option within the patient-triggered modes of ventilation and it can be best described as pressure-limited, continuous flow ventilation with tidal volume guidance or tidal volume targeting.2

It has been designed to combine the advantages of pressure-limited ventilation with the advantages of volume-controlled ventilation, without the inherent disadvantages of either of these modalities when used on their own.3

It is intended to allow the clinician to make careful selection of appropriate tidal volumes with which to ventilate the newborn infant while retaining all of the considerable advantages that pressure-limited ventilation affords. The aim is to provide the newborn infant with, on average, much more stable assisted tidal ventilation from breath to breath, free from the perturbations in tidal volume that pressure-limited ventilation alone produces.4

We hypothesized that the addition of VG before presumed window time of 48 h pre-extubation may help to significantly shorten this window by adding more improvement in respiratory status and other outcome variables.

Aim of the work

The aim of this study was to assess whether volume guarantee (VG) added before presumed window time of 48 h pre-extubation can help to significantly shorten this window by adding more improvement in respiratory status and other outcome variables in infants with respiratory distress syndrome (RDS).

Patients and methods

Study design and interventions

This randomized prospective trial was conducted at Al-Azhar University (Damietta Faculty of Medicine, NICU of Pediatric Department) in collaboration with Mansoura Faculty of Medicine, NICU of Pediatric Department, Egypt, between January 2012 and January 2013. The current study comprised 40 ventilated babies who were randomly assigned during weaning phase to either VG group 1 (10 SIMV + VG & 10 PSV + VG); or no VG group 2 (10 SIMV & 10 PSV). All babies were ventilated by Drager Babylog 8000 ventilator due to respiratory distress syndrome (AC or SIMV as initial mode) evidenced by clinical and radiological criteria.

Patients

Infants were deemed eligible if their gestational ages were ≤34 weeks and had respiratory distress syndrome to warrant assisted mechanical ventilation within 72 h of delivery and they were expected to be extubated within 48 h due to stable blood gases & O2 saturation with low ventilatory parameters. Babies with Endotracheal tube leakage > 30% (as accurate determination of tidal volumes may be compromised); major congenital anomalies; congenital heart disease; pneumothorax; neonatal sepsis or meconium aspiration syndrome were excluded.

Ventilation strategies

The initial modes of ventilation for all infants were A \ C or SIMV mode. However during weaning phase (48 h before extubation) they were switched to VG group 1 (10 SIMV + VG & 10PSV + VG) or no VG group 2 (10 SIMV & 10 PSV). In VG group the VT was set around 5 ml/kg and the PIP limit was set at 15–20% above the average PIP needed to achieve the target VT. In no VG group the PIP limit was set to obtain TV around 5 ml/kg. The ventilator parameters were decreased during the weaning phase guided by each infant’s blood gases and clinical status. Our department protocol of weaning is (FiO2 < 0.4, PIP 10–12 and or to achieve TV 5 ml/kg, rate ≤ 20, PEEP 4–5 and flow of 6–8 L/min). Blood gases’ analysis was measured at 1st and 4th hour after randomization, and then at 4–6 h intervals or more often as needed.

Success outcome criteria for this trial consisted of arterial blood pH 7.25–7.35, PaCO2 45–55 mmHg, PaO2 50–70 mmHg, target FiO2 to maintain SpO2 88–95%, MAP < 8.0 cm H2O and oxygenation index < 10. If successful (> 12 h) extubation occurred. Those babies were extubated to NCPAP.

The reintubation criteria, extubation failure, were the same in both groups, and included at least one of the following: pH < 7.25 and PCO2 > 60 mmHg, SpO2 < 88% on FiO2 > 60%, more than two episodes of apnea/h (defined as cessation of breathing for 20 or <20 s if associated with cyanosis and/or bradycardia) or any episode of apnea that did not respond to tactile stimulation and required bag and mask ventilation.

Data acquisition and analysis

In this trial we compared the mean values of (FiO2, PIP, MAP, TV and ABG) which were recorded at the start of the trial (weaning phase), every 6 h during the trial, pre extubation and post extubation. All infants were monitored using pulse oximetry and blood pressure measurement.

Outcomes recorded in this trial were classified into Primary outcomes (extubation failure, duration of weaning, post extubation NCPAP duration death in hospital, oxygen at 28 days (BPD)) and Secondary outcomes (failure of ventilatory mode, pneumothorax, PDA, weight gain per week in grams, ventilation and hospitalization days). Maternal and neonatal demographic and clinical characteristics were also recorded.

Statistics

Data were entered, cleaned to identify inconsistencies and statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 16. Qualitative data were described as numbers and percentages. χ2 test or Fisher’s exact test was used for comparison between the two groups, as appropriate. Quantitative data were described as means (SD) or medians, as appropriate. They were tested for normality. In the normally distributed variables, independent sample t-test was used; while in non-normally distributed variables, Mann–Whitney test was used for comparison between the two groups.
Forty infants ventilated for RDS were included in the study. During the weaning phase twenty infants were randomly assigned to VG group 1 and the other twenty to no VG group. There were no significant difference between both groups as regards birth weight, gestational age, infant risk, maternal risk, neopuff usage or surfactant administration as seen in Table 1.

The comparative values of the mean FiO₂, MAP, TV, pH, PCO₂ and PO₂ at the weaning phase, extubation and post extubation were recorded. MAP and O₂ index were significantly lower in VG group. There was no significant difference of pre and post extubation blood gases (pH, PCO₂ & PO₂) between both groups (P > 0.05) apart from pre-extubation PCO₂ which shows significant decrease with VG group 2 (P < 0.05) (see Fig. 1 Table 2).

Many outcomes were recorded in both groups as seen in Table 3. There was a significant decrease in duration of weaning and post-extubation NCPAP duration in VG group (P < 0.05) (see Figs. 2 and 3). Moreover extubation failure and hospitalization days were significantly lower in VG. No differences were observed in the incidence of PDA, post-extubation pneumothorax, BPD and death.

Discussion

We conducted a prospective, randomized study to assess the effect of combining volume guarantee mode with various modes of ventilation during weaning of preterm infants with...
respiratory distress syndrome. Infants randomized to VG group achieved weaning success criteria (arterial blood pH (7.25–7.35), PaCO₂ (45–55 mmHg), PaO₂ (50–70 mmHg), target FiO₂ to maintain SpO₂ (88–95%), MAP < 8.0 cm H₂O and oxygenation index <10) faster than those randomized to no VG group (weaning duration, median 14 h in VG group versus median 24 h in no VG group) with *P* value <0.05. Adding VG at the weaning phase resulted in a significant decrease in the MAP (5.6 ± 0.48 in VG group versus 6.1 ± 0.64 in no VG group) and oxygenation index (6.29 ± 0.98 in VG group versus 7.235 ± 1.44 in no VG group) which agree with previous trials (2, 5, 6, 7). This reduction was highest when VG was combined with PSV. 5

In our study, both groups were well-matched regarding baseline clinical characteristics, birth weight, gestational age, gender, weight for gestational age or maternal risk, resulting in a non-significant difference between both groups. Presence of fetal or maternal may be related to RDS severity and prognosis.6–9

In our study tidal volume is 5 ml/kg in both groups matched with 10–13 who recommend starting VG ventilation with set TV of 4–6 ml/kg. As regards to blood gases’ course during our trial (pH, PCO₂ & PO₂) there was no significant difference between both groups, apart from pre-extubation PCO₂ (31.28 ± 2.9) which showed significant decrease with VG group (*P* < 0.05) due to hyperventilation occurred when the ventilator is triggered with every spontaneous breath especially in infants with strong respiratory drive near extubation, this was in agreement with.14,15 Our result was not in agreement with2 who reported that PaCO₂ was significantly higher in the VG group.

In the present study we found that adding VG during weaning phase leads to a significant reduction of MAP, oxygenation index, weaning duration and post extubation NCPAP duration. These results are in agreement with a meta-analysis of 12 randomized trials with a total of 793 preterm infants.17 Only three of these trials were primarily designed to compare the efficacy and safety of VG and conventional modes in RDS treatment.2,4,18 The combined outcome of death or BPD was included in four trials. 4,11,19,20

No individual trial reported a difference in the combined outcome of death or BPD, but the pooled meta-analysis revealed a reduction in this combined outcome. Recently two long term trials were conducted 12,13 and recorded a significant reduction of BPD in VG group. Our study is a short term study (48 h before extubation) unlike other short term studies (20 min to 4 h).3–5,7,16,17

### Table 3 Important outcomes of the studied patients.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>VG (group 1)</th>
<th>No VG (group 2)</th>
<th><em>P</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of weaning (h)</td>
<td>14</td>
<td>24</td>
<td>0.02 *</td>
</tr>
<tr>
<td>Minimum</td>
<td>12</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>72</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Days of post-extubation NCPAP</td>
<td>1 (5.0%)</td>
<td>6 (30.0%)</td>
<td>0.04 *</td>
</tr>
<tr>
<td>Exubation failure</td>
<td>2 (10.0%)</td>
<td>1 (5.0%)</td>
<td>0.89 (NS)</td>
</tr>
<tr>
<td>Days of ventilation</td>
<td>111.8 ± 32.9</td>
<td>112.1 ± 38.2</td>
<td>0.98 (NS)</td>
</tr>
<tr>
<td>Days of hospitalization</td>
<td>24.2 ± 5.1</td>
<td>30.1 ± 8.1</td>
<td>0.01 *</td>
</tr>
<tr>
<td>PDA</td>
<td>3 (15.0%)</td>
<td>6 (30.0%)</td>
<td>0.46 (NS)</td>
</tr>
<tr>
<td>Post-extubation pneumothorax</td>
<td>2 (10.0%)</td>
<td>1 (5.0%)</td>
<td>0.89 (NS)</td>
</tr>
<tr>
<td>BPD</td>
<td>1 (5.0%)</td>
<td>2 (10.0%)</td>
<td>0.89 (NS)</td>
</tr>
<tr>
<td>Death</td>
<td>3 (15.0%)</td>
<td>3 (15.0%)</td>
<td>1.0 (NS)</td>
</tr>
</tbody>
</table>

* Significant value; NS: non-significant.

**Figure 2** Significant decrease of duration of weaning in VG group.

**Figure 3** Significant decrease of post-extubation NCPAP duration in VG group 1.
In our study BPD was 2 (10%) in group 1 and 1 (5%) in group 2 with no significant difference between both groups, which may be attributed to the small sample size and short interventional period.

One limitation of our study is the small sample size. With the increased use of non-invasive ventilation techniques over the last few years, the use of invasive mechanical ventilation has decreased dramatically, which may be attributed to the small sample size and short duration of ventilation (i.e. <48 h) nor who developed sepsis, which was proved bacteriologically; further reduced the number of eligible patients for our study. The non-significant difference of BPD may be attributed to the small sample size. Lake of tcPCO2 monitor, which measures minute to minute PaCO2 leads to unavoidable low PaCO2 in some patients in pre extubation period.

Conclusion

Our results support the findings of previous studies, which demonstrated the reduction of PIP, MAP, oxygenation index and tidal volume variability in VG group. However in our study weaning duration, post extubation NCPAP duration and extubation failure were recorded and showed significant reduction in the VG group. No statistically significant differences were observed in the incidence of pneumothorax, PDA, BPD, weight gain and neonatal sepsis, but the number of cases of these issues was lower and the duration of the trial was short.

Trials with a larger sample size are needed to derive sufficient power to examine differences in all outcomes. Further investigations with different combined VG modes and different tidal volumes are needed in order to derive more precise instructions for clinical practice. Further studies and long term follow up are needed to identify whether VTV modes improve neurodevelopmental outcomes and to compare and refine VTV strategies.

Conflict of interest

None declared.

References