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Randomised controlled trial of weaning by patient triggered ventilation or conventional ventilation

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Abstract. A group of preterm infants ($n = 40$) were entered into a randomised controlled trial to compare the duration and efficacy of weaning by patient triggered ventilation (PTV) or conventional ventilation. Once recovery from respiratory distress had begun, enabling the ventilator rate to be reduced to 40 breaths/min, infants were randomised to either regime. Infants randomised to PTV were weaned by reduction in ventilator pressure only, whereas infants randomised to conventional ventilation were weaned by reduction in ventilator rate only. Only one infant required re-ventilation within 24 h of extubation; this infant had been weaned by conventional ventilation. Three infants, all of less than 28 weeks gestation, did not tolerate weaning by PTV and were subsequently weaned conventionally. The duration of weaning was analysed according to the original randomisation allocation and was significantly shorter in the PTV group, being a median of 30 h (mean 39, range 3–186) compared to a median of 61 h (mean 65, range 15–262) in the conventional group, $P < 0.02$. We conclude PTV is the more advantageous form of weaning in preterm infants of greater than 27 weeks gestational age.

Key words: Patient triggered ventilation – Respiratory distress syndrome – Mechanical ventilation – Prematurity

Introduction

Use of patient triggered ventilation (PTV) is frequently associated with acute improvements in blood gases [10, 12]. Long-term PTV, however, was not successful in infants less than 28 weeks gestation [11]. PTV also failed more frequently than high frequency positive pressure ventilation to adequately support infants with acute respiratory distress syndrome, even though only infants of greater than 28 weeks gestation were randomised [9]. A modified conventional newborn ventilator delivered PTV in both those studies [9, 11] and, although the optimum triggering device [7] was used in the second study [9], there are concerns regarding the performance of both the ventilator [1] and triggering system [8]. Since those studies [9, 11], new purpose-built patient triggered ventilators have become available which have superior performance as evidenced by a very short trigger delay and increased sensitivity [5, 8].

Postnatal age has an important influence on the outcome of PTV. Failure of long-term PTV is commoner in infants commenced on PTV in the first 48 h of life [6]. In contrast, improvements in oxygenation during PTV, compared to conventional ventilation, are greater during the recovery compared to the acute phase of respiratory distress syndrome [2]. These results suggest that PTV may be most useful during weaning, particularly if one of the new purpose-built ventilators is used [5]. The aim of this study was to test that hypothesis by comparing the duration and efficacy of weaning by PTV or conventional ventilation.

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Abbreviations: bpm = breaths per minute; CPAP = continuous positive airway pressure; PTV = patient triggered ventilation

Patients and methods

Methods

Only infants in the recovery stage of respiratory distress were eligible for this study. Prior to trial entry ventilator rate and pressure were reduced until a rate of 60 breaths/min (bpm) was reached. Subsequently weaning was only by rate reduction while peak pressure was held constant. Reduction in rate from 60 to 40 bpm was achieved by extending the expiratory time, keeping the inspiratory time constant [4]. At 40 bpm all infants were commenced on aminophylline or theophylline (4 mg/kg per day) [3] and were then entered into the study, being randomised for further weaning by either PTV or conventional weaning.

One purpose-built patient triggered ventilator (SLE HV 2000) was available to this study. Infants were only recruited and randomised if this patient triggered ventilator was available. Infants randomised to weaning by PTV were transferred to the SLE HV 2000 on the same ventilator settings as during conventional ventilation. After a 30-min period of stabilisation they were then transferred to the patient triggered mode with the ventilator settings unchanged, except that the inspiratory time was shortened to 0.3–0.4 s [11]. Subsequently, weaning was achieved during patient triggered ventilation by reduction in ventilator pressure only. Infants randomised to weaning by conventional ventilation remained on the Sechrist ventilator.

Weaning during conventional ventilation was by reduction in ventilator rate only, inspiratory time was kept constant and the expiratory time progressively increased [4]. In every other respect the protocol for weaning from ventilation was similar in both groups, in particular the criteria used for reduction in ventilator settings and re-intubation.

All changes in ventilator settings were made by the clinical team caring for the infants throughout weaning. The infants' oxygen tension was continuously monitored either by a transcutaneous electrode or a Searle intra-arterial electrode. During weaning blood gases were measured as clinically indicated and routinely every 4 h. Ventilator pressure during PTV or rate during conventional ventilation were reduced if the infant had developed a respiratory alkalosis or the blood gases had been maintained over the 4-h period. The inspired oxygen concentration was reduced if the arterial oxygen pressure exceeded 7.3 kPa, regardless of whether a reduction in ventilator rate or pressure had been made. After a change in ventilation arterial blood gases were checked within 40 min and further reduction (in pressure during PTV or rate during conventional ventilation) made if the infant had a persisting respiratory alkalosis. During PTV ventilator pressure reduction was made in "steps of 2 cmH_2O" until a peak pressure of 14 cmH_2O was reached in infants greater than 28 weeks gestation and 12 cmH_2O in those less than 28 weeks gestation. Infants were then changed to endotracheal continuous positive airways pressure (CPAP). Arterial blood gases were checked after 1 h and if there was no evidence of a respiratory acidosis ($pH < 7.25$) the infant was then extubated. During conventional ventilation ventilator rate reduction was made in "steps of 5 bpm", until the infant was receiving endotracheal CPAP. Again, arterial blood gases were checked after the infant had been receiving CPAP for 1 h and if there was no evidence of a respiratory acidosis ($pH < 7.25$) the infant was then extubated. Infants were reintubated if they developed a respiratory acidosis or frequent troublesome apnoeas or had one major apnoea. The decision to reintubate was made by the clinician caring for the infant.

If, during PTV, no reduction in ventilator pressure could be made over a 24-h period or during conventional ventilation no reduction in rate could be made over a similar period, the infant was transferred to the alternative method of weaning. In addition, if any infant became apnoeic during PTV [6] they were transferred to weaning by conventional ventilation.

Trial size

Using results derived from 20 infants previously ventilated on our unit we calculated that a trial population of 40 infants was necessary to detect with 85% power at the 5% level a difference of 24 h in the duration of weaning between the two groups.

Statistical analysis

Comparison was made between the two groups of:

1. The number of infants who required re-intubation within the 24-h period following extubation.
2. The number of infants requiring transfer to the alternative mode of weaning.
3. The duration of weaning, defined as the time from entering the study until first extubation. To determine whether differences between the two groups were significant either a Fisher's exact test or Wilcoxon rank sum test was used. Infant's data were analysed in the group into which they were originally randomised, regardless of whether that regime had failed and the infants had been transferred to the alternative weaning method.

Patients

Twenty patients were randomised to both groups. All patients were initially ventilated for respiratory distress syndrome by oro-endotracheal tubes using a continuous flow, variable pressure ventilator (Sechrist). There was no significant difference in gestational age, postnatal age, gender distribution, maximum peak pressure or inspired oxygen concentration received before weaning between the two groups (Table 1). Neither was there a significant difference in the number of infants in each group who, before weaning, had developed an air leak, patent ductus arteriosus or pneumonia (Table 2). Pneumonia was characterised by asymmetrical consolidation on the chest radiograph and isolation of bacteria in a previously non-infected infant. Both the peak inspiratory pressure and the inspired oxygen concentration were significantly higher at randomisation in the PTV group ($P < 0.01$).

This study was approved by the King's College Hospital Ethics Committee.

Table 1. Clinical details of patients at trial entry. Results are expressed as the number of infants *(n)* or the median (range)

	PTV	Conventional ventilation
n	20	20
Gestational age (weeks)	29 (26–24)	30 (27–36)
Number of infants < 27 weeks gestational age	4	1
Males *(n)*	12	10
Prior to weaning:		
Maximum peak inspiratory pressure (cmH_2O)	22 (16–38)	22 (13–38)
Maximum inspired oxygen concentration (FiO_2)	73 (32–100)	75 (21–98)
Number of infants who received surfactant	5	3
Airleak *(n)*	2	1
Patent ductus arteriosus *(n)*	3	5
Pneumonia *(n)*	1	1

Table 2. Clinical details of patients at trial entry. Results are expressed as the median (range)

	PTV	Conventional ventilation
Postnatal age (days)	3 (1–21)	3 (1–16)
Fluid input (ml/kg)	75 (40–160)	87 (40–180)
Peak inspiratory pressure (cmH_2O)	18 (14–24)	16 (13–18)
Inspired oxygen concentration (%)	40 (22–64)	29 (21–45)

Results

Only one infant required re-intubation within 24 h of extubation. This infant had been weaned by conventional ventilation and was of 29 weeks gestational age. Three infants required transfer from PTV to conventional ventilation as, in all three infants, no reduction in peak pressure could be during the 24-h period following randomisation. The infants were of 25, 26 and 27 weeks gestational age respectively and represented the most immature infants randomised to PTV. All three infants were eventually weaned conventionally. No infant required transfer from conventional ventilation to PTV because of unsuccessful weaning.

No infant developed a pneumothorax or patent ductus arteriosus during the weaning process. The duration of weaning was significantly shorter in the PTV group being a median of 30 h (mean 39, range 3–186) compared to a median of 61 h (mean 65, range 15–262), $P < 0.02$.

Discussion

Weaning by PTV appears superior to weaning by conventional ventilation in the majority of infants. PTV was associated with a shorter duration of weaning and no infant required reintubation within 24 h of extubation demonstrating that appropriate weaning had been achieved. There was no significant difference between the infants weaned conventionally or by PTV for gestational age or postnatal age. The two groups were also well matched for the severity of their acute illness, as evidenced by their maximum peak inspiratory pressure and inspired oxygen concentration and in the number of infants sustaining complications prior to weaning. Thus it seems likely the shorter duration of weaning in the PTV group reflected the mode of ventilation. However, despite use of a purpose-built patient triggered ventilator and a trigger device with high sensitivity and short trigger delay [5], weaning by PTV failed in three infants, the infants were the most immature included in the study. These results suggest that, even during the recovery phase of RDS, PTV should not be routinely used for infants of less than 28 weeks gestation.

In all infants ventilator pressure was not further decreased as ventilator rate was reduced from 60 to 40 bpm. Above a ventilator rate of 60 bpm, however, the individual clinicians reduced both rate and pressure as they felt appropriate from their assessment of the blood gases, thus at trial entry the infants were receiving a variety of ventilator pressures. Despite randomisation, infants in the PTV group required significantly higher peak inflating pressures and inspired oxygen concentrations at trial entry. Although the PTV group, therefore, might be considered to be at a disadvantage compared to the conventional ventilation group, they still required a shorter duration of weaning.

Only one patient triggered ventilator was available for this study thus, to avoid any possible bias, infants were only entered into the study if that ventilator was ready for use. Infants randomised to PTV were then transferred to the SLE HV 2000 and those randomised to weaning by conventional ventilation remained on the Sechrist ventilator. Differences in ventilator performance did not explain the differences in the duration of weaning. We have previously [1, 5] reported our laboratory assessment of both ventilators. Both maintain airway pressure waveform without inadvertent PEEP at fast rates, even over 100 bpm. At lower rates, as used in this study, in both ventilators peak inflating pressure is generated as a square wave with the duration of the positive pressure plateau the set inspiratory time. Thus, as used in this study, there is no difference between either ventilator's performance.

During PTV, the infants controlled ventilator rate, a positive pressure inflation being delivered on every occasion the change in airway pressure exceeded the critical trigger level. The median peak inflating pressure at randomisation in the PTV group was 18 cmH_2O and infants were extubated at either 12 or 14 cmH_2O, depending on gestational age. In that group infants were weaned by reduction in pressure at "steps of 2 cmH_2O" so theoretically weaning was possible at a faster rate than during conventional ventilation when weaning was by reduction in rate at "steps of 5 bpm", from 40 bpm to endotracheal CPAP. Reduction in pressure or rate respectively, however, was only made if indicated by the infant's arterial blood gases and further reduction made if there was evidence of a respiratory alkalosis in blood gases, checked 40 min after changing ventilator settings. Such a policy enabled rapid weaning, if required by the infant, whether they were in the PTV or conventional group. Despite this, the shorter duration of weaning was via PTV and, as none of the PTV group required re-intubation within 24 h of extubation, this suggests that the speed of weaning had been appropriate.

Although the study was randomised, it was not possible to "blind" the clinicians to the allocation of a particular weaning method. During the months in which the study was performed, a number of physicians were involved and it seems unlikely that they were biased to one particular regime. All infants entered into our study followed our routine policy [4] regarding timing of arterial sampling and which clearly instructs the method of pressure or rate reduction expected, this again reduces the possibility of bias.

Only three infants failed initially to wean and all were in the PTV group. All three infants eventually weaned by conventional ventilation, although in one infant this was 186 h after randomisation. We analysed our data by intent to randomisation and included the three infants in the PTV group, thus our data reflect the longest duration of weaning by PTV. We conclude, as the duration of weaning was shorter by PTV compared to conventional ventilation and no infant required re-intubation within 24 h of extubation, PTV to be the optimum method of weaning. Our results, however, suggest this method of weaning should only be used routinely in infants more mature than 27 weeks of gestation.

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