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What CPAP to use in the delivery room? Bench comparison of two methods to provide continuous positive airways pressure in neonates

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ABSTRACT

Background Continuous positive airway pressure (CPAP) is a recommended first-line therapy for infants with respiratory distress at birth. Resuscitation devices incorporating CPAP delivery can have significantly different imposed resistances affecting airway pressure stability and work of breathing.

Aim To compare CPAP performance of two resuscitation devices (Neopuff T-piece resuscitator and rPAP) in a neonatal lung model simulating spontaneous breathing effort at birth.

Methods The parameters assessed were variation in delivered pressures (ΔP), tidal volume (VT), inspiratory effort (model pressure respiratory muscle (PRM)) and work of breathing (WOB). Two data sequences were required with Neopuff and one with rPAP: (1) set PRM with changes in VT and (2) constant VT (preterm 6 mL, term 22 mL) with increased effort. Data were collected at CPAP settings of 5, 7 and 9 cmH_2O using a 1 kg preterm (Compliance: 0.5 mL/cmH_2O) and 3.5 kg term (1.0 mL/cmH_2O) model.

Results 2298 breaths were analysed (760 rPAP, 795 Neopuff constant VT, 743 Neopuff constant PRM). With CPAP at 9 cmH_2O and set VT the mean ΔP (cmH_2O) rPAP vs Neopuff 1.1 vs 5.6 (preterm) and 1.9 vs 13.4 (term), WOB (mJ) 4.6 vs 6.1 (preterm) and 35.3 vs 44.5 (term), and with set PRM mean VT (ml) decreased to 6.2 vs 5.2 (preterm) and 22.3 vs 17.5 (term) $p<0.001$. Similar results were found at pressures of 5 and 7 cmH_2O.

Conclusion rPAP had smaller pressure swings than Neopuff at all CPAP levels and was thus more pressure stable. WOB was higher with Neopuff when VT was held constant. VT reduced with Neopuff when respiratory effort was constant.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Lung transition from fetal circulation to independent breathing and lung aeration is accompanied by rapid changes in lung compliance with implications for continuous positive airway pressure (CPAP) delivery systems.

⇒ Resuscitation devices used for CPAP have differences in imposed expiratory resistance with implications for pressure stability and work of breathing (WOB).

WHAT THIS STUDY ADDS

⇒ Increased system resistance for Neopuff led to either the reduction of tidal volume with constant effort or increased effort compared with rPAP if the tidal volume was maintained constant.

⇒ Airway pressure stability in CPAP systems can significantly affect the WOB.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ A required higher effort between different CPAP delivery systems at the same CPAP level might lead to respiratory exhaustion and CPAP failure.

⇒ If CPAP is required for long periods related to interhospital transfer, devices with lower expiratory resistance and higher pressure stability may be preferable.

INTRODUCTION

In recent years, respiratory management in the delivery room has shifted towards a less-invasive approach with rising numbers of infants receiving non-invasive respiratory support.[1] Multiple trials have studied the benefits of non-invasive respiratory support for spontaneously breathing preterm infants.[2–4] Systematic reviews and a meta-analysis support the early non-invasive support in preterm infants with findings of reduced incidence of bronchopulmonary dysplasia, death and mechanical ventilation.[5 6]

The European Consensus Guidelines on the management of respiratory distress syndrome (RDS) recommend continuous positive airway pressure (CPAP) as the first-line support for the initial stabilisation of spontaneously breathing preterm infants with respiratory distress.[7] The International Liaison Committee on Resuscitation (ILCOR) introduced CPAP as part of neonatal resuscitation to improve lung recruitment in preterm infants in 2010.[8] Since then the use of CPAP has become increasingly common in

Table 1 Comparison of rPAP and Neopuff: Mean and Coefficient of Variation% for P, tidal volume, pressure respiratory muscle and work of breathing in preterm and term models at different set positive end-expiratory pressure levels

	CPAP (cmH_2O)	P min (cmH_2O)	P max (cmH_2O)	Δ P (cmH_2O)	VT set (ml)	VT measured (ml)	Effort (cmH_2O)	WOB (mJ)
Preterm (1000 g)								
rPAP*	**5**	5.0, 1.0%	5.6, 1.3%	0.7, 13%	6	6.4, 9%	12.7, 8%	4.7, 1.3%
	7	6.8, 1%	7.7, 1%	0.9, 10.1%	6	6.3, 5.5%	12.2, 3%	4.6, 1.1%
	9	8.9, 10%	10.0, 1.0%	1.1, 13%	6	6.2, 6.7%	12.2, 3%	4.6, 1.2%
NP: VT constant	**5**	3.6, 2%	7.5, 2.1%	3.9, 4.7%	6	6.3, 3.3%	13.3, 2.7%	5.2, 0.9%
	7	5.1, 1.7%	10, 1.4%	4.9, 4%	6	6.6, 3.5%	14.3, 3%	5.8, 1.3%
	9	6.6, 1.7%	12.2, 0.9%	5.6, 3.5%	6	6.4, 3.3%	14.8, 3%	6.1, 1.6%
NP: Effort constant	**5**	3.5, 2.6%	7.1, 2.7%	3.6, 6%	NA	5.9, 6.2%	12.2, 4.2%	4.5, 0.8%†
	7	5.4, 1.6%	9.6, 1.5%	4.3, 4.4%	NA	5.7, 3.4%	12.2, 2.9%	4.3, 1.3%†
	9	6.9, 1.9%	11.6, 1.8%	4.7, 6.8%	NA	5.2, 7.8%	12.1, 6.2%	4.1, 1.6%†
Term (3500 g)								
rPAP*	**5**	4.4, 2%	6.1, 2.4%	1.7, 9.4%	22	22.5, 4.7%	24.4, 3.2%	35.2, 1%
	7	6.3, 1.1%	8.1, 1.1%	1.9, 6.9%	22	22.5, 2.8%	24.6, 3%	35.4, 1.1%
	9	8.3, 1.1%	10.2, 1%	1.9, 7.3%	22	22.3, 3.2%	24.4, 3%	35.3, 1.6%
NP: VT constant	**5**	1, 10%	10.5, 1.5%	9.4, 2.5%	22	22.6, 2.9%	28.6, 2.9%	42.7, 1.1%
	7	1.8, 7.8%	13.4, 1.3%	11.7, 2.5%	22	22.3, 3%	29.8, 2.8%	44.4, 0.9%
	9	3.1, 5.9%	16.5,1.3%	13.4, 2.6%	22	21.5, 3.1%	30.6, 2.9%	44.5, 1.3%
NP: Effort constant	**5**	1.4, 8%	9.8, 2.6%	8.4, 3.7%	NA	19.5, 3.1%	24.5, 3.1%	31.6, 1.2%†
	7	2.6, 4.6%	12.4, 1.3%	9.8, 2.6%	NA	18.6, 3%	24.5, 2.9%	30.4, 1.2%†
	9	4.1, 4.3%	15, 1.1%	10.9, 2.8%	NA	17.5, 3.1%	24.5, 3%	29.1, 1.2%†

All differences significant p<0.001, ANOVA repeated measurements
*VT with rPAP remained constant at set effort.
†VT in these simulations reduced and WOB not comparable to constant VT

late preterm and term infants with laboured breathing or persistent cyanosis without sufficient evidence for ILCOR recommendation.[9] Term infants treated with non-invasive ventilation in Australasian Newborn Intensive Care Units have approximately doubled within the last few years.[10] The use of T-piece devices with expiratory flow restriction to produce CPAP in the delivery room has been associated with an increase in pneumothorax, especially in infants with increasing gestational age.[11–13]

Since the first use of CPAP as a mode of non-invasive ventilation for preterm infants by Gregory *et al* in 1971,[14] several devices and methods to generate CPAP have been introduced to clinicians. For resuscitation, the number of devices capable of pressure ventilation with positive end-expiratory pressure (PEEP) to a non-breathing infant and/or providing CPAP to an infant that is breathing is limited. TPR is the most common, but a new alternative is the rPAP.[15] Both have the advantage of easy transition between positive pressure ventilation (PPV) and CPAP, but the resistance to breathing and method of generating CPAP is not similar. Previous research has shown differences in the resultant pressure waveforms between CPAP delivery systems[16–19] and large differences in expiratory resistances.[20]

In respiratory systems, the work of breathing (WOB) is the product of pressure and volume, with the mechanical work needed for breathing referred to as total or physiological WOB. Imposed WOB (iWOB) is the component of work added to the patient by respiratory equipment.[21 22] CPAP can decrease the total WOB in infants with RDS and surfactant deficiency by increasing the functional residual capacity (FRC), splinting airways and optimising breathing.[1 23] However, the WOB may be increased by the added CPAP system resistance from the interface, connectors and device design. It can be investigated in lung models or real patients but is sensitive to changes in breathing patterns such as VT and minute ventilation.[21 24]

The infant's effort to breathe causes fluctuations in the pressure waveform around set CPAP levels. Pressure stability refers to the variation in pressures above and below the set mean pressure, the ΔP. Smaller ΔP when comparing CPAP systems with identical respiratory

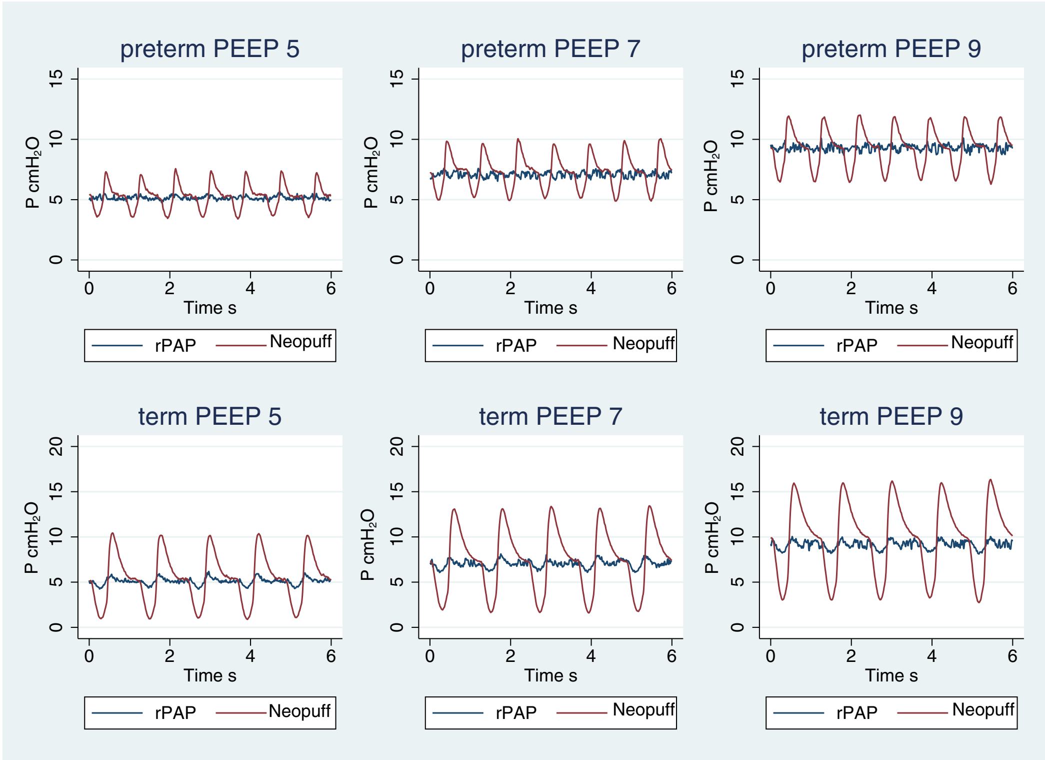


Figure 1 Pressure fluctuations around a set mean pressure of 5,7,9 cmH_2O with simulated spontaneous respiration for rPAP (blue) vs Neopuff (red) with constant tidal volume in term and preterm models. PEEP, positive end-expiratory pressure levels.

parameters can be described as more pressure stable.[17] In bench tests, rPAP has shown lower imposed resistance and more pressure stability with significantly fewer inspiratory and expiratory pressure fluctuations than the Neopuff T-piece resuscitator (TPR).[20] In constant-flow CPAP systems, gas flow continues throughout the inspiratory/expiratory cycle resulting in the need for the patient's expiratory effort to overcome the flow and the resistance of the CPAP generating device during expiration, which leads to an increased expiratory work.[25]

Lung simulators such as the Neonatal Active Lung Model (NALM) are designed to be programmable, dynamic and react to the tested device. They simulate breathing by allowing the user to set airway resistance (R_{aw}), compliance of respiratory system (C_{rs}) and tidal volumes (VT). The muscular effort needed to produce the simulated breath is labelled as the 'pressure of respiratory muscles' (PRM) in NALM.[26] PRM is generated with a moving piston within the NALM. Resistance and compliance can be linear or non-linear and in more complex simulations have more than one compartment. The NALM responds with changes in tidal volumes when system pressure and resistance change. Lung model simulators are thus dynamic, but the response is limited as they cannot react actively by changing the respiratory rate or inspiratory–expiratory ratio.

The NALM calculates the total WOB using the area of a pressure–volume loop of a simulated breath.[21] This includes the simulated effort limited to inspiration with exhalation considered passive. iWOB reflects the added resistance from the CPAP device and is calculated from the pressure–volume loop at the interface. It can be split into an inspiratory and expiratory part. All measurements of WOB are directly affected by changes in VT, and this makes reporting complicated. To standardise the comparison of devices, either the pressure or the targeted tidal volume needs to be maintained stable.[27]

The relationship between simulated effort and VT for resuscitation devices providing CPAP during simulated breathing has not previously been investigated. We aim to compare the delivered CPAP performance of two resuscitation devices with differing imposed resistances in a neonatal lung model simulating spontaneous breathing after birth by examining pressure stability, the effect on delivered tidal volume and simulated WOB.

METHODS

Two CPAP/PPV resuscitation systems were compared: the Inspire rPAP (Inspiration Healthcare) and the Neopuff TPR (Fisher and Paykel Healthcare). Both devices were connected to the NALM (Schaller Medizintechnik, Germany, V1-4.0), which simulated spontaneous breathing modelling a preterm and term newborn infant with respiratory distress.[28–31] Prior to connection to either CPAP device, the NALM was set as per previous researchers for these models[16 19 32 33] on 'spontaneous breathing' and was representative of a term 3500 g (C_{rs}:1 mL/cmH_2O, inflation rate 50/min, inspiratory time 0.4 s) and

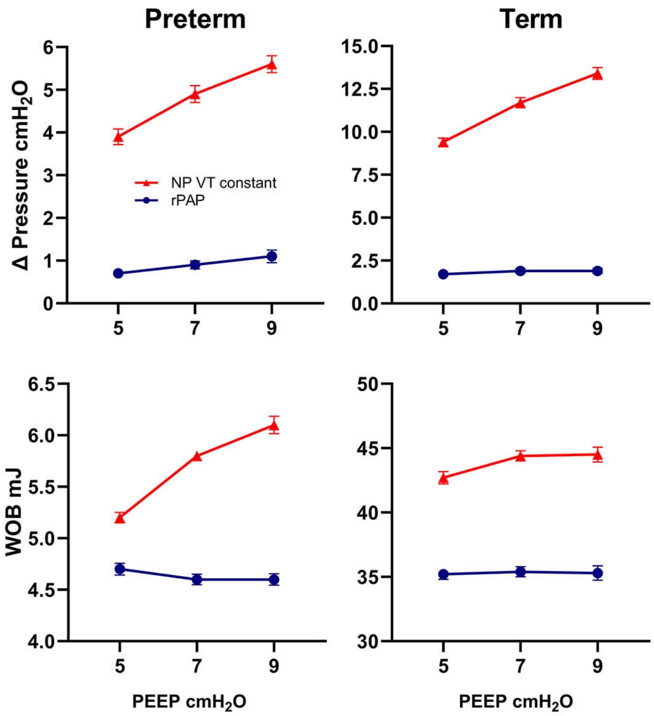


Figure 2 Pressure swings (Δ P in cmH_2O) and WOB (mJ) for preterm and term experiments with constant tidal volumes for Neopuff (red) and rPAP (blue) at PEEP 5,7 and 9. Box plots with mean and coefficient of variation percentage. PEEP, positive end-expiratory pressure levels; VT, tidal volume; WOB, work of breathing.

preterm 1000 g (C_{rs}:0.5 mL/cmH_2O, 70 /min, 0.3 s) infant with respiratory distress (online supplemental material).[19]

Before recording the NALM was equilibrated for 30 min and calibrated. The pressure and flow of the tested resuscitation devices were adjusted using a ventilator calibration analyser (Flow Analyser PF-300 IMT Medical, Buchs, Switzerland). The PEEP was set by adjusting the total flow on Inspire rPAP (7.1 L/min for 5.0 cm H_2O, 9.0 L/min for 7 cm H_2O, 10.7 L/min for 9.0 cm H_2O), Neopuff was set up with a total flow of 10 L/min for all PEEP values. The experiments were conducted without a leak, using non-humidified gas 21% O2 at ambient room temperature and with no facemask interface.

We found a significant drop in delivered VT compared with the set NALM values when connecting the Neopuff TPR to NALM in both term and preterm models. This did not occur with rPAP. To fairly examine the WOB aspect, changes in PRM were adjusted to maintain a constant VT since in a system with a constant compliance, the WOB is proportional to VT.[24] Two data sequences were collected with Neopuff to examine both states of constant VT and constant PRM. As there was no change in rPAP from set NALM values, only one data sequence was collected.

Patient and public involvement

This is a bench study of mechanical properties using a computerised lung simulator. There was no patient or animal involvement.

Data analysis

Data were collected from the NALM over 2 min for each setting. These data were imported into Stata V.18 MP (StataCorp, College Station, USA). Each respiratory cycle was identified by pressure waveform changes of PRM in Stata.

The measured parameters included the mean CPAP pressure, minimum and maximum airway pressures and their difference (Δ P), VT, PRM and WOB (total WOB calculated by NALM). Mean values for those parameters are reported in table 1. Analysis of variance (ANOVA) for repeated measures was used to determine differences in mean and Coefficient of Variation (CV%) for measured parameters at different set PEEP values and compliance between the two tested devices. Differences between means determined by multiway ANOVA were reported with p values adjusted. F test was performed using Box's conservative epsilon; p values of <0.05 were considered statistically significant. Bonferroni corrections of estimates were made to adjust for multiple comparisons.

RESULTS

2298 simulated breaths were analysed comprising 760 with rPAP, 795 with Neopuff with constant VT and 743 with Neopuff and constant PRM.

Pressure

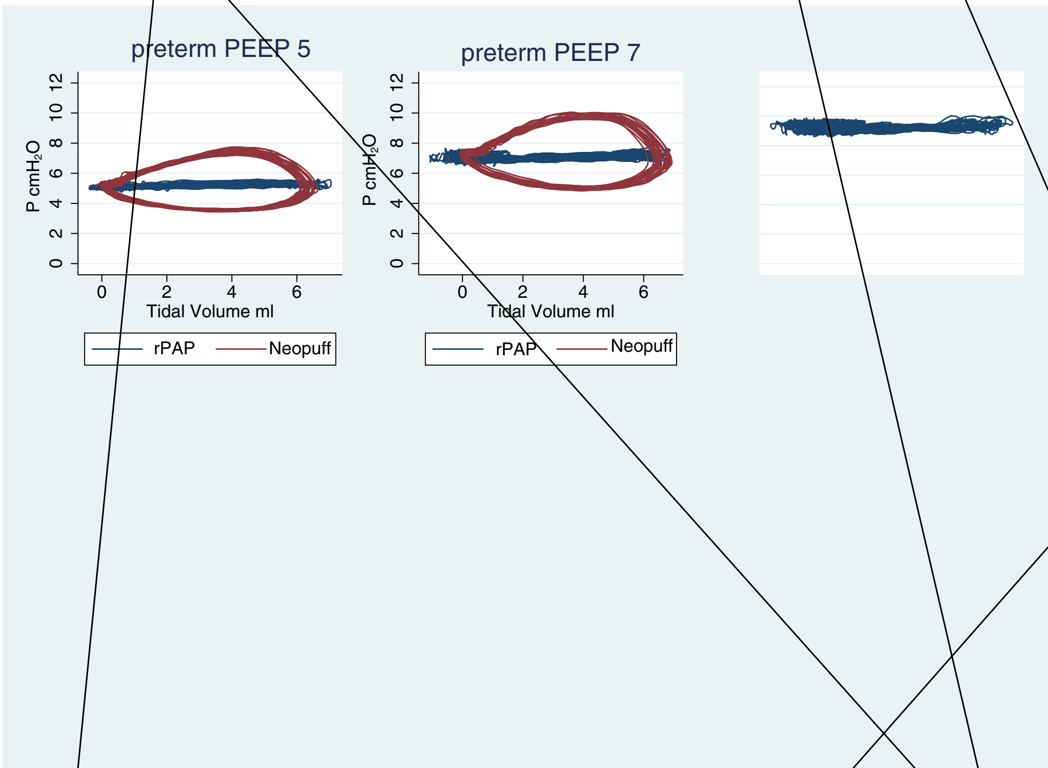
Pressure swings were significantly lower with rPAP compared with Neopuff, across all PEEP values in preterm and term models for both settings (VT or PRM constant) figure 1 and table 1. The largest ΔP was seen at higher PEEP levels in sequence 2 (constant VT) with a mean of 1.1 vs 5.6 cmH_2O rPAP vs Neopuff, CV% 13% vs 3.5% in the preterm model and 1.9 vs 13.4 cmH_2O rPAP vs Neopuff CV 7.3% vs 2.6% in the term model. The high CV% observed with rPAP can be attributed to the noisy signal produced by rPAP (table 1).

A higher PEEP had a greater impact on ΔP with Neopuff compared with rPAP: Mean ΔP 9.4–13.4 cmH_2O Neopuff vs 1.7–1.9 cmH_2O rPAP (ranges for PEEP 5–9, term model).

A larger increase in ΔP was recorded in both term and preterm constant VT models with the Neopuff (mean 5.6 preterm vs 13.4 cmH_2O term) compared with rPAP (1.1 preterm vs 1.9 cmH_2O term).

Tidal volume

In simulations with the constant inspiratory effort (PRM), the largest reduction in VT was seen in the term model at PEEP 9 cmH_2O with Neopuff where VT was reduced to a mean of 17.5 mL compared with rPAP of 22.3 mL.



Similar findings could be observed in the preterm model 6.2 vs 5.2 mL for rPAP vs Neopuff at the highest set PEEP. Showing a VT reduction of 20.5% in the term model and 13.3% in the preterm model (set PEEP 9) with constant inspiratory effort. These findings were less pronounced at lower PEEP levels (table 1 and figure 2).

In the sequence with constant VT, the inspiratory effort (PRM) was adjusted for Neopuff. The highest required PRM were at 9 cm CPAP with a total increase in effort of 2.6 cmH_2O in the preterm and 6.1 cmH_2O in the term model.

WOB

In simulations with constant VT the total WOB was significantly higher with Neopuff. The greatest differences were seen at the highest PEEP level, mean 4.6 vs 6.1 mJ, CV 1.2 vs 1.6% in preterm and 35.3 vs 44.5 mJ, CV 1.6% vs 1.3% in term model rPAP vs Neopuff. A higher increase in WOB between PEEP levels was present with Neopuff (mean 5.2–6.1 mJ preterm and 42.7–44.5 mJ term) compared with rPAP (4.7–4.6 mJ preterm and 35.2–35.3 mJ term). Examples of pressure-volume loops are presented in figure 3.

DISCUSSION

This bench test has confirmed that in both term and preterm NALM models simulating breathing with respiratory distress, the TPR (Neopuff) affects breathing with larger pressure swings around the set CPAP level compared with that measured with rPAP. The increased resistance to breathing was reflected in both ΔP, VTs and the effect on PRM. The overall impact of using Neopuff TRP compared with rPAP to deliver CPAP in our models led to either the VT reducing or a required increase in simulated effort.

Significant differences were also found in WOB levels recorded by the NALM. At a constant compliance, the elastic WOB is proportional to the VT.[34] Interpreting WOB in our dynamic active model is more complex with the calculations being dependent on the VT and, for the total WOB, the simulated effort. Since the added device resistance reduces the VT or requires an increase in simulated effort, this must be accounted for when looking at the absolute values of WOB and is a limiting factor in this bench test. Nonetheless, our findings of WOB are consistent with the in vivo study by Pandit *et al* comparing variable to constant flow CPAP devices[25] but could not be confirmed by Courtney *et al*.[35]

Fluid clearance in transition to breathing happens quickly[36] with dynamic changes in lung compliance and resistance. This transition is difficult to simulate in current lung simulators. Limitations are (1) the bench testing on fixed respiratory function parameters, which are not representative of these dynamic changes after birth; (2) our model was intentionally designed to be leak free; (3) the inability to split the WOB value of the NALM to an inspiratory and expiratory component; and (4) infants alter respiratory rate more than VT to maintain minute ventilation, which cannot be modelled with simulators, and the general translation of this bench model to in vivo results needs further investigation.

Infants breathing on identical respiratory support systems with the same settings might have a different iWOB and different inspiratory flow rates.[21] Increasing the fresh gas flow to Neopuff TPR increased pressure stability.[20] This has not been investigated in our study. A higher flow on Neopuff might be beneficial in terms of less effort, especially for CPAP use over a longer period. An increased iWOB compared with the WOB of spontaneous breathing is assumed to play a role in CPAP failure.[21]

Whether there are benefits of pressure fluctuations in the initial aeration is uncertain, but high resistance might reduce peak flows and tidal volumes. A recent animal study by Kuypers *et al* in intubated preterm rabbits receiving PPV using higher expiratory resistance showed reduced deflation rates and increased the accumulation of FRC over time.[37] Concerns of adverse effects caused by larger pressure fluctuations such as a higher incidence of pneumothorax have been raised.[18] The use of CPAP for newborn stabilisation with a T-piece system has shown an increased rate of pneumothorax, especially in late preterm and term infants.[11 13] This might be associated with faster lung compliance changes in this group. Additionally, high system resistance could increase the risk of inadvertent PEEP due to a shorter expiration time.[38]

Previous clinical and bench studies report larger VTs and greater changes in lung volume in variable versus continuous flow CPAP.[19 20 25] Cook *et al* found VT drops with a constant inspiratory effort on higher PEEP levels, which were less pronounced in CPAP systems with flow opposition.[16] This is confirmed by the findings in our bench test.

Flow opposition CPAP systems showed an advantage regarding extubation success in preterms.[39] A recently performed randomised controlled trial by Donaldsson *et al* comparing the more pressure-stable rPAP to the Neopuff TPR reported a reduced delivery room intubation using the dual flow system.[40] Whether pressure stability of CPAP systems is of importance in the early phase during transition to breathing in newborns requiring airway pressure support needs further investigation. In vivo studies are required to assess the actual imposed (inspiratory and expiratory) WOB in relation to dynamic changes of lung compliance and resistance during transition.

Prolonged support using resuscitation CPAP systems occurs in many settings while awaiting inter-hospital transfer. Our findings of differences in pressure stability and the impact of WOB may be particularly relevant in these clinical scenarios.

CONCLUSION

Our study showed large differences between the two resuscitation systems related to the imposed respiratory resistance of the CPAP devices. The rPAP device had smaller pressure swings than Neopuff at all CPAP levels and was more pressure stable. WOB was higher with a greater respiratory effort with Neopuff when VT was held constant, and VT reduced with Neopuff when respiratory effort was constant. The clinical impact of higher pressure stability and lower iWOB in the stabilisation of newborn infants needs further investigation in in vivo studies.

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