

Which neonatal nasal CPAP device should we use in babies with transient tachypnea of the newborn?

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Continuous positive airways pressure (CPAP) is a distending pressure applied with a few cmH₂O to the airways, usually through the nose. The beneficial effects result from splinting the airways, enhancing lung expansion, promoting a residual lung volume after birth, preventing alveolar collapse during expiration, preserving endogenous surfactant, reducing ventilation/perfusion mismatch, improving oxygenation, improving lung compliance, reducing airway resistance, reducing the work of breathing, and stabilizing the respiratory pattern.¹

There is very good evidence that nasal CPAP started during neonatal resuscitation is very effective for reducing the rate of intubation after birth, reducing the use of CPAP and shortening the duration of mechanical ventilation.²⁻⁵

There are five techniques commonly used for generating CPAP: 1) bubble CPAP, where the pressure is generated by a continuous flow of gas into the circuit and the 'expiratory' limb of the CPAP circuit is placed under a known depth of water to generate the pressure (I put expiratory in quotes because that is the term used but there is no evidence infants expire into the CPAP device); 2) ventilator CPAP, where the pressure is generated by a neonatal ventilator with a continuous flow of gas into the circuit and an expiratory valve modulates the pressure; 3) variable flow ventilator CPAP, where the ventilator modulates the positive end expiratory pressure (PEEP) valve and the circuit flow to maintain the pressure; 4) infant flow driver, or similar device, where the pressure is generated by a high gas flow through a nasal device with increased resistance directing the gas under pressure into the nose. The pressure is determined by the gas flow into the device and the leak from the

prongs; 5) simple nasal cannula, where a high gas flow is delivered into the nose with no resistance other than the baby's nasopharynx. It is controversial how much pressure this delivers to the infants because it appears to vary considerably with the flow, size of the infant, size of the prongs, and nasal obstruction from secretions. It

is most important that all gas flowing into the nose is heated to 37 °C and has 100% humidity. It has been very difficult to determine whether one device is more effective than the others because the comparison techniques have not carefully maintained the prong pressure, measured the delivered pharyngeal pressure or controlled for

gas leaks, and therefore pressure loss at the nose and through the mouth.

Bubble CPAP has variations in the pressure generated by heated humidified gas bubbling quickly under water at a set level, such as 5 cmH₂O. It produces pressure oscillations about 4 cmH₂O around the set CPAP level. If there is a large leak at the mouth or nose, there is not enough flow to generate the pressure and so it stops bubbling. It has been suggested that bubble CPAP is more effective than ventilator CPAP because of these oscillations.⁶ However, Kahn et al.⁷ showed that bubble CPAP pressure oscillations are progressively attenuated distal to the prongs. A short-term crossover study comparing fast bubbling with minimum bubbling did not find any difference in blood gases.⁸ A preterm lamb model comparing bubble CPAP with ventilator CPAP showed bubble CPAP was associated with a higher pH, better oxygenation and ventilation, less ventilation inhomogeneity in the lungs and decreased protein exudate in the alveoli compared with the ventilator CPAP.⁹ The pressure delivered with bubble CPAP is dependent on the flow rate and the leak, whereas the

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Conflicts of interest: The author is a consultant to Fisher & Paykel Healthcare, manufacturer of the Bubble CPAP.

Suggested citation: Morley C. Which neonatal nasal CPAP device should we use in babies with transient tachypnea of the newborn? *J Pediatr* (Rio J). 2011;87(6):466-8.

<http://dx.doi.org/10.2223/JPED.2146>

pressure generated by a ventilator was flow-independent until there are large leaks. Boumecid et al.¹⁰ suggested variable-flow CPAP increased tidal volume and improved thoracoabdominal synchrony compared with conventional CPAP. To date, there have been no studies comparing the different devices that have reported improvements in clinically important outcomes.

In this issue of *Jornal de Pediatria*, Yagui et al.¹¹ report a trial of 40 babies with respiratory distress requiring at least 30% oxygen, on the first day after birth, weighing > 1,499 g, randomized to CPAP from the Fisher and Paykel bubbly bottle device, or the Seimans Servo-i ventilator, that modulates flow and the PEEP valve to maintain the CPAP pressure. Both groups had Fisher and Paykel short binasal prongs and started with 6 cmH₂O CPAP. The primary outcome was CPAP failure, which the authors defined as needing a FiO₂ > 0.4 and a PEEP of 8 cmH₂O or higher. The trial enrolled babies with mean birth weight of about 2.5 kg. Surprisingly, over 90% were born by cesarean section, perhaps because the trial was performed in a private hospital, although about half had been in preterm labor. Unsurprisingly, with babies of this size, over 70% had a diagnosis of transient tachypnea. The rest had RDS or apnea. The CPAP was started at about 2 hours after birth. There was no significant difference in the primary outcome or duration of CPAP and duration of oxygen treatment, which were both about 24 hours. It was not stated whether the nurses were equally familiar with using both devices.

So how should we interpret this trial? It showed no difference in different outcomes in this relatively mature group of preterm babies. This may mean that different CPAP pressure generating devices did not make any difference to the effect because it is the CPAP pressure that was important and not the way it was delivered. It is unusual to report a trial of CPAP in babies who predominantly had transient tachypnea. One interpretation could be that no difference in outcome was seen between the groups because CPAP may have little effect on babies with transient tachypnea of the newborn (TTN). For this comparison there is no control group without CPAP and so it must be pure speculation but about one day's treatment with oxygen is what I would anticipate in babies with TTN.

One problem with all trials of CPAP is that there is no international consensus on what constitutes CPAP failure. In the trials or historical cohort studies where CPAP failure was defined, the definitions were very variable. This trial is unusual with a combination of > 40% oxygen and high CPAP with no reference to a high and rising CO₂ or respiratory failure. The COIN trial² defined CPAP failure as a rising PaCO₂ > 60 mmHg or an FiO₂ > 0.6 or recurrent apnea. The SUPPORT trial³ criteria were: FiO₂ > 0.50 to maintain an SpO₂ > 87% for 1 hour; PaCO₂ > 65 mmHg, or hemodynamic instability. The criteria in the CURPAP trial⁵ were: FiO₂ > 0.4 to maintain SpO₂ of 85% to 92%

for at least 30 minutes unless rapid clinical deterioration occurred, > four episodes of apnea per hour or > two per hour when ventilation with bag and mask was required, pCO₂ > 65 mmHg (8.5 kPa), and pH < 7.2 on an arterial or capillary blood gas sample. The Rojas trial⁴ criteria were: FiO₂ of > 0.75 for > 30 minutes to maintain SpO₂ within set target ranges; persistent desaturation below 80% unresponsive to suctioning and positive pressure ventilation, or pCO₂ of > 65 mmHg and pH of < 7.22 on an arterial or capillary blood gas analysis, with progressive respiratory failure. Ammari et al.¹² defined CPAP failure as: FiO₂ > 0.6, or arterial pH < 7.20 and PaCO₂ > 65 mmHg or frequent apnea requiring repeated stimulation or bag-and-mask ventilation during the first 72 hours of life. It hardly needs stating that the higher the FiO₂ and CO₂ criteria the fewer babies will be reported to fail CPAP.

One problem that can occur in trials of CPAP devices is that the delivered CPAP may not be the same in the two groups. This did not appear to be a problem in this trial. The study was unblinded. This may have biased the results but it would not have been possible to mask the intervention to the staff.

Despite one of the trial objectives being to evaluate the safety of the devices, this was not possible in a trial of only 40 babies, except for very common problems. For example, if a serious event happened in 5% of the infants, there may be only two babies in the trial who had it. A trial investigating safety needs large numbers of patients to confidently report rare but serious adverse effects.

The conclusion from this study seems to be that it does not matter which CPAP device you use. This is good news because it means you can use the cheapest device that the nurses find easiest and are used to using since CPAP success depends largely on nursing skills.

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