REVIEW

Nasal CPAP for neonates: what do we know in 2003?

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Despite the acknowledged clinical usefulness of nasal CPAP, uncertainties regarding aspects of its application remain. Clinical indications for the application of nasal CPAP vary greatly between institutions. Furthermore, defining the optimal nasal CPAP system is complicated by the multiplicity of nasal CPAP devices and techniques available to the clinician. This review aims to identify what we know about nasal CPAP and what important questions remain.

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Continuous positive airway pressure (CPAP) was first used as a method of supporting the breathing of preterm infants in 1971.[1] Since this time several routes of administration have been tried but today the nasal route is most commonly used, largely because it allows better access to the infant.[2] The physiological effects of CPAP, described in a previous review of this topic,[3] include improving oxygenation, maintaining lung volume,[4-7] lowering upper airway resistance,[8 9] and reducing obstructive apnoea.[10]

Nasal CPAP is widely used for a range of neonatal respiratory conditions. In Australia and New Zealand a massive upsurge in the popularity of nasal CPAP has seen its use increase fourfold over the past decade.[11] It is established as an effective method of preventing extubation failure,[12] is used in the management of apnoea of prematurity, and is increasingly seen as an alternative to intubation and ventilation for the treatment of respiratory distress syndrome (RDS).

WHICH NASAL CPAP DEVICE SHOULD BE USED?
Devices in common use for the delivery of nasal CPAP include single and double (binasal) prongs, in both short (nasal) and long (nasopharyngeal) forms.

Single versus double prong devices
Single prong CPAP, using a cut down endotracheal tube,[13] continues to be used widely despite evidence of better results using short binasal devices. The evidence, from a meta-analysis of randomised clinical trials of nasal CPAP devices in very preterm neonates, is that short binasal devices are more effective at preventing re-intubation in the week post-extubation when compared with single nasal prong devices.[14] A randomised trial in more mature preterm infants with early respiratory distress reported better oxygenation, respiratory rate, and weaning success with a short binasal device when compared with single prong nasopharyngeal CPAP.[15]

Probably the main reason that these devices are more effective is that they have a lower resistance, allowing greater transmission of the applied pressure to the airway.[16]

Which short binasal prongs should be used?
There are several short binasal prongs available to the clinician, including the Argyle prong,[17] Hudson prong,[18] infant flow driver (IFD),[19] and INCA prongs.[20]

Benchtop studies using lung models suggested that the prototype IFD, compared with Argyle prongs[19] and Hudson prongs,[21] generated more stable pressures. Full publication of the results of clinical trials comparing short binasal prong devices is awaited.[22 23] Further research is required to define the optimal short binasal prongs.

Can nasal cannulae be used to deliver nasal CPAP?
Nasal cannulae are used to deliver oxygen into the nose at low flow, usually with no intention of generating positive pressures in the airway. However nasal cannulae, with an outer diameter of 3 mm and flows up to 2 l/min, have been reported to deliver CPAP.[24] A study of CPAP via nasal cannulae found it as effective in the treatment of apnoea of prematurity as conventional CPAP prongs.[25] No studies have examined its role in the treatment of RDS or in the post-extubation setting. Our view is that CPAP pressures are unlikely to be delivered effectively to the airway, because flows used are low and leaks around the cannulae large. Monitoring of the pressure generated by a given flow and achieving adequate humidity are problematic.

How effective are nasal masks?
Nasal masks were an early means of applying CPAP to neonates.[2 26] They lost favour because of the difficulty in maintaining an adequate seal and a tendency to obstruct the nasal airway.[27] Recently a new generation of nasal masks have been developed which anecdotally have been noted to deliver CPAP effectively while causing minimal nasal trauma. These promising devices have not yet been subject to proper clinical comparisons with nasal prongs.

HOW SHOULD NASAL CPAP DEVICES BE FIXED?
The most difficult aspect of using nasal CPAP is positioning the device. In common with nasotracheal tubes, CPAP devices have the potential to

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Abbreviations: CLD, chronic lung disease; CPAP, continuous positive airway pressure; ET, endotracheal; IFD, infant flow driver; NIPPV, nasal intermittent positive pressure ventilation; RDS, respiratory distress syndrome

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cause nasal excoriation and scarring if inappropriately applied or infrequently monitored.[28][29] It is important that the biggest prongs that comfortably fit the nostrils are used to avoid loss of pressure. Using prongs of the correct diameter reduces leak. Excessive pressure against the nasal septum causes septal erosion. Damage to the lateral walls of the nostrils and the nasal septum can be avoided by ensuring that the device is straight and not pressed hard against the nasal septum.

There are many different techniques for fixing the devices to the infant. The exact technique does not matter as long as the device is secure and not traumatising the nose, face, or head. More research is needed to define the least traumatic nasal device and method of fixation.

WHAT ARE THE OPTIMAL FLOW CHARACTERISTICS?

The amount of gas flow through the CPAP circuit is important. Insufficient set flow limits the flow available for inspiration, increasing airway pressure fluctuation, and raising the work of breathing. The flow required is affected by the degree of "leak" of gas from the infant's nose and mouth. In our experience this can often be 6 l/min or greater. If the mouth is open the pressure in the pharynx will fall and the flow will need to be increased to maintain it. If the mouth is tightly closed and the nasal prongs are a good fit (that is, minimal "leak") the flow required will be less. The flow required and its dynamics are also affected by the system used to generate the CPAP. The bubbly bottle CPAP pressure generating system has the advantage that the adequacy of flow can be seen and heard. If the leak is high the flow causing the bubbling is too low and the bubbling stops. If the flow is too high the bubbling becomes very vigorous.

Infant flow driver system

Altering the flow into the CPAP device directly changes the delivered pressure with the IFD. It needs flows in excess of 8 l/min to generate pressures around 5 cm H_2O. The actual flow delivered to the airway and the effect of leaks, using "variable flow" devices such as the IFD, has not been studied.[30]

The "expiratory" limb of the IFD is unusual among CPAP devices in that it is open to the atmosphere. Potentially, the baby can inspire with a higher flow than that delivered through the inspiratory limb. This extra gas can be drawn from the expiratory limb ("variable flow"). This reduces the possibility of the pressure falling with large inspirations and therefore may reduce the work the baby expends to take large breaths. More research is needed to clarify the clinical importance of this modification.

Underwater bubble CPAP

Underwater bubble CPAP has been used since the early 1970s.[1] With an underwater blow off system, sufficient flow creates continuous bubbling from the end of the underwater tube, placed at a specified depth underwater, to ensure that circuit pressure is maintained. Although a comparison of underwater bubble endotracheal (ET) CPAP with conventional ventilator derived ETCPAP in preterm neonates suggests that such oscillation contributes to gas exchange,[31] no studies have examined the effectiveness of bubbling on CPAP via the nasal route. Despite this lack of strong evidence it has the advantage of being a relatively simple and inexpensive way of generating CPAP. It also has the advantage that if there is inadequate pressure owing to a large leak the bubbling can be seen to stop.

Conventional ventilators for nasal CPAP

When a ventilator generates CPAP pressure the flow is set, often about 6 l/min. There is no easy way of knowing whether this flow is sufficient for the baby's inspiratory needs. If the flow is too low the work of breathing may be increased. The work of breathing was found to be increased with conventional ventilator driven CPAP (circuit flow limited to 6 l/min)

compared with an IFD system maintaining pressure at the device level with variable flow (set inspiratory flow not specified).[20]

A flow of 6 l/min is certainly sufficient to supply the minute volume of all but the largest, most vigorously breathing infants, but it is not minute volume that determines the flow required in nasal CPAP. The "leak", that is the continuous flow of gas through the nose and out through the mouth, affects how much flow is required to maintain the CPAP pressure in the pharynx. The leak may be several litres per minute; our own measurements suggesting leaks of 6 l/min are common. If this is true then the flow through the device needs to be higher to provide enough flow to maintain the pharyngeal pressure. In theory, too much flow might be better than too low a flow. This is an area requiring more research.

Benveniste device

As with the IFD, altering the flow to the Benveniste device directly alters the pressure at the level of the attached nasal prongs. The Benveniste device[32] requires high gas flows with up to 14 l/minute to generate pharyngeal pressures of between 3 and 10.5 cm H_2O.[33] Comparisons with other flow sources for CPAP generation are lacking.

HOW MUCH PRESSURE SHOULD BE USED?

The purpose of nasal CPAP is to deliver a supporting pressure to the upper airways and lungs. If this is achieved consistently it may not matter which device is used. A pressure of 5 cm H_2O is traditionally used. Some neonatal intensive care units hardly vary this and claim good results. We use higher levels, often starting at 8 cm H_2O. A recent report, studying infants with mild RDS, showed the highest end expiratory lung volume and tidal volume, and the lowest respiratory rate and thoracoabdominal asynchrony, at a pressure of 8 cm H_2O compared with 0, 2, 4, and 6 cm H_2O.[34] The optimal CPAP pressure is not known and may depend on the condition treated.

A baby with RDS, relatively stiff lungs, a high FiO_2, and a chest x ray showing rather opaque lungs may need a higher pressure to support lung volume than a baby with a low FiO_2 treated for apnoeic episodes. Studies in the 1990s have applied CPAP pressures as high as 10 cm H_2O.[35] However caution must be exercised, as the inappropriate use of high pressures in an infant with compliant lungs may restrict pulmonary blood flow, increase the risk of air leak, or cause over-distension leading to hypercapnia. Judging how much pressure is needed is still an art. If an infant shows evidence of worsening lung disease with increasing oxygen requirements, a more opaque chest x ray, and is recessing, we would increase the pressure in increments of 1 cm H_2O, up to 10 cm H_2O, and observe the effect.

HOW DO WE KNOW AN INFANT IS "FAILING" ON NASAL CPAP AND WHAT ARE THE REMEDIABLE CAUSES?

There are no clear definitions of nasal CPAP failure. When used for supporting babies with RDS or preventing re-intubation after extubation there is no clear cut off to decide that the baby should be intubated. The following are typical "failure" criteria for infants treated with nasal CPAP for early RDS: persistent serious apnoeic episodes, $PaCO_2$ of ⩾60 mm Hg (8.3 kPa), FiO_2 of ⩾0.6 to maintain acceptable oxygen saturation. Treatable reasons for apparent failure of nasal CPAP include: insufficient applied pressure, insufficient circuit flow, inappropriate prong size or placement, airway obstruction from secretions, and a baby's open mouth creating a large leak and lowering the pharyngeal pressure.

If neglected the nose can obstruct with secretions with loss of CPAP effect. There are no good data to help decide the frequency of suction of nasal secretions. Excessive suction interferes with CPAP delivery and can traumatise the nose. The

frequency of suctioning needs to be individualised to the infant's requirements.

IS MOUTH CLOSURE IMPORTANT?
The general effect of mouth closure, with a pacifier[33] or by direct closure,[36] is to raise pharyngeal pressure. Our own data have shown that the pharyngeal pressure may fall significantly if the mouth is open even slightly. Chin straps have been used to avoid the fluctuations in the delivered pressure seen with intermittent mouth opening.[4] This appears sensible, although there are no data to show that keeping the mouth closed improves clinical outcomes. There is one theoretical problem with ensuring the mouth is closed. The success of CPAP has been shown in most studies without actively closing babies' mouths. If we now ensure all babies' mouths are closed they will receive higher pharyngeal pressures than when the mouth was left alone.

WHAT IS THE OPTIMAL POSTURE?
Despite the lack of evidence that it is optimal for the baby, the supine position is often used as it facilitates easier care of the CPAP device. However studies have shown that preterm infants nursed prone are less likely to suffer central and mixed apnoea.[37] [38] There is little direct evidence about neck flexion or rotation to guide us. Avoiding excessive flexion, extension, or rotation of the head and neck would appear to be sensible.

SHOULD NASAL CPAP BE USED FOR RESPIRATORY DISTRESS FROM BIRTH?
The role of CPAP as primary support for very premature infants with respiratory distress from birth is not fully defined. Historically, the respiratory support for very premature babies has been intubation and ventilation at birth. Nasal CPAP was usually reserved for the support of larger babies several hours after birth. However, there is a growing popularity for the use of CPAP to manage babies at risk of RDS from birth.

A retrospective analysis of eight different units by Avery and colleagues[39] associated the early use of CPAP with a lower incidence of chronic lung disease. This led to an increase in the use of CPAP, as an alternative to intubation and ventilation, in some units. Subsequent publication of non-randomised studies, with[40–42] and without[35 43] historical controls, reported the benefits of early CPAP in minimising the incidence of mechanical ventilation and chronic lung disease (CLD). Evidence for CPAP as prophylactic therapy for respiratory distress in preterm infants is so far inadequate.[44] What is required is a definitive, prospective, randomised controlled trial of nasal CPAP from birth versus intubation and mechanical ventilation for very preterm neonates.[35 41 42 45–48] The IFDAS trial,[49] currently in abstract form, randomised a total of 234 very preterm neonates into one of four treatment arms: early CPAP after intubation and prophylactic surfactant, early CPAP with or without subsequent rescue intubation and surfactant, early intubation and ventilation with prophylactic surfactant, and management at the physicians' discretion. Although the short term duration of mechanical ventilation was reduced in those receiving nasal CPAP (with or without surfactant) no difference was found in the rate of CLD. Another trial, in process, aims to determine definitively whether nasal CPAP or intubation and ventilation from birth is more effective in promoting survival free of CLD and long term disability.[50]

SHOULD EXOGENOUS SURFACTANT BE ADMINISTERED TO VERY PRETERM INFANTS BEING TREATED WITH NASAL CPAP FROM BIRTH?
The results of the published surfactant trials in ventilated infants should not be extrapolated to infants treated with early CPAP. Some trials have examined the role of prophylactic surfactant in combination with early CPAP. The strategy of a short intubation to deliver surfactant, with subsequent extubation to CPAP, compared with CPAP alone[51] or with ongoing mechanical ventilation[52] has so far shown no difference in CLD incidence, and longer term outcomes remain unresolved. Among the groups of the IFDAS trial,[49] those preterm neonates randomised to early CPAP with prophylactic surfactant had no significant difference in the rate of chronic lung disease or in duration of mechanical ventilation when compared to the group randomised to early CPAP with or without rescue surfactant. A small randomised trial of nebulised surfactant delivered via IFD, versus nasal CPAP alone, showed no differences in short term outcomes.[53]

Despite these trials it is important to recognise that CLD continues to be a significant problem despite surfactant treatment[54] and different modes of ventilation.

IS NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION (NIPPV) A USEFUL METHOD OF AUGMENTING NASAL CPAP?
NIPPV augments CPAP by superimposing ventilator inflations on nasal CPAP. Reviews of randomised controlled trials of NIPPV versus nasal CPAP show that NIPPV is more effective in preventing failure of extubation[55] and may be useful in preterm infants with troublesome apnoea.[56] The availability of ventilators synchronising NIPPV breaths with infants' breaths has reduced concerns about the risk of gastrointestinal perforation.[57] The randomised trials using synchronised NIPPV,[58–60] all via the Infant Star ventilator, provide some guidance on appropriate ventilator settings: positive end expiratory pressure at 5–7 cm H_2O; peak inspiratory pressures 2–4 cm H_2O above pre-extubation level or 16–20 cm H_2O increased to maintain a "measured" pressure of at least 12 cm H_2O; ventilator rate 10–25 per min; flow 8–10 l/min; inspiratory time 0.6 seconds. Further, more definitive studies are needed.

No studies have described the use of NIPPV as first line therapy for early respiratory distress.

DOES NASAL CPAP INCREASE THE RISK OF AIR LEAK?
A randomised trial of early prophylactic CPAP versus oxygen alone[61] showed no difference in the incidence of air leak. No results on the incidence of air leak are yet available from randomised controlled trials comparing early CPAP with mechanical ventilation. Reassuringly observational studies with historical controls, in units that have changed to a policy of promoting early CPAP, have shown no increase in the incidence of air leak.[40 42]

GASTRIC DISTENSION AND CPAP
What is surprising is not that CPAP sometimes causes gaseous distension of the stomach but that it does so rarely. This may be because the tone in the upper and lower oesophageal sphincters is higher than the applied CPAP.[62] It seems appropriate to use a stomach tube open to atmosphere to vent any gas, although our observation is that little comes up. If it occurs, "CPAP belly syndrome" is likely to be benign.[63] The inappropriate fear of "CPAP belly" leads some units to withhold feeds and prolong the use of parenteral nutrition.[40]

HOW SHOULD INFANTS BE WEANED FROM NASAL CPAP?
There are many different methods of weaning infants from nasal CPAP. Our unit practice is to trial an infant off CPAP once they are stable at a low FiO_2 on a pressure of 5 cm H_2O. Some units cycle the infants through periods on and off CPAP before stopping and others recommend weaning to lower pressure settings. In a study by Robertson and Hamilton,[64] preterm infants were randomised at extubation to one of two nasal

CPAP regimens. These were a "weaning regimen", where infants were treated with CPAP immediately after extubation and then weaned, and a "rescue regimen", where extubated infants were treated initially with head box oxygen and had CPAP commenced if predefined "start CPAP" criteria were met. There was no significant difference between the groups in the total duration of nasal CPAP, days of ventilation after initial extubation, CLD, or intraventricular haemorrhage.

CONCLUSIONS

What new things do we know about nasal CPAP for neonates?

- Short double prongs are more effective than single prongs for delivering nasal CPAP.
- Nasal CPAP is effective for the post-extubation support of preterm infants.
- NIPPV is a useful method for augmenting nasal CPAP.
- NCPAP can be used as primary treatment for RDS.

What questions remain?

- Does early nasal CPAP for RDS reduce mortality and morbidity when compared with intubation for very preterm neonates?
- Can more effective and less traumatic nasal CPAP devices and methods of fixation be developed?
- What is the most effective source of pressure for CPAP?
- What is the optimal flow and how should this be measured?
- What is the optimal pressure level and how can this be judged?
- How should babies be weaned from CPAP?

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ECHO...

Screening for retinopathy of prematurity: evaluation and modification of guidelines

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Please visit tbe Archives of Diseases in Childhood: Fetal and Neonatal Edition [www. archdischild.com] for a link to the full article.

Aims: To evaluate current screening guidelines for ROP (retinopathy of prematurity) and to determine whether they can be modified.

Methods: In accordance with the authors' present criterion, infants born in Stockholm County, Sweden, from 1 August 1998 to 31 July 2000, with a gestational age of ⩽32 weeks, were screened for ROP. The effectiveness of screening was studied.

Results: The incidence of ROP was 25.5 % in this study A dropout group comprising almost 20% of the population studied (⩽32 weeks), was never referred, were lost to follow up, or died before screening was completed. No infant with a gestational age of >31 weeks at birth developed severe ROP (stages 3–5) and no infant with a gestational age of >29 weeks was treated for ROP.

Conclusion: 80% of infants in this population with a gestational age at birth of ⩽32 weeks, this screening criterion, were effectively screened for ROP. The authors recommend that the screening criterion be lowered to ⩽31 weeks since no infant with severe ROP would have been missed.

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