An Observational Study of Gas Flow in Preterm Infants Treated with Bubble CPAP

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Keywords

Premature infant
CPAP
Nasal high-flow
Neonatal intensive care
Pressure
Flow

Word count: 2491

ABSTRACT

Objective

To measure the nasal gas flow of infants treated with bubble continuous positive airway pressure (CPAP) and compare that with commonly used flows during nasal high-flow (nHF) treatment.

Design

Prospective, single-centre study. Bubble CPAP pressure was measured at the nasal prongs. Set gas flow was reduced until bubbling in the water-chamber just ceased. Set gas flow without bubbling then approximated flow entering the infant's nose ('delivered flow').

Setting

Neonatal Intensive Care at The Royal Women's Hospital, Melbourne, Australia.

Patients

Clinically stable preterm infants receiving bubble CPAP therapy.

Main outcome measure

Delivered flow (L/min) when bubbling stopped at a range of clinically set CPAP pressures (cm H₂O).

Results

Forty-four infants were studied: mean (SD) gestational age at birth 28.4 (2.2) weeks, birth weight 1154 (419) g. At time of study, infants were a median (IQR) age 4.5 (2 – 12) days with mean (SD) weight 1205 (407) g. Delivered flow ranged from 0.5–9.0 L/min, and increased with higher set CPAP pressures (median 3.5 L/min at CPAP 5 cm H₂O vs. 6.3 L/min at CPAP 8 cm H₂O) and heavier weights (median 3.5 L/min in infants <1000 g vs. 6.5 L/min for infants >1500 g).

Conclusions

Nasal gas flows during bubble CPAP in preterm infants are similar to flows used during nHF and increase with higher set bubble CPAP pressures and in larger infants.

INTRODUCTION

Nasal continuous positive airway pressure (CPAP) is a common form of non-invasive respiratory support for treating preterm infants with respiratory distress.¹⁻³ The primary mechanism of action of CPAP is the delivery of distending airway pressure, which assists with lung aeration, maintains functional residual capacity, improves oxygenation, and reduces work of breathing.^{4, 5} CPAP is produced by the flow of heated, humidified gas against a resistance at the distal end of the circuit. This pressure is partly transferred to the infant's airways through tightly fitting short binasal prongs or a nasal mask. During bubble CPAP, the resistance is a specified depth of the "expiratory tube" under water. The circuit gas flow is set to produce continuous bubbling in the water chamber. Target gas flows to produce bubbling vary between neonatal units.⁶⁻⁸

Nasal high-flow (nHF) is an alternative method of providing non-invasive respiratory support, delivering heated, humidified gas directly to an infant's nose at a set gas flow, typically 2–8 Litres per minute (L/min), through smaller nasal cannulae.² Compared with CPAP, nHF use is associated with lower rates of nasal trauma in preterm infants,⁹ and is preferred by nursing staff and parents due to ease of use and perceived comfort for the infant.^{10, 11} The postulated mechanisms of action of nHF include reduction of dead space through the washout of nasopharyngeal carbon dioxide produced by the 'high' gas flows, and the generation of a distending pressure.^{5, 12-18}

It is suggested that CPAP exerts its effects primarily through generation of distending pressure, and nHF by the high gas flow into the airway. We postulate there may be overlap between the mechanisms of action of the two modes.^{5, 19} Studies, including a recent randomised crossover study by *Liew et al*, have demonstrated that nHF produces some distending pressure,¹³⁻¹⁹ but no studies have measured the gas flow delivered into the nose by CPAP systems.

This study measured the gas flow into the nose and the CPAP pressure at the nasal prongs in preterm infants receiving bubble CPAP. We aimed to compare the range of gas flows delivered to infants treated with bubble CPAP with those commonly used in nHF treatment.

METHODS

Study design

A single-centre study in the Neonatal Intensive Care Unit (NICU) at The Royal Women's Hospital (RWH), Melbourne, Australia, from March to September 2019. The study was prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12619000197134). The protocol was approved by the RWH Human Research Ethics Committee. Infants were eligible if they were born <37 weeks' gestation, were receiving treatment with bubble CPAP (Circuit: F&P 850 System, Fisher & Paykel Healthcare, Auckland, New Zealand; Prongs: Hudson RCI Infant Nasal Prong, Teleflex, USA; or Inca Infant Nasal CPAP Assembly, Cooper Surgical, USA), and were clinically stable as determined by their treating clinician. Prospective, written parental consent was obtained.

Outcomes

The primary outcome was gas flow delivery at the point when bubbling in the water-chamber just ceased ('delivered flow'). Secondary outcomes included this 'delivered flow' and measured CPAP pressures in weight groups at various set CPAP pressures, over a range of set gas flows, and with the infant's chin in a neutral position versus supported (mouth closed).

Procedure

The study was designed to cause minimal interference to the routine care of the infants. Parental consent was obtained, and measurements performed at a time suitable for parents and clinicians. The infant's gestational age at birth, birth weight, and sex were recorded. At the point of measurement, a number of infant demographics were recorded (Table 1). CPAP circuit

pressure was measured with a calibrated respiratory function monitor (Florian, Acutronic Medical Systems, Hirzel, Switzerland) attached to the monitoring port of the nasal prongs. Data from the monitor were continuously sampled at 200Hz, digitised, and recorded using physiological recording software (Spectra, Version 3.0.2.5, Grove Medical, London, UK). At the start of each study, baseline gas flow was measured by visual inspection of the flow meter ball (EZI-FLOW Flowmeter M/N: 515817, Comweld, Victoria, Australia, accurate to within 5% of full scale reading i.e. within 0.75 L/min) to the nearest 0.5 L/min, looking horizontally at the level of the ball to reduce parallax errors. Mean (SD) measured pressure was recorded from a 10-second sample at baseline flow, 10 L/min, 8 L/min, then in 0.5 L/min decrements from the baseline flow until bubbling in the water chamber ceased and the meniscus was maintained at the bottom of the underwater tube. This flow at this point was considered to be the flow of gas applied to the infant's nose as there was nowhere for it to be lost.

After these measurements, gas flow was returned to baseline and the infant's chin was lifted with a finger to close the mouth, as determined by visual inspection. Gas flow and pressure were measured again as above with the infant's chin supported throughout.

Each study took approximately 10 minutes and at completion the original settings were restored (Supplemental Figure 1).

Sample size and statistical analysis

The sample size of this descriptive study with a single mean was calculated based on the precision of the estimate of mean gas flow through the prongs with the mouth position undisturbed. Forty-four infants were required to achieve a margin of error of ± 1.5 L/min, given a standard deviation of 5 L/min, based on previous unpublished data. Statistical analysis was performed using SPSS Statistics (Version 25, IBM, USA), Minitab (Version 19.2, Minitab, USA), and Excel (2016, Microsoft, USA). Demographic data are reported using descriptive statistics.

Mean and standard deviation were used when data were normally distributed; median and interquartile range were used when the data were skewed. For the primary outcome, the delivered gas flow is presented as a median (interquartile range [IQR]) flow at each set CPAP pressure. The relationship between infant weight and delivered flow was determined using the Kruskal-Wallis test in three weight groups: <1000 g, 1000-1499 g, and 1500-2499 g. The effect of mouth closure was determined using the Mann-Whitney test. The effect of gas flow on measured pressure was evaluated by lines of best fit on a plot of measured pressures with increasing set gas flow. P-values <0.05 were deemed to be statistically significant.

RESULTS

Forty-four infants were studied (Figure 1): 23 (52%) were male; mean (SD) gestational age at birth was 28.4 (2.2) weeks, and birth weight 1154 (419) g. At the time of study, infants had a median (IQR) age of 4.5 (2–12) days and mean (SD) weight of 1205 (407) g. All infants had an orogastric feeding tube *in situ*; 31/43 (72%, one record missing), a nasal barrier dressing (Neo-Guard, Readmed Inc, Jiangsu Province, China) *in situ*; and 4 (9%) infants had a chinstrap fitted. Set CPAP pressures ranged from 5–9 cm H₂O (Table 1). Baseline flow (gas flow set by bedside staff) ranged from 6.0–10.5 L/min (Table 2).

With the chin unsupported in a neutral position, delivered flow at bubbling cessation ranged from 1.0–9.0 L/min (median [IQR] 4.5 [3.5–6.0] L/min). Higher set CPAP pressures were associated with greater delivered flow (Figure 2): at a set CPAP pressure of 5 cm H₂O, the median (IQR) delivered flow was 3.5 (2.6–4.5) and at a set CPAP pressure of 8 cm H₂O it was 6.3 (4.1-8.0) L/min.

When the chin was supported, delivered flow (at bubbling cessation) ranged from 0.5-8.5 L/min (median flow [IQR] 4.0 [3.0–5.0] L/min). There was no significant difference (p=0.31) in delivered flow between the chin neutral and chin supported states (Table 3). With the chin

supported, the median (IQR) delivered flow at set CPAP pressures of 5 and 8 cm H₂O, was 3.3 (1.0-4.5) and 5.3 (3.9–6.6) L/min, respectively (Table 2).

There was a significant difference in the mean delivered flow at which bubbling ceased between infants in the three weight groups, with the chin both neutral and supported ($p=0.02$ and $p=0.04$ respectively). Delivered flow increased with weight, with median (IQR) flow of 3.5 (1.5–5.5) L/min in infants <1000 g; 4.5 (3.5–5.3) L/min in infants 1000-1499g; and 6.5 (4.5–8.0) L/min in infants > 1500 g (chin neutral measurements) (Table 3).

At baseline flows, measured pressure at the nasal prongs approximated set CPAP pressure. We observed increasing measured pressure with increasing set gas flow; as flow was increased to 10 L/min, measured pressure exceeded set CPAP pressure by approximately 1 cm H₂O. Conversely, as flow was reduced below baseline, measured pressure fell below the set CPAP pressure by up to 1 cm H₂O (Supplemental Figure 2).

Table 1. Infant demographics.

Characteristic	N = 44
At birth	
Gestational age – mean weeks (SD)	28.4 (2.2)
Birth weight – mean grams (SD)	1154 (419)
Male sex – no. (%)	23 (52.3)
At time of study	
Postmenstrual age – mean weeks (SD)	29.7 (1.7)
Postnatal age – median days (IQR)	4.5 (2 - 12)
Weight – mean grams (SD)	1205 (407)
Infant position – no. (%) (n = 43)^	
Prone	20 (46.5)
Back	8 (18.6)
Side	15 (34.9)
Other features	
Orogastric tube present – no. (%)	44 (100)
Nasal barrier dressing present – no. (%) (n = 43)^	31 (72.1)
Chinstrap in place – no. (%)	4 (9.1)
Median fraction of inspired oxygen (IQR)	0.23 (0.21 – 0.26)
CPAP nasal prong type and size – no. (%)§	
Hudson Prong 0	26 (59.1)
Hudson Prong 1	13 (29.6)
Hudson Prong 2	2 (4.6)
Inca Prong‡	3 (6.8)
Studies at each set CPAP Pressure (cm H₂O) – no. (%)	
5	14 (31.8)
6	14 (31.8)
7	9 (20.5)
8	6 (13.6)
9	1 (2.3)

^ Data missing in one measurement for infant position and nasal barrier dressing presence. Percentages calculated excluding the missing values (i.e. n = 43)

§ Hudson prongs (Teleflex, USA); Inca Prongs (Cooper Surgical, USA).

‡ Inca prong sizes were 9.0 French and 10.5 French.

Table 2. Primary outcome - baseline and delivered gas flow at bubbling cessation for each set CPAP pressure, with chin neutral and supported.

Outcome	Set CPAP Pressure (cm H ₂ O)				
	5	6	7	8	9*
Number of infants (n = 44)	14	14	9	6	1
Chin neutral (n = 44)					
Baseline set flow – median (IQR) L/min	7.0 (7.0 – 8.0)	7.5 (6.9 – 8.0)	8.0 (7.8 – 10.0)	8.3 (8.0 - 8.6)	*
Delivered flow when bubbling ceased – median (IQR)L/min	3.5 (2.6 – 4.5)	4.5 (3.9 – 5.6)	6.0 (3.3 – 7.5)	6.3 (4.1 – 8.0)	*
Chin supported (n = 43)^					
Baseline set flow – median (IQR) L/min†	7.0 (7.0 – 8.0)	7.5 (6.9 – 8.0)	8.0 (7.6 – 9.5)	8.3 (8.0 - 8.6)	*
Delivered flow when bubbling ceased – median (IQR) L/min	3.3 (1.0 - 4.5)	4.0 (2.9 – 5.1)	4.0 (3.6 – 7.4)	5.3 (3.9 – 6.6)	*

* Measurements at CPAP 9 cm H₂O excluded from analysis as only one measurement recorded.

^ Data not obtained from one infant at CPAP 7 cm H₂O due to lack of bubbling with chin supported.

† Baseline set flow measurements with chin supported are the same as those when chin is neutral excluding the above missing data point.

Table 3. Secondary outcomes

Effect of chin support on delivered flow when bubbling stopped				
	Chin neutral – median flow (IQR) n=44	Chin supported – median flow (IQR) n=43 [^]	Difference (95% CI)	p-value (Mann- Whitney test)
Delivered flow when bubbling ceased – L/min	4.5 (3.5 – 6.0)	4.0 (3.0 – 5.0)	0.5 (-0.5 – 1.5)	0.31
Effect of infant's weight on delivered flow when bubbling stopped				
Descriptive analysis by weight – Delivered flow when bubbling ceased – L/min	Chin neutral (n = 44)		Chin supported (n = 43) [^]	
	Number	Median flow (IQR)	Number	Median flow (IQR)
<1000 grams	15	3.5 (1.5 – 5.5)	15	3.5 (1.0 – 5.0)
1000 – 1499 grams	22	4.5 (3.5 – 5.3)	22	4.3 (3.0 – 5.0)
1500 – 2499 grams	7	6.5 (4.5 – 8.0)	6	6.5 (3.8 – 7.4)
Kruskal-Wallis test [†]	Chin neutral (n = 44)		Chin supported (n = 43) [^]	
	df ^a	P-value	df ^a	p-value
Difference in delivered flow when bubbling ceased between weight subgroups	2	0.02*	2	0.04*

[^] n = 43 due to data not obtained from one infant at CPAP 7 cm H₂O due to lack of bubbling with chin supported.

[†] Kruskal-Wallis test comparing delivered flow between weight groups <1000 g, 1000-1499 g, 1500-2499 g. Infants were divided into weight groups based on most recent weight at the time of measurement.

^a df – degrees of freedom in the comparison.

* denotes significant p-values <0.05

DISCUSSION

In preterm infants receiving bubble CPAP, we found that the delivered nasal gas flow ranged from 0.5-9 L/min, similar to gas flows prescribed during nHF.² The delivered gas flow into the nose during bubble CPAP changed little when the mouth was closed by supporting the chin.

We found that the pressure and flow delivered during bubble CPAP varied with the set pressure, set flow, and weight of the infant. More flow was delivered into the nose when set CPAP pressures were higher. Murki *et al.* previously showed that reducing the set flow to barely produce bubbling resulted in lower CPAP pressures than a higher set flow of 5 L/min.²⁰

Our findings suggest that during bubble CPAP similar gas flows are delivered into the nose as flows delivered during nHF. Therefore, benefits conferred by high gas flow may be similar in both types of support. These findings may not apply during CPAP generated using other devices. Several studies have already indicated overlapping actions by demonstrating that nHF can generate some distending pressure similar to CPAP.¹³⁻¹⁸ The main differences between the two systems are that the desired pressure is set by the clinician during bubble CPAP, whereas with nHF the clinician does not set, and is not aware of, the delivered pressure. In both systems, the device set pressure and the delivered prong pressure is likely to be higher than the pressure transmitted into the airway. Nasal CPAP prongs are selected to fill the nares in order to reduce leak and therefore better deliver the set pressure, although in practice this may be difficult to achieve. Nasal HF prongs are intended to be loosely fitting and leak in order to facilitate nasopharyngeal washout. Pressure produced during nHF is generated by the high gas flow into the nasopharynx, and resistance to it leaving the nose and mouth.

The position of the infant's mouth (unsupported in a "neutral" state versus gently closed by supporting the chin with a finger) had little effect on the delivered gas flow (Table 3). This could indicate that gas leak during CPAP is primarily around the nasal prongs rather than through the

mouth, despite the intention to fill the nostrils with snug fitting prongs. This variable was not able to be well controlled, as infants naturally open and close their mouths, and we did not ensure that an infant's mouth was open prior to taking "neutral" measurements.

Bubbling ceased at higher flows in larger infants suggesting more leak around the nasal prongs in this group (Table 3). The routine use of nasal barrier dressings in infants born <30 weeks' gestation and/or with birth weight <1250 g at our study site may have resulted in a better seal around the nasal prongs and reduced leak. However, we did not compare the delivered flow between those with nasal barrier dressings *in situ* and those without.

We observed a number of trends with the use of bubble CPAP in this study. Firstly, a higher set flow was typically used in infants with higher set CPAP pressures, with the median baseline flow being 7.0 L/min for a set CPAP of 5 cm H₂O vs. 8.3 L/min for a set CPAP of 8 cm H₂O.

Secondly, in infants with higher set CPAP pressures, delivered flow when bubbling ceased was higher than in those with lower set CPAP pressures. Median delivered flow at bubbling cessation was 3.5 L/min at a set pressure of 5 cm H₂O compared with 6.3 L/min at set CPAP of 8 cm H₂O when the mouth was neutral (Table 2; Figure 2). One possible reason for this is that the increased circuit pressure may result in higher leak from the nose and mouth. Thirdly, the measured pressure may be influenced by the set flow: measured CPAP pressure increased with increasing set flow at the same set CPAP pressure. For any given set CPAP pressure, at lower set flows (3–4 L/min), measured pressure was lower than the set CPAP pressure by around 0.5 cm H₂O. Conversely, at higher set flows (8–10 L/min), measured pressure exceeded the set CPAP pressure by around 1 cm H₂O. Although lower baseline flows were not used in our study (the lowest was 6 L/min), higher set flows are commonly used to achieve bubbling, especially when leak is an issue. This may result in higher circuit pressures than those prescribed. Although the design of bubble CPAP system allows the escape of excess pressure

through the underwater tube, we speculate that at higher flows, resistance to gas flow escaping from the underwater tube may increase circuit pressure.

Our study is the first to record the flow of gas into the nose of infants during bubble CPAP. The procedure used was quick, safe, simple, and easy to replicate. Whilst we measured pressure at regular decrements of set flow, the procedure could be easily performed by simply turning the flow down until bubbling stopped and recording that flow. As the set CPAP pressure was not altered, infants continued to receive appropriate CPAP (set ± 1 cm H₂O) throughout the procedure, although the beneficial effects of CPAP bubbling were removed during this short period. Blinding was not possible, however attempts to reduce bias included utilising a standard case report form, a consistent procedure for data collection in each infant, and by having a standardised criterion for judging when bubbling ceased. An estimate of the fit of the nasal prongs, as performed in this study, is necessarily subjective. The visualisation of mouth closure was also subjective. However, in both cases, the flow into the nose represented flows similar to that of nHF. We used the flow meter that was used clinically rather than a calibrated scientific flow meter because changing the flow meter for each study may have affected CPAP delivery, potentially causing instability. The same researcher was present at each study and used a standardised process for collecting the data.

The implication of these results is that bubble CPAP is delivered with a nasal gas flow rate in a similar range to that used to deliver nasal high-flow treatment, and this may be one reason why the two treatments produce similar results in terms of respiratory support in some studies. Further research exploring the delivery of nasal high-flow through the bubble CPAP apparatus would assist understanding of these mechanisms.

CONCLUSIONS

Delivered gas flows into the nose during bubble CPAP are similar to set flows used during nHF.

Delivered flows are higher with higher set CPAP pressures and in larger infants.

ACKNOWLEDGEMENTS

The authors would like to thank the following: the parents and families of the participants for making the project possible; the doctors and nurses working in NICU at RWH for facilitating the project; Dr Jennifer Dawson for assistance with equipment and protocol development; Ms Emily Twitchell, Ms Bernice Mills, and Ms Brenda Argus for assisting with recruitment and data collection; and Dr Megan McKimmie-Doherty, Ms Grace Elliot and Ms Bridget Howard for their assistance in data collection.

COMPETING INTERESTS

The authors report no competing interests. Prof Colin Morley is a consultant to Fisher and Paykel Healthcare.

FUNDING

Program Grant #1113902 for equipment used in this project.

CONTRIBUTORSHIP STATEMENT

Authors: C.M. formulated the original study concept and protocol framework. P.D., B.M., L.O., K.H., and C.P. planned and developed the protocol, completed the ethics application, collected data, and result analysis. All authors were responsible for interpreting results, drafting and revising the manuscript, had final approval of the submitted manuscript and supporting data. All authors also agree to be accountable for the accuracy and integrity of the study.

Contributors: J.D. assisted with equipment and protocol development. E.T., B.M., and B.A. assisted with recruitment and data collection. M.M., G.E., and B.H. assisted with data collection.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

Continuous positive airway pressure and nasal high-flow are commonly used non-invasive respiratory supports for the treatment of neonatal respiratory diseases.

Conventionally, CPAP is thought to provide pressure support, whilst nHF provides support through high gas flow.

nHF therapy is associated with the generation of some distending pressure.

WHAT THIS STUDY ADDS?

This study is the first to measure gas flow delivered into the infant's nose during bubble CPAP.

Nasal gas flows during bubble CPAP are similar to set gas flows during nHF.

Higher nasal gas flow occurs when set CPAP pressures are higher.

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