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Bubble CPAP versus CPAP with variable flow in newborns with respiratory distress: a randomized controlled trial

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Abstract

Objective: To evaluate the efficacy and safety of nasal continuous positive airway pressure (NCPAP) using devices with variable flow or bubble continuous positive airway pressure (CPAP) regarding CPAP failure, presence of air leaks, total CPAP and oxygen time, and length of intensive care unit and hospital stay in neonates with moderate respiratory distress (RD) and birth weight (BW) ≥ 1,500 g.

Methods: Forty newborns requiring NCPAP were randomized into two study groups: variable flow group (VF) and continuous flow group (CF). The study was conducted between October 2008 and April 2010. Demographic data, CPAP failure, presence of air leaks, and total CPAP and oxygen time were recorded. Categorical outcomes were tested using the chi-square test or the Fisher's exact test. Continuous variables were analyzed using the Mann-Whitney test. The level of significance was set at $p < 0.05$.

Results: There were no differences between the groups with regard to demographic data, CPAP failure (21.1 and 20.0% for VF and CF, respectively; $p = 1.000$), air leak syndrome (10.5 and 5.0%, respectively; $p = 0.605$), total CPAP time (median: 22.0 h, interquartile range [IQR]: 8.00-31.00 h and median: 22.0 h, IQR: 6.00-32.00 h, respectively; $p = 0.822$), and total oxygen time (median: 24.00 h, IQR: 7.00-85.00 h and median: 21.00 h, IQR: 9.50-66.75 h, respectively; $p = 0.779$).

Conclusion: In newborns with BW ≥ 1,500 g and moderate RD, the use of continuous flow NCPAP showed the same benefits as the use of variable flow NCPAP.

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Introduction

Respiratory distress (RD) is the most common condition leading to newborn admission to the neonatal intensive care unit. Its etiologies include respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), meconium aspiration syndrome, and pulmonary infections.

Restoration of functional residual capacity using positive pressure is one of the pillars of RD treatment. This can be achieved using non-invasive techniques, such as nasal continuous positive airway pressure (NCPAP), an alternative to mechanical ventilation that may avoid many of the risks

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associated with it.[1] NCPAP has many benefits, such as promoting an increase in transpulmonary pressure, chest stabilization, pulmonary compliance, ventilation/perfusion ratio, and airway patency, and can be administered using continuous or variable flow systems.

Continuous flow was first described by Gregory et al. in 1971 as a system consisting of an apparatus in which the expiratory limb is submersed in a water seal that defines the positive end expiratory pressure (PEEP) level. This model is known as bubble continuous positive airway pressure (CPAP) and is still in use today.[2] Bubble CPAP is inexpensive and is easy to adapt for newborns[3]; however, if the interface is not well adapted or if there is leakage through the nose or mouth, the PEEP level is not guaranteed. The device has a continuous flow, which is delivered via an oxygen blender connected to a flow meter, a heated humidifier, a respiratory circuit (i.e., inspiratory and expiratory tubing), and a chamber containing sterile distilled water that is attached to a threshold resistor. The level of pressure is changed by submerging the expiratory limb of the tubing into the chamber at the depth of the desired CPAP.[4]

In an attempt to ensure more stable pressures even in the presence of air leaks, new devices that use variable flows have been developed, providing flow on the basis of the newborn's demand. The electronic ventilator for variable flow NCPAP (VF-NCPAP) has a variable resistance valve placed at the expiratory limb. The set CPAP pressure is consistently maintained by adjusting the flow rate based on the patient's condition, up to a maximum of 33 L/min; this is done by using bias flow to facilitate patient's triggering. According to the manufacturer, the system responds to deviations from the set CPAP pressure, which are sensed, fed back to the electronic ventilator controller valves and regulated several times during each breath. A precise gas delivery support maintains a continuous, predetermined pressure.[5]

The use of systems with variable flow, such as VF-NCPAP, is known to reduce the work of breathing and to increase lung recruitment compared to continuous flow devices.[3,6] Nevertheless, there are few randomized controlled trials that compare these different CPAP apparatuses with respect to respiratory outcomes, particularly among infants with birth weight (BW) ≥ 1,500 g and moderate RD, which frequently use NCPAP as a non-invasive respiratory support. Therefore, the aim of this study was to compare continuous flow NCPAP (CF-NCPAP) (delivered by a bubble CPAP device) and VF-NCPAP (delivered by an electronic ventilator) with regard to the rate of nasal support failure, barotrauma, total CPAP and oxygen time, and length of hospital stay in infants with BW ≥ 1,500 g and moderate RD who required positive pressure associated with oxygen therapy.

Materials and methods

Between October 2008 and April 2010, a randomized controlled trial was conducted at Hospital Israelita Albert Einstein, São Paulo, Brazil. The study was approved by the hospital Ethics Committee. Infants with BW ≥ 1,500 g requiring NCPAP for moderate RD until 24 h after birth were eligible for the study after informed parental consent. In this study, moderate RD was defined when newborns needed a fraction of inspired oxygen (FiO_2) ≥ 0.30 for a target saturation of 88-94%, associated with RD (characterized by the presence of at least two of the following symptoms: expiratory grunting, intercostal or xiphoid retractions, thoraco-abdominal distortions, nares dilatation), requiring positive airway pressure. At our unit, NCPAP is routinely indicated when the previous situation occurs. Exclusion criteria included the presence of major congenital malformations, severe birth asphyxia, hemodynamic instability, and previous intubation.

A total of 40 babies were randomized into two study groups: variable flow group (electronic ventilator, mode CPAP with variable flow, Servo-i – Siemens Elema Inc., Solna, Sweden) and continuous flow group (CPAP with continuous flow at 8 L/minute, bubble CPAP device, Fisher & Paykel Healthcare, Panmure, Auckland, New Zealand), using computer-generated random numbers contained in sealed envelopes, which were opened at the moment of patient inclusion. Both groups used short binasal prongs, model BC 161 (Fisher & Paykel Healthcare, Panmure, Auckland, New Zealand), provided by Maquet Inc. (Bridgewater, NJ, U.S.). An initial evaluation form was completed for every patient. After CPAP stabilization, the parameters (namely, PEEP and FiO_2) were adjusted as necessary to maintain transcutaneous oxygen saturation between 88 and 94%. All infants were monitored routinely by recording vital signs every 2 h, repositioning nasal prongs when necessary and checking the delivery of CPAP by measuring the underwater tube position (as well as ensuring bubbling on the bubble CPAP unit) until their discharge.

The primary outcome was CPAP failure with indication of conventional mechanical ventilation (as determined by routine criteria, such as the need for a $FiO_2 > 0.40$ plus PEEP level ≥ 8 cmH_2O). The secondary outcomes were: length of oxygen and CPAP use, presence of barotraumas, and length of intensive care unit and hospital stay. NCPAP use was suspended when its parameters (FiO_2 and PEEP pressure) were below 0.25 and equal to 5 cmH_2O respectively, and when clinical RD was overcome.

Categorical outcomes were tested using the chi-square test or the Fisher's exact test. Continuous variables were analyzed using the Mann-Whitney test. All data were analyzed using SPSS version 17 software (SPSS Inc., Chicago, IL, U.S.). The level of significance was set to $p < 0.05$. Data are presented as mean ± standard deviation (SD) or median

and interquartile range. Sample size calculations indicated that 40 subjects randomized would be sufficient to reject the hypothesis of equivalence between devices regarding CPAP failure, with 80% probability using an alpha of 0.01, given that proportions of CPAP failure varied between 25 and 55%.

Results

A total of 40 infants were randomized. One baby was excluded from the variable flow group because the nasal prong interface was changed due to the development of nasal injury and damage to the septal mucosa; therefore, the patient was not able to continue using the interface designed for this study. Table 1 summarizes the clinical data at the time of enrollment.

The primary causes of RD are shown in Table 2. Among the 29 newborns, the most common etiology was TTN.

There were no differences between groups regarding the initial parameters or the time to install NCPAP (Table 3).

The primary and secondary outcomes analyzed are shown in Table 4. There were no differences between the study groups regarding the primary outcomes analyzed, which included CPAP failure. In both groups, CPAP failure occurred in four newborns. These infants had a gestational age of 35.4±3.3 weeks (mean ± SD) and BW of 2,445±839 g; moreover, half of them were diagnosed with RDS and half with TTN. All of them initiated conventional mechanical ventilation after CPAP failure. Barotrauma was found in only one baby in the continuous flow group and in two babies in the variable flow group. All three infants with barotrauma had good evolution without necessity of thorax drainage. Similar results were found in both study groups for all secondary outcomes analyzed (Table 4).

Discussion

Using a randomized clinical trial to compare the use of continuous and variable flow CPAP devices, we found no differences in any of the outcomes analyzed among neonates having BW ≥ 1,500 g and moderate RD.

While many studies have been conducted to determine the advantages of different CPAP systems, there is remarkably little agreement on how NCPAP should be applied, including the specification of initial parameters, the most appropriate NCPAP system for use and the choice of interface.

Table 1 - Baseline characteristics of patients (variables are expressed in mean ± standard deviation or percentage)

	Variable flow group (n = 19)	Continuous flow group (n = 20)	p
Birth weight (g)	2,602±585	2,518±598	0.663
Gestational age (weeks)	35.8±0.5	35.7±0.4	0.863
Male sex (%)	68.4	70.0	0.915
5-minute Apgar score	9.5±0.6	9.6±1.0	0.246
Cesarean section (%)	94.7	90.0	1.000
Preterm labor (%)	47.4	40.0	0.643
Antenatal steroids (%)	31.6	10.0	0.127
Infection risk (%)	31.6	40.0	0.584
Rupture of membranes ≥ 18 h (%)	5.3	5.0	1.000
Multiple birth (%)	42.1	25.0	0.257

Table 2 - Main etiology of respiratory distress

	Variable flow group (n = 19)	Continuous flow group (n = 20)	Total
Other	5 (26.3%)	5 (25.0%)	10 (25.6%)
TTN	14 (73.7%)	15 (75.0%)	29 (74.4%)

Other = includes respiratory distress syndrome and apnea; TTN = transient tachypnea of the newborn.
Fisher's exact test: p = 1.000.

Table 3 - Initial CPAP parameters and time delay to CPAP installation (values are expressed in median and interquartile range)

	Variable flow group (n = 19) Median (IQR)	Continuous flow group (n = 20) Median (IQR)	p
Initial CPAP (cmH_2O)	6.0 (5.0-6.0)	6.0 (5.5-6.0)	0.714
Initial FiO_2	0.28 (0.25-0.34)	0.30 (0.30-0.30)	0.332
Time of CPAP installation (min)	120 (90-203)	135 (50-225)	0.978

CPAP = continuous positive airway pressure; FiO_2 = fraction of inspired oxygen; IQR = interquartile range (Mann-Whitney rank sum test).

Table 4 - Primary and secondary outcomes analyzed (values are expressed in percentage or median and interquartile range)

	Variable flow group (n = 19)	Continuous flow group (n = 20)	p
CPAP failure (%)	21.1	20.0	1.000
Barotrauma (%)	10.5	5.0	0.605
Length of CPAP use (h)	22.00 (8.00-31.00)	22.00 (6.00-32.00)	0.822
Length of oxygen use (h)	24.00 (7.00-85.00)	21.00 (9.50-66.75)	0.779
Length of ICU stay (days)	4.00 (2.00-6.00)	4.50 (2.50-6.00)	0.745
Length of hospital stay (days)	9.00 (5.00-21.00)	7.50 (3.50-14.50)	0.390

CPAP = continuous positive airway pressure; ICU = intensive care unit.
Mann-Whitney test and Fisher's exact test.

In our study, we chose to use the same interface for both groups, that is, short binasal prongs, because they have been found to be superior to single or long nasal prongs.[7] In doing so, we eliminated potential confounders.

In terms of initial parameters, we used the same CPAP level in both groups (6 cmH_2O), with FiO_2 between 0.28 to 0.30 to aim for an hemoglobin saturation between 88 and 94%, as previously described in literature.[4,8] These parameters changed little from baseline values and did so in similar ways in both groups. Our CPAP failure criteria (FiO_2 > 0.40 and PEEP ≥ 8 cmH_2O) were in accordance with previous studies.[3]

There are several systems that can be used to apply NCPAP. A recent study comparing five different NCPAP systems, including bubble CPAP, flow opposition, and the same electronic ventilator we used in our study, showed that electronic ventilator was the only system that averaged the desired CPAP during ventilation.[9]

There are currently no reports that have compared continuous and variable flow CPAP using bubble CPAP and electronic ventilator in neonates weighing 1,500 g or more. Indeed, most of the literature comparing different CPAP systems has focused on comparing bubble CPAP (for continuous flow) and flow opposition devices, such as infant flow driver CPAP (IFD CPAP) (for variable flow).

Based on our analysis of previous studies, there is no consensus regarding which is the best device to ventilate patients with BW ≤ 1,500 g. Some studies have shown that variable flow IFD CPAP is better than continuous flow with bubble CPAP regarding lung recruitment,[6] decreased effort for breathing, less respiratory asynchrony,[3] decreased requirement for endotracheal ventilation,[10] and decreased oxygen use time.[11,12]

However, one author found that IFD CPAP was as effective as conventional CPAP in the prevention of extubation failure among extremely low BW infants and in the post-extubation management of infants with RDS.[13] Another author also found that bubble CPAP may reduce the use of mechanical ventilation in that population.[14] Furthermore, in infants ventilated for less than 14 days, bubble CPAP was associated with a higher rate of successful extubation and a reduced duration of CPAP support.[15]

The differences seen in outcomes using bubble and IFD CPAP devices may be due to differences in the application of positive airway pressure. Studies have shown that the stochastic resonance produced by the bubble CPAP may promote airway opening due to the fact that the noisy pressure waveform of the device superimposed on pressure fluctuations that result from spontaneous breathing.[2,16] It has been shown that flow can affect the delivered CPAP, even in the presence of leakage. Because of this, the measurement of pressure at the level of the prongs is imperative in the prevention of lung overdistension. Some authors have shown that the oscillations provided by the bubble CPAP under conditions of increased flow may improve gas exchange.[2,16,17] However, other authors disagree with this and note that the attenuation of the waveform at the level of the alveoli makes such improvement unlikely.[17] As such, we did not change the flow rate in the bubble CPAP (which was continuous at 8 L/min), although we acknowledge that one limitation of our study is the lack of evaluation of the real pressure delivered to the newborns through manometers placed at the level of the nasal prongs.

In contrast, the IFD CPAP is a device with variable flow in which CPAP is set by an opposition flow that diverts into a separate expiratory branch.[1,7,13] CPAP values may vary from cycle to cycle in response to the infant's demand. Another difference between bubble and infant flow driver devices is that the CPAP level is always monitored in the latter device; thus, it presumably provides a stable mean airway pressure.

In contrast to prior studies, the two groups showed similar outcomes. This may be due to the fact that IFD CPAP utilizes a different mechanism for delivering PEEP as compared to electronic ventilator, although both use variable flow. In the former, the pressure is delivered by a system of opposition flow through the Coanda effect, while, in the latter, the pressure is delivered using an expiratory valve.

We speculate that another reason that CF-NCPAP and VF-NCPAP showed the same results in our sample may be related to the gestational age of the population of newborns studied, which do not require the lung recruitment effect attributed to VF-NCPAP that was exhibited in newborns with BW ≤ 1,500 g. In addition, the beneficial effects of VF-NCPAP were reported with respect to post-extubation or more severe RD, as demonstrated in the studies cited above.

Our mean BW was between 2,500 to 2,600 g, and the most frequent RD etiology was TTN. In our study, this basic pathophysiology might have benefited from the simple use of CPAP because of its relatively low severity and complexity in comparison with the inclusion criteria described in the previous studies. Two infants in the variable flow group and one in the continuous flow group had barotraumas; we believe that this was associated with the fact that we randomized only infants with moderate RD, as demonstrated by the total CPAP failure rate of 20.5% among all randomized infants, with necessity of intubation and conventional mechanical ventilation.

Although our study was a relatively small, single-center trial, we found that both bubble and VF-NCPAP (electronic ventilator) devices showed similar outcomes; thus, both are indicated for use in infants with BW greater than 1,500 g and moderate RD. As a result, decisions concerning which device to use in this population can be made based on staff's familiarity with the device and the cost of the device relative to the medical service provided.

Conclusion

In newborns with BW ≥ 1,500 g and moderate RD, the use of CF-NCPAP showed the same results as the use of VF-NCPAP.

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