RESEARCH PAPER

Nasal Mask *Versus* Nasal Prongs for Delivering Nasal Continuous Positive Airway Pressure in Preterm Infants with Respiratory Distress: *A Randomized Controlled Trial*

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Objective: To compare the effectiveness of nasal continuous positive airway pressure delivered by Nasal mask *vs* Nasal prongs with respect to continuous positive airway pressure failure.

Study design: Randomized, controlled, open label, trial.

Setting: Tertiary care level III neonatal unit.

Participants: 118 preterm infants-gestational age (27-34 weeks) requiring nasal continuous positive airway pressure as a primary mode for respiratory distress, who were treated with either nasal mask (*n*=61) or nasal prongs (*n*=57) as interface.

Primary outcome: Need for mechanical ventilation within 72 h of initiating support.

Results: Nasal continuous positive airway pressure failure occurred in 8 (13%) of Mask group and 14 (25%) of Prongs group but was statistically not significant (RR 0.53, 95% CI 0.24-1.17) (*P* = 0.15). The rate of pulmonary interstitial emphysema was significantly less in the Mask group (4.9% *vs.* 17.5%; RR 0.28, 95% CI 0.08-0.96; *P* = 0.03). Incidence of moderate nasal trauma (6.5% *vs* 21%) (*P*=0.03) and overall nasal trauma (36% *vs* 58%) (P=0.02) were significantly lower in mask group than in the prongs group.

Conclusion: Nasal continuous positive airway pressure with mask as interface is as effective as prongs but causes less nasal trauma and pulmonary interstitial emphysema.

Keywords: *Management, Mechanical ventilation, Non-invasive ventilation, Respiratory distress*.

Nasal continuous positive airway pressure (NCPAP) is a simple, low cost and non-invasive method of ventilating a sick newborn [1]. Bubble CPAP is the most commonly used modality for delivery of NCPAP [2,3]. Traditionally, short bi-nasal prongs have remained the standard of care for delivery of NCPAP. The limitations of delivering NCPAP with prongs include mechanical difficulties in maintaining the nasal prongs, poor tolerance of the infant to the apparatus, difficulties in positioning the neonate, columella injury and septal deformities [4-6].

Nasal masks are increasing being used for delivering CPAP in recent times due to their ease of application [7]. A randomized trial in neonates <31 weeks gestation comparing nasal mask with binasal prongs showed less intubation rate within 72 hours for the treatment of respiratory distress syndrome (RDS) or in post-extubation setting with nasal mask [8]. A recent randomized controlled trial (RCT) from India reported a 6% reduction in the oxygen requirement at 2 hours of CPAP initiation with nasal mask as compared to nasal prongs [9]. Nasal trauma has been reported with the use of both nasal masks and prongs and occurs equally with each interface [10,11]. There is need for more evidence before nasal masks can replace short binasal prongs. Our aim was to compare the effectiveness of these two modes of CPAP delivery in an Indian scenario using Bubble CPAP.

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Methods

This randomized controlled trial was conducted at a Level III neonatal intensive care unit (NICU). It was conducted from March 2014 to February 2015, following approval from the Institutional ethics committee. Infants were eligible for inclusion if they were born between 27-34 weeks gestation by best obstetric estimate (dated by early obstetric ultrasound or last menstrual period) and had respiratory distress at birth. Babies were initially

stabilized in the labor room and then transported to the NICU. Randomization was done post-initial stabilization if eligibility criteria was met. For the purpose of this study, respiratory distress at initiation was defined as Silverman-Anderson score (SAS) of 3-6 with FiO_2 requirement between 21-60% to maintain SpO_2 between 90-95%. Babies with 5 minute Apgar scores ≤5, those with major congenital malformation, and those with antenatally diagnosed congenital heart disease were excluded from the study. Written informed consent was taken prior to enrolment.

Intervention: Enrolled infants were randomized to receive either Nasal mask (group 1) or Nasal prongs (group 2) as a mode of NCAP delivery interface. Randomization was done using a computer generated randomization chart with sealed opaque, sequentially numbered envelopes. The physician on call opened sequentially numbered sealed opaque envelopes and randomized infants to respective groups. Access to envelopes was restricted to designated physicians. Blinding of intervention and outcome measurement was not feasible because of the nature of intervention

Infants in the Mask group were delivered NCPAP using Fisher and Paykel Infant Nasal Mask in small (BC800), medium (BC801) and large (BC802) sizes based on best estimate using the nasal mask scale provided by the company. Masks were connected to Fisher and Paykel 'Bubble CPAP system'(BC151) using Fisher and Paykel 'Flexi Trunk Midline Interface' (BC191 - 70 mm) and appropriate sized Fisher and Paykel 'Infant Bonnet' depending on Head circumference (BC300 - small, BC303 - medium, BC306 – large). Infants in the Prong group were delivered NCPAP using appropriate sized Hudson RCI Infant Nasal Prong CPAP cannula system (size 0 and 1). The prongs were connected to Fisher and Paykel 'Bubble CPAP system'(BC151) directly using pins and rubber bands over appropriate sized bonnets provided with the Hudson Nasal prong CPAP cannula system.

CPAP was initiated at a pressure of 5 cms of H_2O with FiO_2 sufficient to maintain SpO_2 of 90-95%. CPAP pressure and FiO_2 were titrated to baby's requirements to a maximum of 60% FiO_2 and CPAP of 8 cms H_2O. Flows were adjusted to maintain adequate bubbling, not exceeding 8 litres/min. Nasal toilet was provided every 4 hourly and the nursing staff evaluated for nasal trauma daily in each shift. Nasal trauma was classified at point of CPAP removal as: Mild trauma: erythema/tenderness; Moderate trauma- excoriation/crusting/bleeding; and Severe trauma- narrowing of the passage. Repositioning of the interface and external massage was given for mild nasal trauma. Mupirocin ointment was applied for moderate/severe trauma to prevent it from further worsening. Weaning from CPAP was achieved initially by stepwise reduction of FiO_2 to 30%, and then subsequently, CPAP was decreased gradually with removal at 4 cms of water.

Babies in both the groups were administered natural bovine surfactant (Survanta) at a dose of 100mg/Kg in 4 equal aliquots by INSURE (Intubation, Surfactant and Extubation) technique if FiO_2 requirement was >30%, as per routine unit protocol. A repeat dose of surfactant was given if the FiO_2 requirement did not come down to <30% after 12 hours of first dose. All infants enrolled in the study received a loading dose of 10 mg/kg caffeine base and then 2.5 mg/kg 24 hours after the loading dose and daily thereafter. The regular dose of caffeine was increased to a maximum of 5 mg/kg caffeine base daily if the baby had apneic spells on CPAP. All babies were started on trophic feeds of human milk by 48-72 hours, if hemodynamically stable.

Outcomes: The primary outcome was CPAP failure, defined as the need for intubation and mechanical ventilation within 72 hours of initiation of respiratory support. Infants were intubated and ventilated if they met 2 or more of 5 failure criteria, at maximum CPAP settings of pressure 8 cms and FiO_2 60% *viz*. (*i*) worsening clinical signs of respiratory distress (increasing tachypnea, expiratory grunting, intercostal, subcostal, and/or sternal recession); (*ii*) apnea treated with positive pressure ventilation (PPV) by mask on two or more occasions in 1 hour; (*iii*) FiO_2 >0.6 to maintain SpO_2 ≥90% for >30 minutes; (*iv*) pH <7.2 on two arterial blood gases taken >30 minutes apart; and (*v*) PCO_2>60 mm Hg on two arterial blood gases taken >30 minutes apart.

The secondary outcomes related to respiratory support were duration of CPAP support, duration of supplementary oxygen requirement, maximal flow, PEEP and oxygen requirement, incidence of air leaks and Broncho-pulmonary dysplasia. Other outcomes included incidence of patent ductus arteriosus (PDA), intraventricular hemorrhage (IVH) grades 3 and 4, necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP) ≥stage 3, culture-proven early and late-onset sepsis, time to full feeds, length of hospital stay, mortality and nasal trauma.

Infants were monitored as per standard nursing protocols. All babies on NCPAP had a large bore oro-gastric tube placed open to the atmosphere in vertical position, to avoid distension of the stomach. Data collection of maternal variables included maternal complications, mode of delivery and antenatal steroids.

Infant variables included birth weight, gestational age, presence of IUGR (weight <10th on Lubchenco percentile), need for resuscitation, FiO_2 requirement and SAS score at initiation of NCPAP support. Vital signs, FiO_2 requirement, CPAP settings, SAS scores and blood gases of the infant were recorded at regular intervals as per unit policy.

PDA was diagnosed clinically and confirmed by echocardiography wherever possible. IVH was defined by bed side sonography using the Papile classification [12]. NEC was classified according to Bell's classification, as modified by Kliegman and Walsh as stage II or greater [13]. ROP was defined according to the international classification of retinopathy of prematurity [14]. BPD was defined according to the National Institutes of Health consensus definition [15]. Full feeds were defined as feeds that reached 150 mL/kg per day and sustained for 3 consecutive days. All secondary outcomes were determined before discharge home from hospital unless stated otherwise.

On the basis of NICU data from previous two years before this study, around 40% of infants with a completed gestational age <34 weeks who received NCPAP as primary treatment of respiratory distress required intubation and invasive ventilation in our NICU. The interface on which infants started was not recorded but was likely to be prongs in the majority. We hypothesized that using nasal mask would reduce the need for intubation and mechanicical ventilation to 20% (an absolute reduction of 20%). With a two sided alpha error of 0.05 and beta error of 0.2 (power 80%), the estimated sample size was 118 (59 in each group).

Statistical analyses: Baseline characteristics and outcome measures on nominal scales were analyzed by chi square test or Fisher exact test as appropriate. Baseline characteristics and outcome measures on continuous scales were analyzed by using two sample t test or Mann Whitney U test as appropriate. Statistical significance was considered if the *P* value was <0.05. Statistical analysis was performed by applying intention to treat principle. SPSS software for Windows version 18 (IBM SPSS, Inc, Chicago, IL) was used for statistical analysis.

RESULTS

A total of 340 infants born at <34 weeks gestation were admitted in NICU during the study period, out of which 181 infants were assessed for inclusion (***Fig.* 1**). 118 infants were randomly assigned with 61 to Mask and 57 to Prongs group**.** The baseline demographic characteristics of enrolled infants were similar ***(Table* I)**.

CPAP failure was seen in 13% infants on nasal mask and in 25% infants on nasal prongs, but failed to reach statistical significance (*P* = 0.15) **(*Table* II)**. Incidence of pulmonary interstitial emphysema was significantly lesser in infants on nasal mask as compared to nasal prongs (*P*=0.03), although higher flows were required in mask group which was statistically significant [6.2 (0.7) *vs* 5.9 (0.4) L/min, *P*= 0.008]. There was a significant lower incidence of overall nasal trauma in mask group as compared to prongs (36% *vs* 58%; RR 0.62, 95% CI 0.41-0.93; *P*=0.02). In terms of severity of nasal trauma, the infants in mask group had lower incidence of moderate trauma as compared to those in prongs group (7% *vs.* 21%; RR 0.31, 95% CI 0.10-0.91; *P*=0.02) which was statistically significant. The two groups were similar in terms of mild (*P*=0.55) and severe (*P*=0.48) nasal trauma.

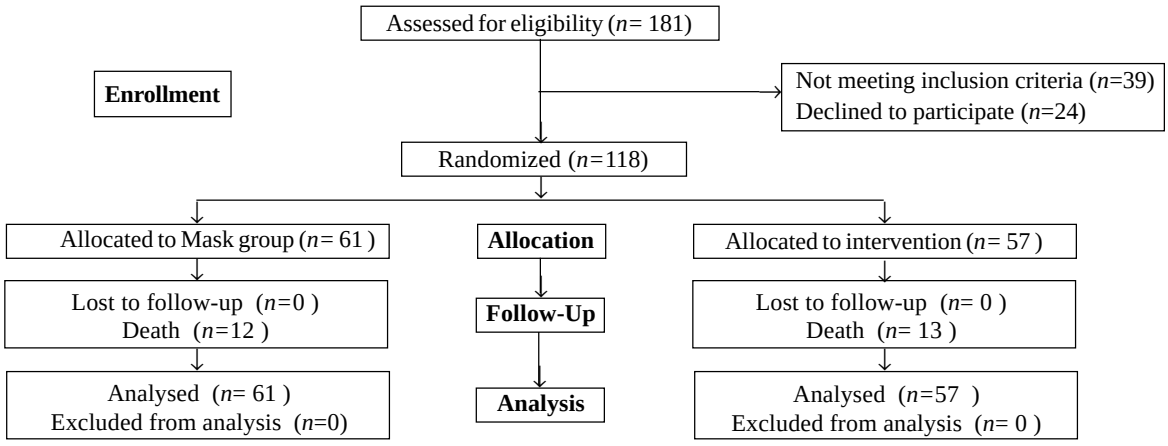

FIG. 1 *The flow of participants in the study.*

TABLE I BASELINE CHARACTERISTICS OF THE STUDY POPULATION (*N*=118)

Baseline Characterstics	*Nasal Mask (n=61)*	*Nasal Prongs (n=57)*
Gestational age (wks)	30.7 (2.2)	30.3 (2.2)
Birthweight (g)	1218 (201)	1176 (191)
Male, *n* (%)	32 (52)	27 (47)
Vaginal delivery, *n* (%)	48 (78)	40 (70)
IUGR, *n* (%)	14 (23)	10 (17)
PPROM, *n* (%)	22 (36)	17 (30)
Antenatal steroid, *n* (%)	36 (59)	35 (62)
Resuscitation need, *n* (%)	28 (46)	23 (40)
Apgar score 5 min	9 (8,9)	8 (7,9)
Age at respiratory support (h)	1.8 (0.5)	1.8 (0.4)
Surfactant	36 (59)	29 (51)
Multiple doses, *n* (%)	12 (20)	10 (18)
Age (h)	2.8 (0.8)	2.8 (1.5)
Initial FiO2 (%)	36.7 (7.1)	37.2 (8.1)
Maximum FiO_2 (%)	41.0 (8.0)	42.0 (8.3)
Maximum flow (L/min)	6.2 (0.7)	5.9 (0.4)
Maximum CPAP*	6 (5,6)	6 (5,7)

*All values in mean (SD) unless indiated; *median (interquartile range); CPAP: Continous positive airway pressure; PPROM: Preterm premature scripture of membranes; IUGR: Intrauterine growth retardation.*

All the infants in the study with mild and moderate nasal trauma recovered fully before hospital discharge except one with columella necrosis who had prolonged NCPAP support with prongs for 3 weeks.

DISCUSSION

In our study, we found a reduced NCPAP failure within 72 hours of initiation of respiratory support in preterms in the mask group when compared with the prongs group; however, this difference was statistically not significant. Incidence of PIE was significantly lower in the Mask group than the Prongs. There was a significantly lower inci-dence of moderate and overall nasal trauma in Mask group.

The major limitation of our study was its non-blinded design with potential for bias in particular with assessment of nasal trauma due to the very nature of the intervention. When we planned the study, we assumed NCPAP failure rate of 40% in Prongs group and 20% in Mask group. On completion of our study we found these rates were 25% and 13%, respectively. Our study was therefore underpowered to demonstrate difference, if any, between the two intervention interfaces. Another limitation of our study was it being a single center study, as NCPAP failure rates may vary in other units.

TABLE II COMPARISON OF OUTCOMES BETWEEN NASAL MASK AND NASAL PRONGS GROUPS

Outcomes	*Nasal Mask (n=61)*	*Nasal Prongs (n=57)*	*RR (95 % CI)*	*P value*
NCPAP Failure, n (%)	8 (13)	14 (25)	0.53 (0.24-1.17)	0.15
Duration of CPAP (d) *	6.1 (3.0)	5.3 (2.3)	1.15 (0.97-1.37)	0.09
Duration of supplementary oxygen (d)[#]	5 (3.5,8)	4 (4,9)	1.16 (0.32-4.13)	0.49
Pulmonary interstitial emphysema, *n* (%)	3 (4.9)	10 (17.5)	0.28 (0.08-0.96)	0.03
Pneumothorax, *n* (%)	3 (4.9)	2 (3.5)	1.40 (0.24-8.08)	1.00
PDA, *n* (%)	11 (18)	14 (24.5)	0.73 (0.36-1.48)	0.49
IVH, grades 3 and 4, *n* (%)	3 (4.9)	7 (12.2)	0.40 (0.10-1.47)	0.19
ROP ≥ stage 3, *n* (%)	4 (6.5)	6 (10.5)	0.62 (0.18-2.09)	0.51
BPD, *n* (%)	4 (6.5)	3 (5.2)	1.24 (0.29-5.32)	1.00
NEC, *n* (%)	3 (4.9)	5 (8.7)	0.56 (0.14-2.23)	0.48
EOS, *n* (%)	11 (18)	9 (16)	1.14 (0.51-2.55)	0.80
LOS, *n* (%)	15 (25)	12 (21)	1.16 (0.59-2.27)	0.66
Feeding intolerance, *n* (%)	12 (20)	15 (26)	0.74 (0.38-1.45)	0.51
Time to full feeds (d)*	13.9 (3.3)	14.5 (3.2)	0.96 (0.88-1.04)	0.38
Duration of hospital stay (days)[#]	22 (15,27)	19 (15,28)	1.08 (0.65-1.77)	0.95
Mortality, *n* (%)	12 (20)	13 (23)	0.86 (0.42-1.73)	0.48

** mean (SD); [#]median (interquartile range)*

BPD: Bronchopulmoary dytsplasia; PDA: Patent ductus arteriosis; IVH: Intraventricular haemorrhage; ROP: Retinopathy of prematurity; NEC: Necrotizing enterocolitis; EOS: Early-onset sepsis (culture proven); LOS: Late-onset sepsis (culture proven).

WHAT IS ALREADY KNOWN?

- Nasal Continuous Positive Airway Pressure (CPAP) can be delivered by using Nasal mask or Nasal prongs as an interface in preterm infants with respiratory distress.

WHAT THIS STUDY ADDS?

- Nasal mask is as effective as prongs for NCPAP delivery in preterm infants but causes less nasal trauma and pulmonary interstitial emphysema.

A study by Kerian, *et al*. [8], compared mask *vs* prongs using IFD, and found that in terms of NCPAP failure, nasal mask was superior than prongs which was statistically significant (28% *vs* 52%). Our overall CPAP failure rate was comparable to the previously done studies [16,17]. Air leaks are known complications of CPAP therapy [18]. We found low incidence of PIE in the mask group which was an unexpected finding in our study. Similar findings in the mask group have been previously reported [8], though not reaching statistical significance. Paradoxically, we found that delivering NCPAP with nasal masks required higher flows than prongs which was statistically significant. We assume that need for higher flows could be due to some leak at the interface level, which could have played a protective role for air leaks in the mask group. Further studies are required to elucidate, if any, the causal relation between the interface and air leaks.

Nasal trauma has been found to be a major drawback associated with NCPAP use. Injury pattern in the nasal mask group was primarily seen at the base of nasal bridge with occasional injuries at the junction between the nasal septum and the philtrum sparing the columella and septum. This may be because the mask rests on the nasal bridge and philtrum with constant pressure hampering local tissue perfusion which triggers breach of skin barrier leading to inflammation and nasal trauma. Injury pattern in prong group was mainly seen at columella and anterior part of nasal septum which may be due to constant pressure between the two prongs. These findings of different sites of injury are consistent with the pattern described in a previous study of nasal trauma [11].

We conclude that NCPAP with mask as interface is equally effective as providing NCPAP with short bi-nasal prongs, but causes less PIE and nasal trauma. We have used Bubble CPAP as a primary mode of respiratory support thus making our results more generalizable and applicable in resource-limited settings. As masks and prongs cause nasal trauma in differing distribution, we suggest that the interface to be alternated after every 72 hours if NCPAP to be used for prolonged duration. We recommend more multicentric RCTs with appropriate sample size to evaluate impact of various delivery interfaces on NCPAP success along with associated side effects.

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Contributors: SG, JM, HP: conceived and designed the study; JM, AU, SM: were involved in patient care; SG, DGH, HP: collected the data; SG, HP: analysis and interpretation of data; SG, DGH, JM: Drafting the manuscript. All authors approved the final manuscript.
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