



Effectiveness of Low Flow Oxygen Delivery through Nasal Prongs during Neonatal Endotracheal Intubation

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Abstract

Introduction: Significant disturbances in physiological parameters commonly accompany neonatal endotracheal intubation. Neonates who endure the procedure often experience adverse events, including bradycardia and severe oxygen desaturations. Thus, a study is needed to evaluate whether the oxygen system of nasal prongs reduces the risk of desaturation and bradycardia during neonatal intubation.

Methods: This hospital-based comparative observational study, conducted in AJ Institute of Medical Sciences, Neonatal Intensive Care Unit from July 2022 to April 2024, included 52 neonates fulfilling the inclusion criteria. Based on the study conducted by Kate A. Hodgson et al. (1) to detect a difference of 5bpm (L) in the heart rate between the two groups, assuming a 95% confidence interval and 80% power with a pooled SD of 6 bpm, the sample size was estimated.

Result: In this single-centered study, no statistically significant difference was observed. Successful intubation on the first attempt without physiological instability. Also, the two groups didn’t show any difference in the number of intubation attempts per procedure or duration of each intubation. The time to apply nasal prongs was an average of 30 seconds. Both groups didn’t show any significant difference in desaturation or bradycardia. The propensity for serious adverse effects was the same in both groups. The length of hospital stay or the number of esophageal intubations did not vary among the two groups. No correlation was found with modes of delivery.

Conclusion: Low-flow oxygen delivery through nasal prongs during neonatal endotracheal intubation is ineffective for newborn apneic ventilation as no positive findings were observed from our study. Better, more cost-effective methods need to be established.

Keywords: Nasal prongs, apneic oxygenation, neonatal intubation, desaturation and bradycardia during intubation, safe apnea time

Introduction

Neonatal endotracheal intubation is commonly accompanied by significant disturbances in physiological parameters. (2) Meanwhile, the opportunities for pediatricians to become proficient in neonatal intubation have decreased. (3,4) The use of noninvasive ventilation devices like CPAP and HFNC and minimally invasive procedures like LISA have reduced the need for intubation. (5,6)

Because of the lower functional residual capacity and greater metabolic demand of newborns than older children and adults, a neonate's condition is often clinically unstable during intubation. (8) Neonates who endure the procedure often experience adverse events, including bradycardia and severe oxygen desaturations. (9) Through bradycardia is rare, fall of oxygen saturation by 20% or more from the pre-intubation baseline level in approximately 50% of the caeses.(7) Complications of neonatal intubation are known to be increased with an increased number of attempts.(5) Safe and effective airway management of neonates requires unique knowledge and clinical skills(11), and interventions to improve the rates of safe and successful intubation in neonates are needed.

About 20-30secs can be taken for neonatal intubation during resuscitation. During endotracheal intubation, the safe apnea time is extended by using nasal oxygen. (1) This is based on the principle of apneic oxygenation which is basically the oxygenation of the newborn with no patient or external effort to move the lungs.(7) The physiological principle underlying apnoeic oxygenation is a ventilatory mass flow: in the apnoeic patient, as

oxygen moves from the alveoli into the bloodstream, alveolar pressure becomes subatmospheric. This, in turn, facilitates the movement of oxygen (applied via nasal prongs) down a pressure gradient from the atmosphere into the alveoli. (13)

Apnoeic oxygenation is used as an adjunct to preoxygenation in anesthesia, to prolong the period of time prior to desaturation in patients in whom definitive securing of the airway is expected to be difficult (due to anatomy), impossible (due to airway surgery), or the time to desaturation short (due to patient comorbidities).(14)

This study aims to demonstrate apneic oxygenation via low-flow oxygen delivery. A small amount (2l/min) of oxygen is delivered via low-flow nasal prongs. Nasal prongs provide a FiO₂ of 24-40 %, and are simple to use, and have good tolerance. (15) All prior studies done are on high-flow nasal prongs, and the high-flow system is not routinely available in a low-resource setting and poses a financial burden on the family of the neonate. The need for study is to evaluate if this system of oxygen delivery reduces the risk of desaturation and bradycardia during neonatal intubation.

Materials and Methods

Methodology

Primary Objectives: Successful intubation on the first attempt without physiological instability (defined as an absolute decrease in the peripheral oxygen saturation of >20% from the pre-intubation baseline level or bradycardia with a heart rate of <100 beats per minute in the newborn.)

Secondary Objectives

1. Peripheral oxygen saturation (%)
2. Heart rate (bpm)\
3. Number of intubation attempts per procedure

4. Duration of each intubation(sec)
5. Time to apply nasal prongs(sec)
6. Intubations in which desaturation occurred
 - a. Time to desaturate
 - b. Duration of desaturation
7. Intubations in which bradycardia occurred
 - a. Time to bradycardia
 - b. Duration of bradycardia
8. Serious adverse effects
 - a. CPR /Epinephrine administration within 1 hour after intubation attempt
 - b. Pneumothorax diagnosed within 72 hrs after randomizationc.
 - c. Death within 72hrs after randomization
9. Oesophageal intubation
10. Length of hospital stay

Source Of Data: All neonates undergoing oral endotracheal intubation in the delivery room or in the Neonatal Intensive Care Unit (NICU) at AJ Institute of Medical Sciences, Mangalore between the period of July 2022 and August 2024.

Study Design: A hospital based prospective comparative observational study.

Sample Size: 52 (26 in each group)

Study place: Neonatal intensive care unit of AJIMS, Mangalore-575004

Study Period: July 2022 to April 2024

Inclusion Criteria: A hospital based prospective comparative observational study.

Exclusion Criteria

- Neonates whose parent/ guardian do not consent for this study.
- Nasal intubation
- A heart rate of less than 120 beats per minute immediately before randomization

- Cyanotic congenital heart disease
- Preterm less than 28weeks

Data Collection Procedure: Informed consent will be obtained from the parents of neonates who fulfill the inclusion criteria. A detailed history will be obtained from the parents including family history, antenatal, natal and postnatal history. Vital signs, general examination, and systemic examination will be recorded. Clinico-etiological diagnosis will be made based on history and clinical examination. Hospital records and discharge summaries will be reviewed wherever available to collect extra information on the antenatal, natal and neonatal period. The newborns selected based on inclusion criteria will be grouped into two groups by purposive sampling. Group 1 will be given oxygen via nasal prongs during endotracheal intubation while group 2 will be subjected to standard intubation practice with no nasal prongs. Sedation will be done with MIDAZOLAM. Subsequent intubation episodes in the same neonate could be included in the analyses if there was at least 1 week. The preintubation fraction of inspired oxygen, the use of pre-oxygenation, duration, and termination of the intubation attempt will be at the discretion of the clinician leading the procedure. All infants will be monitored with the use of a low perfusion Massimo pulse oximeter . In intubations assigned to the nasal prongs group, an investigator will apply appropriately sized basal prongs immediately after removing the preexisting respiratory support interface before laryngoscopy. The tubing circuit will be secured behind the infant's head without adhesive tapes, and the gas flow was set to 2 liters per minute, which provides a FiO₂ of 28 %. (16) Oxygenation will be continued throughout laryngoscopy; after the first intubation attempt, it will be discontinued. In the intubations

assigned to the standard-care group, the intubation attempt will proceed without any oxygen delivery during intubation.

Statistical Analysis

Descriptive statistics will be used to describe the baseline data. Z test will be used to test the significant difference in the outcomes such as heart rate, Spo2, time taken to desaturate. Chi square test will be used to test significant difference in the outcome between groups. P value <0.05 will be considered statistically significant. Based on the study conducted by Kate A. Hodgson, Louise S. Owen, C. Omar F. Kamlin, Calum T. Roberts, Sophie E. Newman, Kate L. Francis et al, in order to detect a difference of 5bpm (L) in the heart rate between the two groups assuming 95% confidence interval and 80%power with pooled standard deviation (SD) of 6 bpm, sample size estimated for the study is 22.5 approximately equal to 23 in each group, Assuming 10% drop out rate, the final sample size estimated for the study is 25 in each group.

Sample size calculation:

$$n = \frac{(z(1-\alpha/2)+z(1-\beta/2))^2 2SD^2}{L^2}$$

The total number of samples obtained was 52, and that has been used for statistical analysis.

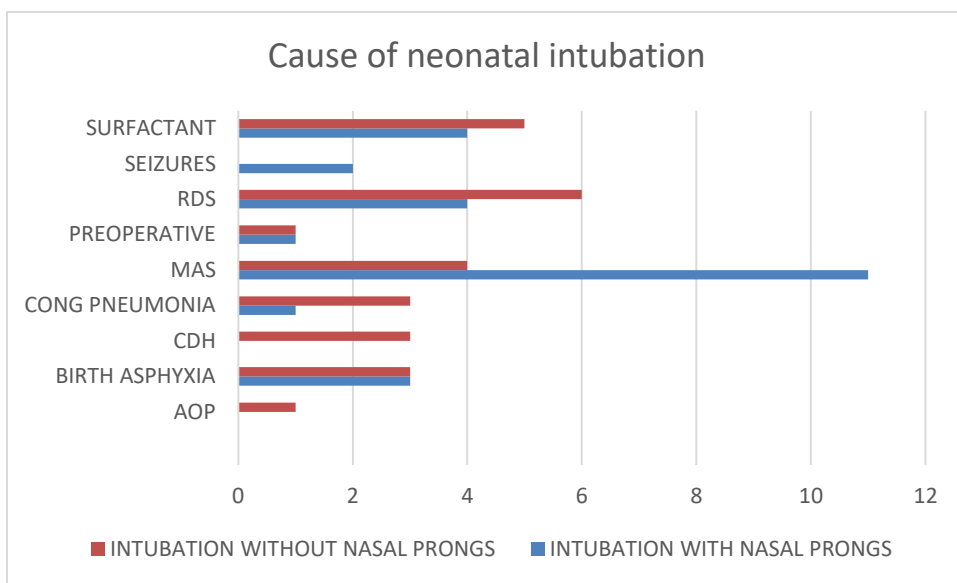
Ethical Considerations: The research was reviewed and approved by the Institutional Ethics Committee (DCGI Reg. No. EC/NEW/INST/2020/741) dated 25/07/2022). Written informed consent was taken from the patient’s parents/ guardian prior to enrolment in the study.

Results

The baseline characteristics are represented in Table 1. In the group where intubation was done with nasal prongs, the most common cause for intubation was meconium aspiration syndrome (42.31%). In contrast, in the other group, the major cause was respiratory distress syndrome (23.08%). (Figure 1). The baseline characteristics in the two groups didn’t show any statistically significant difference.

		Nasal prongs used during intubation	Nasal prongs not used during intubation	P value
Gender	Male	9	13	0.262
	Female	17	13	
Weight for gestational age	LGA	2(7.7%)	0	0.221
	AGA	24 (92.3%)	25(96.2%)	
	SGA	0	1 (3.8%)	
Gestational age	Preterm	9 (34.6%)	15 (57.7%)	0.126
	Term	17 (65.4%)	11(42.3%)	
Mode of delivery	LSCS	16(61.5%)	21 (80.8%)	0.095
	Vaginal	10 (38.5%)	5 (19.2%)	

Table 1: Baseline characteristics



Graph 1: Cause of neonatal intubation

		Nasal prongs used during intubation	Nasal prongs not used during intubation	P value
Successful intubation on the first attempt	No	12 (46.2 %)	14 (53.8%)	0.579
	Yes	14 (53.8%)	12 (46.2 %)	
Desaturation >20 %	No	22 (84.6%)	19 (73.1%)	0.308
	Yes	4 (15.4%)	7(26.9%)	
Bradycardia	No	26(100.00%)	23(88.50%)	0.235
	Yes	0	(3)11.50%	
Time to apply nasal prongs	<30secs	13(50%)	NA	
	>30secs	13 (50%)	NA	
Esophageal intubation	0	14 (53.8%)	13(50%)	0.415
	1	10 (38.5%)	7 (23.90%)	
	2	2 (7.7%)	5 (19.20%)	
	3	0	1(3.8%)	

Table 2: Outcomes with respect to (i) Successful intubation on the first attempt (ii) Desaturation >20 % (iii) Bradycardia (iv)Time to apply nasal prongs (v) Oesophageal intubation

In the group where nasal prongs were used for intubation, 53.8% were successfully intubated on the first attempt, while in the other group 46.2% were successful in the first attempt although this difference was not statistically significant. In nasal prongs used category, 15.4% had desaturation more than 20%, while

the rest had desaturation less than 20%. Similarly, in intubations done without nasal prongs, 26.9% had desaturation more than 20% while 73.1% did not. It was observed that when intubation was done with nasal prongs, none of the newborns had bradycardia. In the other group where intubation was done without nasal prongs, three newborns (11.50%) had bradycardia. None of these results showed statistically significant difference between the two groups. Both categories each account for exactly 50% of the total instances, with 13 occurrences. This suggests the time it takes to perform this task, indicating that individuals are equally

likely to take less than 30 seconds or more than 30 minutes to apply a nasal prong.

In the group where nasal prongs were used during intubation, the median number of intubations per procedure is 1.0000, with an IQR of (2-1), while for the no group, the median is 1.5000, with an IQR of (2-1). With a p-value of 0.455, thus, there is no significant difference in the number of intubations per procedure between patients who received the nasal intervention and those who did not. In both groups, the median duration of each intubation is 30 seconds, with a p-value of 0.903. (Table 3)

		Median	IQR	U- value	P-value
Number of intubation per procedure	nasal prongs used	1	(2-1)	301	0.455
	nasal prongs not used	1.5	(2-1)		
Duration of each intubation	nasal prongs used	30	(35-25)	331.5	0.903
	nasal prongs not used	30	(38-20)		

Table 3: Number of intubations per procedure and duration of each intubation

	Nasal prongs used	N	Mean	Std. Deviation	t value	p value
Time to desaturate	YES	4	22.5	9.574	0.253	0.805
	NO	7	21.429	4.756		
Duration of desaturation	YES	4	23.75	24.281	0.196	0.849
	NO	7	25.71	9.322		
Time to bradycardia	YES	0 ^a				
	NO	3	23.33	11.547		
Duration of bradycardia	YES	0 ^a				
	NO	3	11.67	2.887		

a-t cannot be computed because at least one of the groups is empty.

Table 4: Time and duration of Desaturation and bradycardia

When nasal prongs were used for intubation, in the four newborns that desaturated, the time to desaturate was 22.5 ± 9.574 and duration of desaturation being $23.75 + 24.281$. while when intubation was done without

nasal prongs, in the seven newborns who desaturated, the time to desaturate was $21.429 + 4.756$ with the duration of desaturation being $25.71 + 9.322$, the p-value of both being statistically insignificant. When

nasal prongs were used for intubation, no newborn had bradycardia. When intubation was done without nasal prongs, three newborns had bradycardia, and the time to bradycardia was 23.33 ± 11.547 with duration of bradycardia of 11.67 ± 2.887 . (table 4)

Both groups have identical distributions: 3.8% of cases resulted in DAMA, 50.0% in death, and 46.2% in discharge. (Figure 2) In the group where nasal prongs was used for intubation, the majority of 17(65.39%) patients had stays of less than 15 days, followed by 6(23.08%) for 15-30 days, and 3(11.54%) had more than 30 days of hospital stay. In the group where intubation was done without nasal prongs, 12(46.15%) had hospital stay of less than 15 days, also 12(46.15%) for 15-30 days, and 2(7.690%) were in the hospital for more than 30 days. (Figure3)

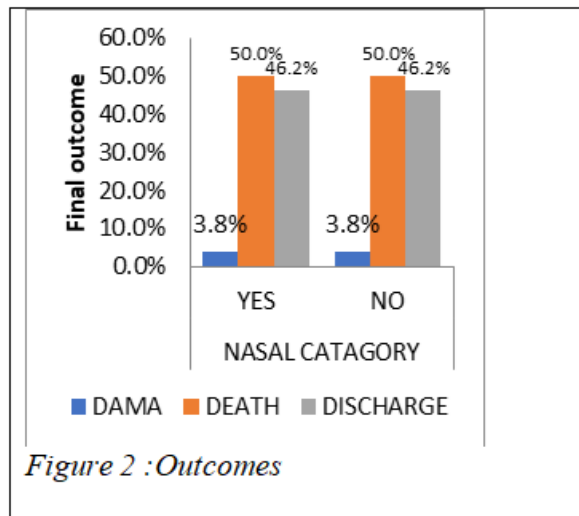


Figure 2 :Outcomes

Graph 2:

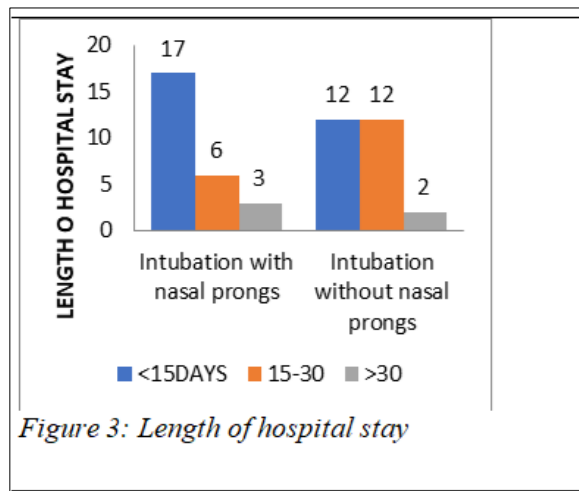


Figure 3: Length of hospital stay

Graph 3:

		Nasal prongs used		chi square	p value
		Yes	No		
CPR/Epinephrine administration within 1 hour after intubation attempt	No	26 (100%)	24(92.3%)	2.08	0.149
	Yes	0	2(7.7%)		
Pneumothorax diagnosed within 72 hrs after randomization	No	26 (100%)	24(92.3%)	2.08	0.149
	Yes	0	2(7.7%)		
death within 72hrs after randomization	No	24 (92.3%)	20(73.9%)	2.364	0.124
	Yes	2(7.7%)	6 (23.1%)		

Table 5: Serious adverse effect

In the group where intubation was done without nasal prongs, two newborns needed CPR and epinephrine administration within 1 hour after the intubation attempt and two newborns developed pneumothorax. The chi-square value calculated for this data is 2.080 with a p-value of 0.149 is not statistically significant. In the group where nasal prongs was used during intubation, two children succumbed within 72 hours while in the newborns who were intubated without nasal prongs, 6 newborns died within 72hrs of randomization. Though the number of deaths appears to be higher in newborns intubated without nasal prongs, the calculated chi-square value for this dataset is 2.364, resulting in a p-value of 0.124 showing no statistical significance. (table 5)

Discussion

In this single-centered study, we sought to determine the effectiveness of using nasal prongs during neonatal intubation. Among the participants who received intubation with nasal prongs, 9 were females (34.6%), and 17 were males (65.4%). Conversely, among those intubated without nasal prongs, 13 were females, making up 50.0%, and 13 were males, also making up 50.0%. Among those intubated with nasal prongs, the weight for majority was AGA with 24 participants (92.3%) and a smaller proportion, comprising two newborns (7.7%), fell into the LGA category. For participants who were intubated without nasal prongs, the majority were classified as AGA with 25 (96.2%). Only one newborn (3.8%), was SGA. For participants intubated with nasal prongs, 9 (34.6%) were preterm, while the rest (65.4%) were term newborns. In the other group, newborns were intubated without nasal prongs; 57.7% were preterm, while 42.3% were term. The baseline characteristics in both the groups, including Gender, period of gestational,

and weight in relation to their gestation age in both groups, did not show any statistically significant difference.

The most common cause for intubation was meconium aspiration syndrome in the group using nasal prongs for intubation, while in the other group, it was respiratory distress syndrome. The likelihood of successful intubation on the first attempt without physiological instability in the newborn didn't have any significant difference compared with standard care. Our study didn't reveal any significant difference with respect to heart rate and saturation levels in the two groups. The time to apply nasal prongs was an average of 30 seconds. Time to desaturate in the four newborns that desaturated in the nasal prongs group was $22.5 + 9.574$ with a duration of desaturation of 23.75 ± 24.281 while in the other group, it was $21.429 + 4.756$ with a duration of desaturation of 25.71 ± 9.322 none of which were statistically significant. No bradycardia was noted in the group where intubation was done with nasal prongs, while in the other group, the time to bradycardia was $23.33 + 11.547$ with the duration of bradycardia of 11.67 ± 2.887 .

In terms of final outcome categorized as death, discharge against medical advice or discharge, the two groups didn't not reveal any statistically significant difference. The use of nasal prongs didn't reduce the number of attempts of intubation. Though the number of newborns needing CPR or epinephrine administration within one hour, death within 72 hours of randomization and newborns developing pneumothorax were less when nasal prongs were used for intubation, these results were not statistically significant. As hypothesized, there was no statistically significant reduction in the number of oesophageal intubations or length of hospital stay. No

significant correlation was observed with respect to the mode of delivery. For participants who were intubated with nasal prongs used, 16 (61.5%) were born via LSCS. In the newborns intubated without nasal prongs, 80.8% were delivered via LSCS, and the rest (19.2%) were delivered vaginally ($\chi^2 = 2.768$, $p = 0.095$), hence not statically significant.

No similar studies have been published to date, though the use of high-flow nasal cannula for intubation has been elucidated.

According to the study by Kate A. Hodgson et al. 1, who used HFNC for apnoeic oxygenation, the median oxygen saturation during the first intubation showed a 5.0 percentage-point difference in the median values (95% CI, 1.1 to 8.9). Among the infants with an episode of oxygen desaturation, the mean time to desaturation in the high-flow group was longer (44.3 seconds) than in the standard care group (35.5 seconds). The other secondary outcomes that included the median number of intubation attempts, the duration of the first and any subsequent intubation attempts, the percentage of intubations that were oesophageal intubations, and the percentage of intubations in which a serious adverse event occurred were similar in the two treatment groups.

A Patel and S A R Nouraei used Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE), and this study showed that using THRIVE increases the apnoea time in patients. No patient experienced arterial desaturation < 90%. They concluded that it has the potential to transform the practice of intubation by changing the nature of securing a definitive airway in emergency and difficult intubations from a pressured stop-start process to a smooth and unhurried undertaking. (14)

An RCT – THRIVE in children showed Transnasal humidified rapid-insufflation ventilatory exchange prolongs the safe apnoea time in healthy children but has no effect to improve CO₂ clearance. The Stabilisation with nasal High flow during Intubation of NEonates (SHINE) trial is a multicentre, randomized controlled trial comparing the use of nasal high flow during neonatal intubation with standard care (no nasal high flow). This trial also aimed at the evaluation of the effectiveness of HFNC during endotracheal intubation and is still ongoing. (15)

Our trial has several limitations. Firstly, the treatment assignments were not concealed. Secondly, intubation is a skill-dependent procedure. Though all the performers were NRP trained, there could still be some bias. Thirdly, the long-term outcome could also depend on the patient's condition. For example, a newborn with severe meconium-stained amniotic liquor would have a relatively poorer outcome compared to a moderate preterm with RDS.

Conclusion

Neonatal intubation is one of the most common procedures performed in the NICU. It's an evolving process that provides scope for improvement in techniques and modifications. Apneic ventilation is one window for the same. This study, we sought to determine the effectiveness of low-flow nasal prongs during neonatal intubation. According to this study, the use of nasal prongs didn't have any significant effect on bradycardia or desaturation. While the current study did not produce positive results, it underscores the need for continued research and potential refinements in techniques for neonatal intubation. Future studies should focus on exploring more effective methods to

improve outcomes for newborns requiring intubation and apneic oxygenation.

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