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Original Article

A Comparison between Nasal Intermittent Positive Pressure Ventilation and Nasal Continuous Positive Airway Pressure Ventilation in the Treatment of Neonatal Respiratory Distress Syndrome

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ABSTRACT

***Background*:** Nasal intermittent positive pressure ventilation (NIPPV) is a non-invasive ventilatory mode, which delivers mechanical ventilation via nasal tubes or prongs. The present study was conducted to compare the efficacy of NIPPV and nasal continuous positive airway pressure ventilation (NCPAP) in reducing the need for intubation in preterm infants with respiratory distress syndrome (RDS).

***Methods*:** This randomized, clinical trial was conducted at the neonatal intensive care unit of Imam Reza Hospital, affiliated to Mashhad University of Medical Sciences during eight months since April 2014. Preterm infants with RDS were recruited before showing any indications for endotracheal intubation after birth. The NIPPV and NCPAPV groups were matched in terms of clinical characteristics. Each infant was randomized to receive either NIPPV or NCPAPV immediately after extubation. Nasal ventilation was deemed successful if intubation was not required within at least 72 hours. Brain sonography was carried out on the third day of life in all infants. Data were recorded for all neonates until hospital discharge.

Results: In total, 28% (15/53) and 26.4% (14/53) of infants in the NIPPV and NCPAPV groups were intubated within the first 72 h after birth, respectively (P=0.168). Neither of the procedures induced major adverse effects, although the incidence rate and severity of intraventricular hemorrhage were higher in the NIPPV group, compared to the NCPAPV group (P=0.026).

***Conclusion*:** Although NIPPV is confirmed as the first-line treatment for the management of neonatal RDS, this mode of ventilation showed no superiority over NCPAPV in eliminating the need for mechanical ventilation in the present study.

Keywords: Nasal continuous positive airway pressure, Nasal intermittent positive pressure ventilation, Preterm infant, Respiratory distress syndrome

Introduction

Transfer from the intrauterine liquid environment to the extra uterine environment after birth is a critical developmental stage. Therefore, the lungs should start to exchange gas through their epithelial surface (1). Some infants suffering from prematurity or asphyxia will develop respiratory problems due to disturbance in this transitional period. In fact, respiratory problems are the most common cause of neonatal hospitalization; as a result, proper management of these infants is of pivotal importance.

Due to surfactant deficiency, lung compliance is diminished in preterm infants, leading to alveolar hypoventilation and diffuse atelectasis (1). These infants become cyanotic in the room air and present with significant respiratory distress and retractions in the first hours of life (2). The condition of these infants normally deteriorates within the subsequent 48 hours, thus necessitating intubation and assisted ventilation in the majority of cases.

Today, the management and prognosis of respiratory distress syndrome (RDS) are

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comprised of exogenous surfactant therapy and assisted ventilation (2). Generally, mechanical ventilation via endotracheal tubes has improved neonatal survival over the past 30 years. However, this procedure is deemed to be invasive, leading to multiple complications such as chronic obstructive pulmonary disease, pulmonary air leaks, endotracheal tube complications (e.g., tube displacement, obstruction, occlusion, atelectasis after extubation, palatal grooves and subglottic stenosis), bronchopulmonary dysplasia (BPD), chronic lung disease, infections (e.g., pneumonia and septicemia), impaired cardiac function, intracranial hemorrhage, patent ductus arteriosus (PDA), retinopathy of prematurity, delayed enteral feeding and complications of parenteral nutrition (3, 4).

Continuous positive airway pressure (CPAP) by delivering oxygen with high pressure throughout the respiratory cycle, particularly during exhalation, can prevent airway and alveolar collapse, deter neonatal hypoxia and reduce breathing efforts (5). Moreover, early use of nasal CPAP ventilation (NCPAPV), accompanied by surfactant administration, can significantly reduce neonatal morbidity and mortality (2).

In comparison with CPAP, nasal intermittent positive pressure ventilation (NIPPV), especially if synchronized, can lead to a greater decline in breathing efforts and frequency of apnea in preterm infants by providing intermittent ventilation and increasing minute ventilation (7). Several studies have confirmed the efficacy of NIPPV in reducing extubation failure and apnea in preterm infants (2). In the present study, we aimed to study the efficacy of NIPPV and NCPAPV in reducing the need for intubation in preterm infants with RDS immediately after birth.

Method

This study was performed on preterm infants (28-34 weeks of gestation) with a birth weight of 800-2500 g, admitted to the neonatal intensive care unit of Imam Reza Hospital due to respiratory distress (i.e., tachypnea, intercostal retraction and cyanosis in room air). Neonates with severe asphyxia or major congenital anomalies were excluded from the study.

After explaining the procedures to the families of infants and obtaining written informed consents, oxygen was delivered to the patients via short binasal prongs, suitable for the neonate's size. The infants were randomly allocated into two groups and were matched in terms of birth weight and gestational age at birth. Each group received oxygen immediately after birth via either NCPAPV (NCPAP pressure: 6 cmH_2O) or NIPPV (peak inspiratory pressure: 18-20 cmH_2O and positive end-expiratory pressure: 4-5 cmH_2O). The fraction of inspired oxygen was set as 21-50% to maintain SpO_2 at 85-95%.

The neonates were monitored, using pulse oximetry. Blood gas assessments were carried out in order to determine the need for intubation and mechanical ventilation. The intubation criteria included severe apnea, $pCO_2 > 60$, $pH < 7.25$ and refractory hypoxemia despite receiving > 50% O_2. The intubation-surfactant-extubation (INSURE) method was applied for surfactant administration (100 mg/kg/dose of Curosurf or Survanta) by associate professors of neonatology at Mashhad University of Medical Sciences, Mashhad, Iran.

The obtained data were recorded, using SPSS version 20. For inter-group comparisons, Chi-square test and student's t-test or Mann-Whitney test were performed. P-value less than 0.05 was considered statistically significant.

Results

From April to November 2014, 106 infants, who met the inclusion criteria, were randomly allocated into two separate groups in order to receive either NCPAPV (n=53) or NIPPV (n=53) immediately after birth. The two groups were matched in terms of birth weight, gestational age, cesarean section, antenatal steroid therapy, Apgar score, prenatal problems and RDS grade (Table 1).

The mean gestational age of the infants was 31.4 weeks (SD=1.9 weeks) and the mean birth weight was 1,636 g (SD=447.9 g); no significant difference was observed between the two groups in terms of these variables (P=0.113 and 0.534, respectively). In total, 55% and 43% of patients were male and female, respectively. Based on the results, 72% of newborns were delivered through cesarean section, while others were born via natural vaginal delivery.

As the results indicated, 15% of newborns did not receive antenatal steroid therapy. Prolonged premature rupture of membranes for more than 18 h was reported in 22.65% of subjects; however, no significant difference was detected between the two groups (P=0.165). Also, maternal diabetes and hypertension were reported in 8.5% and 20% of patients, respectively, and no significant difference was observed between the two groups (P=0.256 and 0.148, respectively).

The neonates were ventilated non-invasively through NCPAPV or NIPPV immediately after birth and surfactant was prescribed if needed, using the

INSURE method (i.e., intubation, surfactant administration and extubation for nasal ventilation). Overall, surfactant was administered in 52% of infants, and no significant difference was observed between the NCPAPV and NIPPV groups (P=0.130). These neonates were carefully observed for any indications of intubation during hospitalization.

According to the findings, 27% and 16% of patients required mechanical ventilation via endotracheal tubes in the first 72 h of life and after 72 h of hospital admission, respectively

Table 1. Demographic characteristics of infants in the two groups

	NCPAPV	NIPPV	P-value
Number of patients	53	53	
Gestational age (weeks)	31.1(2)	31.8(1.7)	0.113
Birth weight (g)	1650(486)	1622(437)	0.534
Gender (male)	64.2%	45.3%	0.025
Corticosteroid therapy	77.6%	66%	0.075
Prenatal steroid therapy	83%	86.8%	0.185
One-minute Apgar score (mean)	6.4	6.4	0.717
Five-minute Apgar score (mean)	7.7	7.8	0.614
Maternal conditions:			
Preterm premature rupture of membranes	20.8%	24.5%	0.165
Diabetes mellitus	9.4%	7.5%	0.256
Hypertension	17%	22.6%	0.148

Table 2. Outcomes of subjects in the two groups

	NCPAPV	NIPPV	P-value
Intubation:			
<72 h of birth	26.4%	28.3%	0.168
>72 h of birth	11.3%	20.8%	0.090
Duration of mechanical ventilation (days)	3.1	4.5	0.394
Duration of initial intubation (h)	30.5	36	0.812
Duration of nasal ventilation (days)	3.4	4.2	0.079
Duration of oxygen therapy (days)	7.4	8.5	0.337
Surfactant administration	49.1%	54.7%	0.130
Complications during nasal ventilation:			
Intraventricular hemorrhage	17%	28.3%	0.026*
Apnea	17%	24.5%	0.121
Hypercapnia	11.3%	13.2%	0.222
Sepsis	11.3%	13.2%	0.222
Air leaks	9.4%	17%	0.120
Pneumonia	5.7%	5.7%	0.322
Pulmonary collapse	6.7%	7.5%	0.281
Gastrointestinal complications	7.5%	9.4%	0.258
Pulmonary hemorrhage	3.8%	5.7%	0.319
Nasal damages	7.5%	11.3%	0.164
Patent ductus arteriosus	9.4%	11.3%	0.237
Bronchopulmonary dysplasia	3.8%	7.5%	0.319
Death	13.2%	13.2%	1.000
Length of hospital stay (days)	15.8	14.8	0.534

(Table 2). No significant difference was observed between the two groups in terms of need for intubation (P=0.168 and 0.090 for <72 h and >72 h, respectively) or even the time of initial intubation (P=0.812). As the results indicated, the mean duration of oxygen therapy and nasal ventilation was 8 and 3.8 days, respectively (P=0.337 and 0.079, respectively).

Complications leading to neonatal intubation included severe apnea (20.75%), hypercapnia (12.25%) and refractory hypoxia (30.7%). The occurrence of complications during nasal ventilation such as PDA, pulmonary hemorrhage, sepsis, severe nasal damages, necrotizing enterocolitis and pulmonary collapse was not significantly different between the groups. Intraventricular hemorrhage (IVH) occurred in 22.6% of patients. In fact, the incidence rate and severity of IVH were higher in the NIPPV group, compared to the NCPAPV group (P=0.026).

BPD, defined as dependence on oxygen therapy for more than 28 days, was reported as an important associated complication in 5.65% of patients (P=0.237). The mean duration of hospitalization was 15.3 days and 13.2% of patients died during this period; however, there was no significant difference between the two groups (P=0.534 and 1.00, respectively).

Discussion

Based on the present findings, there was no significant difference between NCPAPV and NIPPV in terms of intubation or ventilation rate within the first 72 h of birth. Additionally, the incidence of BPD, mortality rate and ventilation time were similar in the NCPAPV and NIPPV groups. However, the two groups were significantly different in terms of IVH, which was more prevalent in the NIPPV group.

The advantages of NIPPV over NCPAPV in the treatment of neonatal apnea and prevention of reintubation after extubation have been documented in several previous studies. However, conflicting results have been reported regarding the early use of NIPPV as the primary treatment for RDS. In this regard, Kishore evaluated 76 neonates (gestational age of 24-34 weeks) during the first 48 h of life and showed that NIPPV could reduce the risk of mechanical ventilation (8). In contrast, according to a study by Belcastro in 2007, risk of intubation due to the failure of non-invasive ventilatory support was similar between the NIPPV and NCPAPV groups, whereas pCO_2 level and risk of apnea were significantly lower in the NIPPV group (9).

In a study by Kugelman in 2007on 84 neonates, NIPPV significantly reduced the need for intubation within the first 72 h of life (25% vs. 49% for NIPPV and NCPAPV, respectively, P=0.04) and decreased the risk of BPD (2% vs. 17%, P=0.03) (10). In their research, similar to a recent study by Armanian, no significant difference was observed between NIPPV and NCPAP regarding intubation rate due to the failure of non-invasive ventilatory support. However, the length of hospital stay and need for oxygen support decreased in the NIPPV group, compared to the NCPAP group in Armanian's study (11).

In a study by Meneses on 200 neonates, NIPPV could not reduce the risk of intubation during the first 72 h of life (12). However, in a meta-analysis by Meneses, NIPPV primarily reduced the risk of intubation, although this decline in the intubation rate did not reduce the occurrence of BPD (13). Moreover, in the largest review study by Kirpalani on 1007 neonates (< 1000 g) during the first week of life, there was no significant difference between NIPPV and CPAP as either the primary or secondary treatment options after extubation (2).

Additionally, Hyeon-Soo Lee in 2014 evaluated 30 premature neonates requiring intubation in the delivery room. After the administration of surfactant within two hours after birth, the neonates were extubated and NIPPV or CPAP was commenced as secondary ventilatory support. As the results indicated, NIPPV was significantly more successful than NCPAP (14).

Gestational age and birth weight of infants in the present study were similar to Kugelman's research, whereas the values of these variables were higher in studies by Armanian and Kirpalani. In the study by Armanian, a statistically significant difference was found between the two groups in terms of gestational age and birth weight (P=0.012 and 0.01, respectively). It should be mentioned that in the present study, the first 72 hours after birth (when RDS has a progressive course) were evaluated, while in studies by Armanian and Kishore, assessments continued only for 48 hours after birth (8, 11).

In the majority of similar studies, surfactant was administered via the INSURE method, except Lee's research in which all neonates were intubated immediately after birth and surfactant was administered after extubation. In fact, mechanical ventilation even for a short period of time could induce lung injuries; therefore, the difference between the present results and previous findings is justifiable (14).

Compared to Kugelman's study, the mean Apgar score was lower in the present research. Despite the fact that neonates with a five-minute Apgar score of 5 were eliminated from our study, partial respiratory depression at birth might have influenced the final results. It should be mentioned that in other similar studies, the Apgar score was not considered.

Prophylactic treatment with aminophylline was applied for all neonates in our study, while in other similar research, use of aminophylline was quite limited and restricted to apnea (if occurred) as an adjuvant treatment. Overall, prophylactic treatment with aminophylline in neonates, who are candidates for non-invasive ventilatory support, may reduce the intubation rate and affect the overall results of non-invasive ventilatory support.

IVH as an important associated complication may occur due to severe fluctuations in cerebral blood flow or PaO_2 level. Although in previous studies, the occurrence of IVH was reported to be similar in NIPPV and NCPAPV, in the present study, this complication was surprisingly more common in the NIPPV group. Overall, use of appropriate nursing care can comfort the neonates under ventilation and use of synchronized methods for ventilation can reduce blood pressure fluctuations, decrease the risk of IVH in NIPPV and improve the final outcomes.

Kugelman showed that NIPPV could significantly reduce the incidence of BPD, whereas in the study by Kirpalani and the present research, no significant difference was observed between the two groups in terms of this variable (10, 2); this discrepancy may be justified by the higher Apgar scores and lower rate of IVH in Kugelman's study.

Overall, mortality rate in our study was estimated at 13.2% due to two major factors, i.e., sepsis and IVH, none of which had a direct association with the mode of non-invasive ventilation. Broadly speaking, the difference between the present findings and other similar studies may be due to variations in our study method, the study population and reported complications. Overall, although NIPPV, similar to CPAP at birth, can be applied to reduce the risk of intubation, further scientific studies are required before the routine use of this method, given the high occurrence of IVH, which may be the main cause of treatment failure in these infants.

Conclusion:

Overall, although NIPPV, similar to CPAP at birth, can be applied to reduce the risk of intubation, further scientific studies are required before the routine use of this method, given the high occurrence of IVH, which may be the main cause of treatment failure in these infants.

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