http:// ijp.mums.ac.ir
Original Article (Pages: 8339-8346)

A Comparative Study of Treatment Response of Respiratory Distress Syndrome in Preterm Infants: Early Nasal Intermittent Positive Pressure Ventilation versus Early Nasal Continuous Positive Airway Pressure

Mohammad Kazem Sabzehei[1], *Behnaz Basiri[1], Maryam Shokouhi[1], Maryam Naser[1]

[1]Department of Pediatrics, Hamadan University of Medical Sciences, Hamadan, IR Iran.

Abstract

Background

Infant respiratory distress syndrome (IRDS) is one of the main causes of serious complications and death in preterm infants. Both Nasal Continuous Positive Airway Pressure (NCPAP) and Nasal Intermittent Positive Pressure Ventilation (NIPPV) are known as the most common treatment strategies for IRDS. The present study intended to compare NCPAP and NIPPV in the treatment of preterm infants with respiratory distress syndrome.

Materials and Methods

To this double blind clinical trial study during a one-year period (2016 to 2017) in Fatemieh Hospital in Hamadan city (Iran), about 60 preterm RDS infants were randomly assigned into two treatment groups; the NIPPV group received the PIP (14–20 cmH2O), RR: 30-50/min, PEEP (5–6 cmH2O), FiO2 up to 60%. The NCPAP group received PEEP (5-6 cmH2o), Flow: 6-7 L/min, and FiO2 up to 60%

Results

There was not any significant difference in the mean values of gestational age (30.07±1.50 vs. 30.07±2.05; P>0.05), birth weight (1259±263 vs. 1235±285; P>0.05), and 1-minute Apgar score (5.53±1.13 vs. 5.33±1.34; P>0.05) between NIPPV and NCPAP treatment groups. Besides, the rate of recovery, mortality and disease complications was not significantly different between both groups. However, the duration of respiratory support was less in NIPPV than NCPAP (34.9±33.8 vs. 68.4±32 h; P=0.001).

Conclusion

According to the results, there was not significant advantage between the NIPPV vs. NCPAP methods in the treatment of RDS in preterm infants with very low birth weight.

Key Words: Infant, NCPAP, NIPPV, Preterm Infants, Respiratory Distress Syndrome.

*Please cite this article as: Sabzehei MK, Basiri B, Shokouhi M, Naser M. A Comparative Study of Treatment Response of Respiratory Distress Syndrome in Preterm Infants: Early Nasal Intermittent Positive Pressure Ventilation versus Early Nasal Continuous Positive Airway Pressure. Int J Pediatr 2018; 6(10): 8339-46. DOI: **10.22038/ijp.2018.31577.2795**

Corresponding Author:

Behnaz Basiri (M.D), Department of Pediatrics, Hamadan University of Medical Sciences, Hamadan, Iran. Fax: +98- 8138262151

Email: behnazbasiri@yahoo.com

Received date: Mar.23, 2018; Accepted date: Apr. 22, 2018

1- INTRODUCTION

Respiratory distress syndrome (RDS), caused by deficiency of surfactants, is one of the main causes of disease complications and death in preterm infants. As the gestational age decreases, the prevalence of respiratory distress syndrome rises. Surfactant therapy is known as an effective factor in shortening the time required for supportive ventilation. On the other hand, the survival of preterm infants with respiratory failure is mainly dependent on the mechanical ventilation devices whose usage increases the likelihood of complications including Bronchopulmonary dysplasia (BPD) and poor outcome of neurodevelopment (1, 2). In order to reduce the serious complications of invasive mechanical ventilation, the increasing use of non-invasive respiratory support strategies, esp. in preterm infants with RDS, is become popular (3).

Non-invasive ventilation is an appropriate alternative to invasive mechanical ventilation, with known effects on the treatment of respiratory distress syndrome in preterm infants, which is done through either Nasal Continuous Positive Airway Pressure (NCPAP) or Nasal Intermittent Positive Pressure Ventilation (NIPPV) that does not require an endotracheal tube and allows spontaneous breathing during positive pressure applied through nasal cannula. In the past, NCPAP was known as the main non-invasive ventilation strategy in premature infants while NIPPV has become more common in the recent years. Research has shown the superiority of NIPPV over NCPAP that is because the former strategy has been more successful in minimizing the need for invasive mechanical ventilation within the first 72 hours of neonatal life than NCPAP. Nevertheless, there was not any significant difference in the survival rate of preterm infants without bronchopulmonary dysplasia between NIPPV and NCPAP strategies (4- 6). Due to the increasing use of non-invasive ventilation (NIV) in neonatal intensive care units (NICUs), relatively few research on the potential merits and demerits of each of these strategies and diversity in research methods, indications and values of intended parameters, studies have led to different results and a few have recommended NIPPV as the preferred strategy for early respiratory protection (7). Therefore, the present study intended to compare the use of NCPAP and NIPPV for the treatment of respiratory distress syndrome in preterm infants with very low birth weight.

2- MATERIALS AND METHODS

2-1. Study design

The present randomized double blind clinical trial study was conducted at a level III neonatal care unit of Fatemieh Hospital in Hamadan city, Iran, during a one-year period from October 2016 to September 2017.

2-2. Inclusion and exclusion criteria

The inclusion criteria were: all admitted preterm infants with a gestational age of 28 to 34 weeks, who had respiratory distress syndrome after birth based on clinical examinations and chest X-ray. The exclusion criteria were an Apgar score of < 3 minutes reported at 5 minutes after birth, premature rupture of membranes of > 3 weeks, major anomalies, cyanotic heart disease, chromosomal anomalies such as trisomy 13-18-21, and pneumothorax upon birth.

2-3. Sample size

The sample size of the present study was estimated using ratio comparison formula:

$$n = \left(\frac{(z_{1-\alpha/2} + z_{\beta})^2 (P_1(1-P_1) + P_2(1-P_2))}{(P_1 - P_2)^2} \right)$$

Where:

α = %5

β = %20
P_1 = frequency of complications in the first strategy,
P_2 = frequency of complications in the second strategy,

Accordingly, previous studies (8) obtained almost 30 infants through this formula:

$$n = \left(\frac{\left(z_{1-0.05/2} + z_{.02}\right)^2 \left(5.37(1-5.37) + 9.39(1-9.39)\right)}{(5.37-9.39)^2} \right) \sim 30$$

2-4. Intervention

The preterm infants with spontaneous breathing and two or more respiratory distress symptoms (including retraction, grunting, nasal flaring and respiration rate of >60 per minute), or those with Silverman-Anderson score of 6 to 7 within the first 6 hours of birth were randomly divided into two treatment groups namely NIPPV, the first group, and NCPAP, the second group. Both treatment groups were ventilated through nasal cannula (prong) using a mechanical ventilation device.

The initial setting of the ventilation device was as follows for the NIPPV group: RR: 30-50/min, PIP (14-20 cmH_2o), PEEP (5-6 cmH_2o), I/T: 0.3-0.35 sec, Flow: 6-7 L/min, and Fio_2: up to 60%.

The initial setting of the ventilation device was as follows for the NCPAP group: PEEP (5-6 cmH_2o), Flow: 6-7 L/min, Fio_2: up to 60%.

The target oxygen saturation was 90-95 per cent. The device setup in both groups was based on ABG indices and clinical parameters. During the treatment period, a nasogastric tube was permanently fixed to the infants of both groups. Intratracheal surfactant was initially administered for both groups at the first two hours of birth based on Ntubation-SURfactant-Extubation (INSURE).

Weaning criteria from ventilation device included: lack of retraction or mild retraction, respiration rate of 30-60 per minute and oxygen saturation over %90 with PEEP< 5 and Fio_2< 30%. All the infants were monitored for 7 days in terms of their need for mechanical ventilation and likelihood of disease complications. Meanwhile, any evidence of pneumothorax, pulmonary hemorrhage, PDA and NEC was recorded.

2-4. Ethical consideration

The present study has been approved by the Ethics Committee of Hamadan University of Medical Science, No. P/4201/9/35/16 and was registered in Iranian Center for Clinical Trial under IRCT2014072618598N1.

2-5. Statistical analysis

All the observed data were analyzed based on chi-square and two-independent-samples t-test using $SPSS_{19}$. In all the aforesaid tests, the significance level was less than 0.05.

3- RESULTS

In the present study to compare NCPAP and NIPPV in the treatment of preterm infants with respiratory distress syndrome, 60 preterm infants were randomly assigned into two treatment groups. There was not any significant difference in the mean values of gestational age between NIPPV and NCPAP treatment groups (30.07±1.50 vs. 30.07±2.05; P> 0.05), birth weight (1259±263 vs. 1235±285; P> 0.05), and 1-minute Apgar score (5.53±1.13 vs., 5.33±1.34; P> 0.05), respectively. Moreover, there was not any statistically significant difference between both groups in terms of other intended variable except for NIPPV in which the amount of prenatal steroid was lower (P=0.029), and the analysis of arterial blood gases (ABG) was significantly worse before the onset of treatment (P=0.014). There was not any significant difference between NIPPV and NCPAP treatment groups after the therapy (**Table.1**). The results of **Table.2** indicate

there was not any evidence of sepsis in NCPAP or any necrotizing enterocolitis and pneumothorax in NIPPV group. Furthermore, PDA and pulmonary hemorrhage was less in NIPPV than NCPAP; while the likelihood of sepsis was higher in NIPPV than NCPAP, though the difference was not significant. Additionally, there was not any statistically significant difference between both groups in terms of the need for mechanical ventilation and rate of recovery. Nonetheless, NIPPV group required less time for respiratory support (34.9±33.8 vs. 68.4±32 hour; P=0.001).

Table-1: Demographic characteristics of population study

Variables	NIPVV (n=30)	NCPAP (n=30)	P-value
Birth weight (mean ± SD)	1259±263	1235±285	0.733
Gestational Age(mean ± SD)	30.07±1.50	30.07±2.05	1.000
Gender Male Female	 20(54.1) 10(43.5)	 17(45.9) 13(56.5)	0.596
Mode of delivery Cesarean NVD	 24 (47.1) 6 (66.7)	 27 (52.9) 3 (33.3)	0.472
Multiple Birth Singleton Multiple	 16 (44.4) 14(58.3)	 20 (55.6) 10(41.7)	0.215
Prenatal steroids Yes No	 6(28.6) 24(61.5)	 15(71.4) 15(38.5)	0.029
Apgar_1th	5.5 ± 1.1	5.3 ± 1.3	0.537
Apgar_5th	8 ± 1.1	7.5 ± 1.5	0.218
Max_PEEP	6 ± 0.4	6 ± 0.7	0.989
Min_PEEP	4.2 ± 0.6	3.7 ± 1.3	0.095
Max_Fio2	75.6 ± 15.4	63.2 ± 25.1	0.025
Min_Fio2	34.2 ± 28.6	33.9 ± 22.2	0.956
PH_Pre	7.1	7.2	0.014
PCO2_Pre	50.6 ± 5.6	43.4 ± 9.9	0.001
PO2_Pre	51.3 ± 7.3	65.7 ± 20	0.001
HCO3_Pre	16.8 ± 1.9	19 ± 2.6	0.001
PH_Post	7.3	7.2	0.291
PCO2_Post	42.6 ± 4.6	40.8 ± 11.9	0.452
PO2_Post	67.8 ± 13.3	73.6 ± 13.9	0.107
HCO3_Post	20.6 ± 2	20.4 ± 2.5	0.696

SD: Standard deviation; NVS: Normal vaginal delivery; PEEP: Positive end expiratory pressure; Fio2: Fraction of inspired oxygen; PCO2: Carbon dioxide partial pressure; HCO3: Bicarbonate; NIPVV: Nasal Intermittent Positive Pressure Ventilation; NCPAP: Nasal Continuous Positive Airway Pressure.

Table-2: Outcome of population study

Variables	NIPVV (n=30)	NCPAP (n=30)	P-value
Complications			
Yes	6(37.5)	10(62.5)	0.430
No	24(54.5)	20(45.5)	
Complication			
Pneumothorax	0(0)	1(3)	0.233
Pulmonary hemorrhage	3(10)	4(13)	
PDA	1(3)	2(6)	
NEC	0(0)	3(10)	
Sepsis	2(6)	0(0)	
Mechanical ventilation			
Yes	6(46.2)	7(53.8)	0.754
No	24(51)	23(49)	
Mechanical ventilation duration (mean ± SD) day	3.5 ± 8.8	1.5 ± 4.8	0.267
Strategy duration_(mean ± SD), hour	34.9 ± 33.8	68.4 ± 32	0.001
Length stay (mean ± SD) day	16.5 ± 9.3	19.2 ± 13.8	0.376
Survive	23(76.6)	23(76.6)	1.000

SD: Standard deviation; PDA: patent ductus arteriosus; NEC: Necrotizing enterocolitis; NIPVV: Nasal Intermittent Positive Pressure Ventilation; NCPAP: Nasal Continuous Positive Airway Pressure.

4- DISCUSSION

According to the results of the present study, there was not any statistically significant difference between NIPPV and NCPAP methods in reducing the need for mechanical ventilation. Some studies have been done in this regard, most of which suggest that the use of NIPPV is more beneficial while less complicated than NCPAP. However other studies in infants weighing less than 1,500 grams show no disadvantages. Meneses et al. studied 200 preterm infants (into 2 groups) with respiratory distress. They found that the need for mechanical ventilation was significantly less in NIPPV than NCPAP even though believing that further studies need to be conducted in this regard (4). Sai Sunil et al. showed that the initial use of NIPPV, compared to NCPAP, reduced the need for intubation and mechanical ventilation in preterm infants with respiratory distress (8). In a meta-analysis, Tag et al. conducted 14 case-control studies on 1,052 infants. They found that the use of NIPPV, compared to NCPAP, had more effects on reducing the need for intubation, increasing successful extubation and reducing the incidence of premature apnea. Moreover, the used of NIPPV led to fewer cases of death or BPD (9). Some past studies have also found more or less similar results indicating more advantages and less complications of NIPPV in comparison to NCPAP (5,10 - 13). In a comprehensive study, Robert et al. stated that although various studies had considered the use of NIPPV, as an initial respiratory support, more beneficial than NCPAP, it is a demanding job to generalize this finding to clinical practice due to the distinct methodology of these studies; thus, there is not any solid evidence to admit the superiority of NIPPV and BiPAP over NCPAP in reducing death and disease complications such as bronchopulmonary dysplasia and further studies are required (7). In the present study, there was not any statistically significant difference between NIPPV and NCPAP in terms of the incidence of such complications (sepsis, NEC, PDA, pulmonary hemorrhage and pneumothorax), the need for mechanical ventilation and rate of mortality.

Moreover, the parameters of ABG analysis were not significantly different in both groups after the therapy while they were significantly worse in NIPPV than NCPAP before starting RDS treatment. Furthermore, the amount of pre-natal steroid was significantly lower in NIPPV which resulted in RDS severity. In general, however, there was not any statistically significant difference between both groups in terms of disease complications. Chen et al. (14) and Shah Farhat et al. (15) found that there was not any significant difference between NIPPV, as an initial respiratory support for preterm infants with RDS treated with surfactant, and NCPAP in reducing intubation and subsequent complications of the disease, which was consistent with the findings of the present study.

In a meta-analysis, Li et al. found that although the need for invasive ventilation was significantly lower in the NIPPV group than NCPAP for preterm infants with RDS, esp. those treated with surfactant, NIPPV could not reduce the need for invasive ventilation for infants with GA $\leq$ 30 weeks or BW< 1,500 grams. Therefore, larger interventional studies are necessary to be conducted to investigate the difference between the initial outcomes and complications associated with both non-invasive respiratory supports. Since the present study included infants with BW< 1,500 g and mean GA of 30 weeks, it was consistent with the findings of new studies in this area with the same BW and GA group.

Consequently, it can be concluded that the reason for the preference of NIPPV in previous studies was examining both preterm and term infants with RDS (1); however, there was not any significant difference between both groups in a study on very preterm, GA< 32 weeks, due to the severity of RDS (16). It can be, in general, concluded that the lack of difference between NIPPV and NCPAP in reducing the need for mechanical ventilation, in the present study, was due to the intended infants being very preterm and VLBW as well as RDS severity in NIPPV group (10); the other reason was using Non-synchronized NIPPV in this study, but Gizzi et al. (17), and Moretti et al. (18) compared synchronized NIPPV and NCPAP. Despite all the aforesaid points, the time required for respiratory support was lower in NIPPV than NCPAP (34.9±33.8 vs. 68.4±32; P< 0.001) in the present study, which was in line with the findings of Armanian et al. (11); while there was not any significant difference between NIPPV and NCPAP in terms of disease complication, which was not consistent with the findings of Chen et al. (14).

5- CONCLUSION

According to the results, there was not a significant advantage between the NIPPV vs. NCPAP methods in the treatment of RDS in preterm infants with very low birth weight. However, the duration of respiratory support was less in NIPPV than NCPAP group.

6- ABBREVIATION

BPD: Bronchopulmonary dysplasia,
NCPAP: Nasal Continuous Positive Airway Pressure,
NEC: Necrotizing enterocolitis,
NIPPV: Nasal Intermittent Positive Pressure Ventilation,
NICU: Neonatal Intensive Care Unit,
PDA: patent ductus arteriosus,
PIP: Peak inspiratory pressure,
PEEP: Positive end expiratory pressure,
RR: Respiratory Rate,
RDS: Respiratory Distress Syndrome,
VLBW: Very low birth weight infants.
GA: Gestational age,
Fio2: Fraction of inspired oxygen.

7- CONFLICT OF INTEREST: None.

8- ACKNOWLEDGMENTS

The researchers of the present study would like to express sincere gratitude to all the respected staff of neonatal intensive care unit working in the Fatemieh Hospital in Hamadan province. The resent study was retrieved from a thesis in assistantship, No. 92503001, approved by the Vice-chancellor of Research and Technology of Hamadan University of Medical Sciences. It's worth mentioning that the present research was conducted without any fund from any financial institution or organization.

9- REFERENCES

1. Gallacher DJ, Hart K, Kotecha S. Common respiratory conditions of the newborn. Breathe. 2016; 12(1):30-42. doi:10.1183/20734735.000716.

2. Natarajan G, Pappas A, Shankaran S, et al. Outcomes of extremely low birth weight infants with bronchopulmonary dysplasia: impact of the physiologic defi nition. Early Hum Dev. 2012; 88(7):509–15.

3. Kugelman A, Feferkorn I, Riskin A, Chistyakov I, Kaufman B, Bader D. Nasal intermittent mandatory ventilation versus nasal continuous positive airway pressure for respiratory distress syndrome: a randomized, controlled, prospective study. J Pediatr. 2007; 150(5):521–6.

4. Meneses J, Bhandari V, Alves J. Nasal intermittent positive-pressure ventilation vs nasal continuous positive airway pressure for preterm infants with respiratory distress syndrome. Arch Pediatr Adolesc Med 2012;166(4):372-376.

5. Silveira CS, Leonardi KM, Melo AP, Zaia JE, Brunherotti MA .Response of Preterm Infants to 2 Noninvasive Ventilatory Support Systems: Nasal CPAP and Nasal Intermittent Positive-Pressure Ventilation. Respir Care. 2015; 60(12):1772-6. doi: 10.4187/respcare.03565.

6. Kirpalani H, Millar D, Lemyre B, Yoder BA, Chiu A, Roberts RS.A trial comparing noninvasive ventilation strategies in preterm infants. N Engl J Med 2013; 369(7):611-20.

7. Roberts CT, Davis PG, Owen LS.Neonatal Non-Invasive Respiratory Support: Synchronised NIPPV, Non-Synchronised NIPPV or Bi-Level CPAP: What Is the Evidence in 2013? Neonatology. 2013; 104(3):203-9.

8. Sai Sunil Kishore M, Dutta S, Kumar P. Early NIPPV versus CPAP for respiratoy distress syndrome. Acta Paediatr. 2009; 98(9):1412-5.

9. Tang S, Zhao J, Shen J, Hu Z, Shi Y. Nasal Intermittent Positive Pressure Ventilation versus Nasal Continuous Positive Airway Pressure in Neonates: A Systematic Review and Meta-analysis. Indian Pediatr. 2013; 50(4):371-6. Epub 2012 Oct 5

10. Shi Y, Tang S, Zhao J, Shen J. A prospective, randomized, controlled study of NIPPV versus nCPAP in preterm and term infants with respiratory distress syndrome. Pediatr Pulmonol. 2014;49 (7):6738.

11. Armanian A, Badiee Z, Heidari GH, Feizi A, Salehimehr N. Initial Treatment of Respiratory Distress Syndrome with Nasal Intermittent Mandatory Ventilation versus Nasal Continuous Positive Airway Pressure: A Randomized Controlled Trial. Int J Prev Med. 2014 Dec; 5(12): 1543–51.

12. Jasani B, Nanavati R, Kabra N, Rajdeo S, Bhandari V. Comparison of non-synchronized nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure as post-extubation respiratory support in preterm infants with respiratory distress syndrome: a randomized controlled trial. J Matern Fetal Neonatal Med. 2016;29 (10): 154651.

13. Bahman-Bijari B, Mahdian R, Niknafs P, Baneshi MR. Nasal intermittent positive pressure ventilation vs. nasal continuous positive airway pressure in preterm infants with respiratory distress. Zahedan J Res Med Sci. 2014; 16(11): 9-14.

14. Chen L, Wang L, Li J, Wang N, Shi Y. Noninvasive Ventilation for Preterm Twin Neonates with Respiratory Distress Syndrome: A Randomized Controlled Trial. Scientific

Reports. 2015; 5: 14483.

15. Shah Farhat A, Mohammadzadeh A, Saeidi R, Noorizadeh S. A Comparison between Nasal Intermittent Positive Pressure Ventilation and Nasal Continuous Positive Airway Pressure Ventilation in the Treatment of Neonatal Respiratory Distress Syndrome. Iranian Journal of Neonatology 2015; 6(4):1-6.

16. Li W1, Long C, Zhangxue H, Jinning Z, Shifang T, Juan M, et al. Nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure for preterm infants with respiratory distress syndrome: a meta-analysis and up-date. Pediatric Pulmonology. 2015; 50(4):402–409. Gizzi C, Papoff P, Giordano I, Massenzi L, Barbàra CS, Campelli M, et al. Flow-Synchronized Nasal Intermittent Positive Pressure Ventilation for Infants <32 Weeks' Gestation with Respiratory Distress Syndrome. Critical Care Research and Practice, 2012; 301818.

17. Moretti C, Giannini L, Fassi C, Gizzi C, Papoff P, Colarizi P. Nasal flow-synchronized intermittent positive pressure ventilation to facilitate weaning in very low-birthweight infants: unmasked randomized controlled trial. Pediatr Int 2008; 50: 85-91.