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# Comparing the Efficacy of NCPAP and NIPPV in Infants with RDS after Extubation; A Randomized Clinical Trial

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**Abstract**

**Background:** Respiratory distress syndrome (RDS) is the most common respiratory disorder of premature infants and leading cause of mortality. The main progress in RDS management is attributable to prescription of surfactant for fastening pulmonary maturation.
**Objectives:** In this study we aimed to compare nasal continuous positive airway pressure (NCPAP) with nasal intermittent positive pressure ventilation (NIPPV) in infants with RDS lower than 1800 gr of birthweight.
**Methods:** In this randomized clinical trial, infants with confirmed diagnosis of RDS who underwent treatment with surfactant and mechanical ventilation were randomly allocated to two NCPAP and NIPPV groups. Duration of hospitalization, oxygen therapy, respiratory protection, need for re-intubation and complications were recorded in a pre-designed checklist.
**Results:** Eventually 60 (37 males and 23 females) infants with mean gestational ages of 31.73±1.72 weeks in NCPAP and 32.6±1.92 weeks in NIPPV group underwent analysis (p=0.096). Infants in NCPAP group underwent mechanical ventilation for a mean duration of 3.3±1.7 days; while it was 2.4±0.96 days for infants in NIPPV group (p=0.026). The mean received doses of surfactant was 2.36±0.66 in NCPAP and 1.9±0.25 in NIPPV group (p=0.005). After intervention, infants in NCPAP group had a mean arterial oxygen saturation of 91.36±3.03%; while it was 91.3±4.03% for those in NIPPV group (p=0.669). Mean arterial oxygen pressure was 67.6±6.91 mmHg in NCPAP group and 75.2±7.2 mmHg in NIPPV group after intervention (p=0.045).
**Conclusion:** We found that NIPPV is more effective than NCPAP in decreasing need for reintubation and invasive mechanical ventilation in premature infants with respiratory distress syndrome and it also shortens the duration of hospitalization.

*Keywords:* Mechanical ventilation, NCPAP, NIPPV, Respiratory distress syndrome

## 1. Background

Involving 60% of infants with gestational ages of less than 30 weeks and 42% of infants with birthweight of lower than 1500 gr, respiratory distress syndrome (RDS) is the most common respiratory disorder of premature infants and leading cause of mortality (1,2). Also known as hyaline membrane disease (HMD), RDS may occur immediately or some hours after birth which may lead to respiratory failure if no effective action is taken (3).

The main progress in RDS management is attributable to prescription of surfactant for fastening pulmonary maturation. Respiratory protection, such as mechanical ventilation and nasal continuous positive airway pressure (NCPAP), and surfactant are building blocks of disease treatment (4-6). However; infants under mechanical ventilation are at higher risks of pulmonary damage and up to 30% get chronic respiratory disease (7-9). Previous studies have indicated that using NCPAP in early minutes after birth is associated with lower incidence of chronic respiratory disease, bronchopulmonary dysplasia and intracranial hemorrhage; so it has turned into a common method of respiratory protection (10-12).

On the other hand, using NCPAP has some clinical limitations. Problems with placing nasal prongs in infants' small nostrils and septal trauma are among these limitations (13,14). Nasal intermittent positive pressure ventilation (NIPPV) is a relatively newer method of respiratory protection which has been successfully applied in adults and older children (15). Some previous studies have mentioned NIPPV as primary treatment of infants with RDS and reported its preventing effects on intubation (16,17). Considering that no similar studies have been yet conducted in Iran, we aimed to compare NCPAP with NIPPV in infants with RDS lower than 1800 gr of birthweight.

## 2. Objectives

To compare NCPAP with NIPPV in infants with RDS lower than 1800 gr of birthweight.

## 3. Methods

This randomized clinical trial was conducted between March 2016 and October 2016 in Najmiyeh university hospital, Tehran, Iran. This study was registered at ethics committee of Baqiyatallah University of Medical Sciences (Ref. No:IR.BMSU.REC. 1395.174) and Iranian Registry of Clinical Trials (Ref. No: IRCT2017050517413N25). Figure 1 shows a flowchart of the trial. Infants with confirmed diagnosis of RDS who underwent treatment with surfactant and mechanical ventilation were assessed

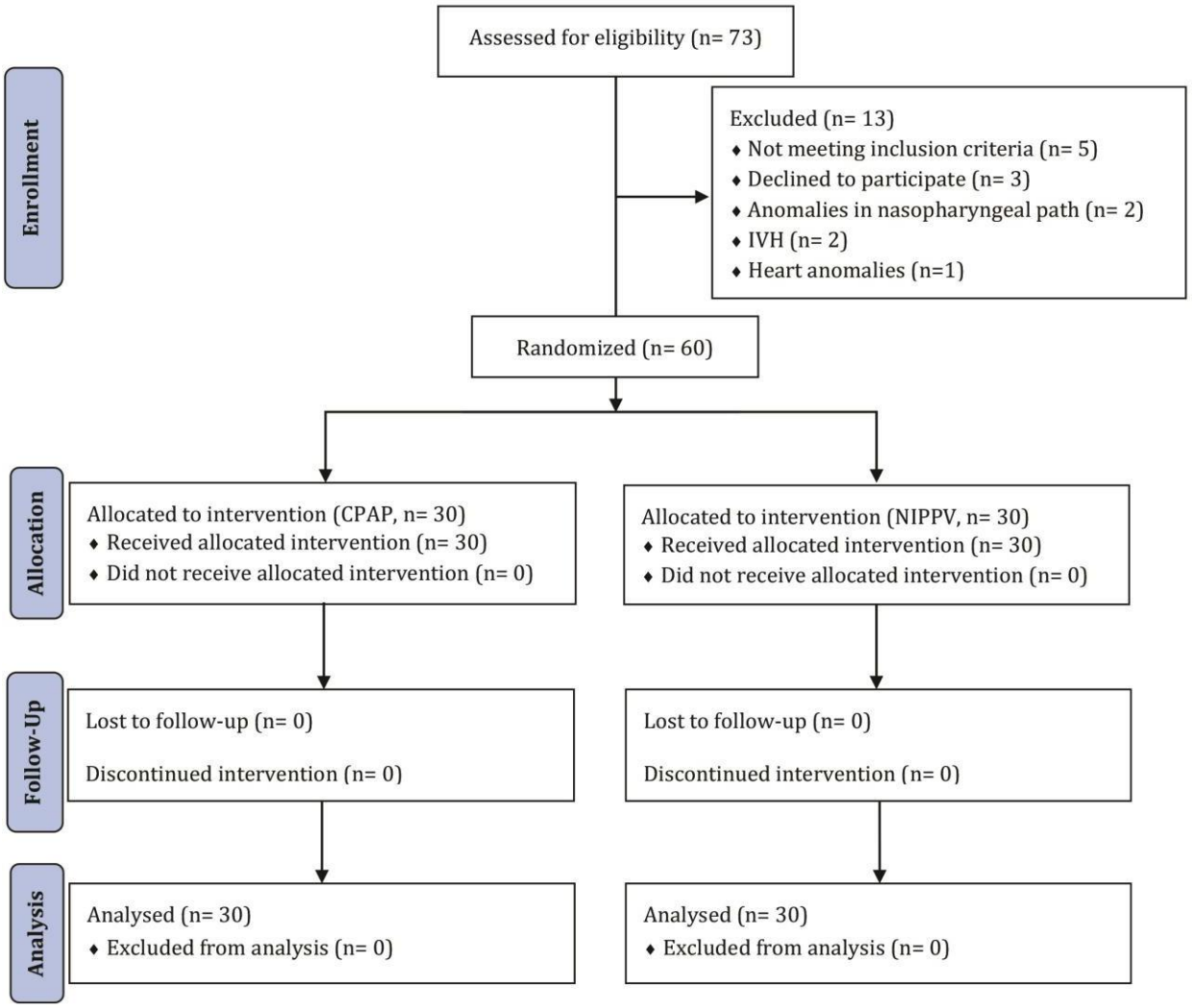


**Figure 1.** Study flowchart

for eligibility. Patients were selected using simple random selection. Diagnosis was made based on chest radiography, respiratory rate, arterial blood gas (ABG), grunting, cyanosis and physical examination by a single neonatologist. Patients with gestational ages of less than 34 weeks, birthweight of less than 1800 gr, respiratory distress despite receiving surfactant and mechanical ventilation and needed $FIO_2$ of less than 60% after extubation were included in the study. Infants with anomalies in nasopharyngeal path, heart or lungs, chromosomal anomalies, intraventricular hemorrhage (IVH) and those not willing to participate were excluded from the trial.

After primary care and extubation, infants were randomly allocated to two groups using random number table; the first group underwent respiratory support by NCPAP using small mask and the second group received NIPPV using nasal prongs. Mean positive end-expiratory pressure (PEEP) was 5 $cmH_2O$ and mean $FIO_2$ was 60% in CPAP group. In NIPPV group, mean applied peak inspiratory pressure (PIP) was 18 $cmH_2O$, mean rate was 40 and mean $FIO_2$ was 66.6%. Demographic information as well as the required duration of hospitalization, oxygen therapy, respiratory protection, the need for re-intubation and complications were recorded in a pre-designed checklist.

Data were analyzed using SPSS software version 21 (SPSS Inc., Chicago, IL) for Microsoft Windows. Normal distributed variables (approved by 1-sample Kolmogorov-Smirnov test) were compared using independent sample *t*-test between the groups. The chi square test was used to compare categorical variables in the two groups. Mean and standard deviation (SD) were used for describing categorical variables. A p value of less than 0.05 was considered as statistically significant.

## 4. Results

Eventually 60 (37 males and 23 females) infants with mean gestational ages of 31.73±1.72 weeks in

**Table 1.** Treatment complications of study individuals

| Complication | NCPAP (N=30) | NIPPV (N=30) | p Value |
|---|---|---|---|
| Distention N (%) | 3(10%) | 2(6.7%) | 0.573 |
| Pneumothorax N (%) | 0 | 0 | - |
| Intraventricular Hemorrhage N (%) | 2(6.7%) | 0 | 0.00 |
| Bronchopulmonary Disease N (%) | 0 | 0 | - |
| Necrotizing Enterocolitis N (%) | 0 | 0 | - |

**Table 2.** Demographic information of study individuals

| | NIPPV | NCPAP | p Value |
|---|---|---|---|
| **Mean Birthweight (gr)** | 1529.3±225.7 | 1490±265.09 | 0.511 |
| **Mean Gestational Age (week)** | 32.6±1.92 | 31.73±1.72 | 0.096 |
| **Surfactant (Doses)** | 1.9±0.25 | 2.36±0.66 | 0.005 |
| **Respiratory Support (days)** | 2±0.18 | 2.6±0.67 | <0.001 |

NCPAP and 32.6±1.92 weeks in NIPPV group underwent analysis (p=0.096). All infants in both groups were born by caesarean section. Mean birthweight was 1490±265.09 gr in NCPAP and 1529.3±225.7 gr in NIPPV group (p=0.511). Infants in NCPAP group underwent mechanical ventilation for a mean duration of 3.3±1.7 days; while it was 2.4±0.96 days for infants in NIPPV group (p=0.026). Mean received doses of surfactant was 2.36±0.66 in NCPAP and 1.9±0.25 in NIPPV group (p=0.005). Patients underwent respiratory support with NCPAP for 2.6±0.67 days and 2±0.18 days with NIPPV (p<0.001). After intervention, infants in NCPAP group had a mean arterial oxygen saturation of 91.36±3.03%; while it was 91.3±4.03% for those in NIPPV group (p=0.669). Mean arterial oxygen pressure was 67.6±6.91 mmHg in NCPAP group and 75.2±7.2 mmHg in NIPPV group after intervention (p=0.045) (tables 1 and 2). Table 1 shows treatment complications of study individuals. Abdominal distention was the most prevalent complication among infants in both NCPAP (10%) and NIPPV (6.7%) groups. Respiratory distress syndrome occurred in 7 (23.3%) infants following treatment with NCPAP and in 3 (10%) infants who underwent treatment with NIPPV (p=0.045). Mean respiratory rate was 64.5±4.97 in NCPAP and 56.8±5.79 in NIPPV group (p=0.01). Mean duration of hospitalization was 18.36±1.14 days in NCPAP and 11.8±5.6 days in NIPPV group (p=0.026). Two (6.7%) infants in NCPAP group and no infants in NIPPV group required reintubation (p=0.161). Feeding intolerance was recorded for 3 (10%) infants in NCPAP and 3 (10%) infants in NIPPV group.

## 5. Discussion

In the present study, we found that duration of treatment with NIPPV was about half day shorter than treating the infants in NCPAP group. Also, mean arterial oxygen pressure was significantly higher and respiratory rate was significantly lower in infants who underwent treatment with NIPPV. Abdominal distention was the most prevalent complication among both groups of study. Respiratory distress syndrome less frequently occurred in NIPPV group infants in comparison with those in NCPAP group. Infants in NIPPV group were hospitalized for about 7 days less than infants in NCPAP group.

In a similar study by Barrington et al., they concluded that using NIPPV decreases failure of extubation; however, there was no significant improvement in the incidence of prematurity apnea in NIPPV (18). In their study, NIPPV was effective only after onset of infants' respiratory effort and while epiglottis was open; while NCPAP provided a constant flow of oxygen for infants. In Barrington et al. study, incidence of respiratory acidosis was significantly lower in NIPPV group.

In Khalaf et al. study, the rate of successful extubation was reported as 94% and 60% in infants who underwent treatment with NIPPV and NCPAP, respectively (19). They mentioned that NIPPV decreased inconsistency between thoracoabdominal muscles as well as resistance of nasal tube flow leading to chest wall stability.

Although there was no significant difference between NIPPV and NCPAP groups in terms of the need for reintubation in Khorana et al. study, but sepsis and atelectasia were more prevalent in NIPPPV group as the reasons of reintubation (20). In addition, incidence of treatment-related complications such as apnea, abdominal distension and necrotizing enterocolitis was not significantly different between the two groups. In Gao et al. study, nasal synchronized intermittent mandatory ventilation (NSIMV) has been mentioned as the preferred method for decreasing the need for reintubation which is not in agreement with the results of the present study (21). They mentioned that infants in NSIMV group showed lower incidence of hypercarbia and hypoxia in comparison to those in NCPAP group.

Moretti et al. randomized infants to nasal flow-synchronized intermittent positive pressure ventilation (NFSIPPV) and NCPAP. They reported that most of the infants (94%) were successfully extubated to NFSIPPV; while only 61% of the infants in NCPAP group showed response to treatment (22). NCPAP group infants failed extubation mostly because of apnea and hypercapnia. None of the procedures were

associated with major adverse effects.

O'Brien et al. compared biphasic nasal continuous positive airway pressure (BP- NCPAP) and infant flow NCPAP in infants less than 1250 gr after extubation for the first time following mechanical ventilation (23). They concluded that there was no difference between the two groups for incidence of sustained extubation. Also complications and short-term results were similar between the two groups. However, retinopathy of prematurity (ROP) was most prevalent in BP-NCPAP group.

Infants with birthweight of less than 1000 gr and gestational ages of less than 30 weeks were randomized to NIPPV and NCPAP in Kirpalani et al. study (24). They reported that 38.4% of infants in NIPPV group died or survived with bronchopulmonary disease (BPD); while it was 36.7% in NCPAP group which reveals no significant difference. In addition, incidence of complications such as air leak or necrotizing enterocolitis as well as duration of respiratory support and time to full feeding was not different between the two groups.

## 6. Conclusion

In conclusion, we found that NIPPV is more effective than NCPAP in decreasing the need for reintubation and invasive mechanical ventilation in premature infants with respiratory distress syndrome and also shortens the duration of hospitalization. Also we realized that NIPPV is a safe method with no additional complications which reduces the risk of intraventricular hemorrhage. So, application of NIPPV in infants who do not receive surfactant is suggested.

Further studies are suggested to evaluate the long term effects and complications of these two methods with longer duration of follow up. Also we recommend that future studies assess the risk for incidence of retinopathy of prematurity (ROP) in infants underwent treatment with NIPPV or NCPAP. Efficacy of both methods without prescription of surfactant needs to be investigated in future researches.

## Compliance with Ethical Standards

Conflict of interest: There is no conflict of interest for any of the authors of the present manuscript.

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Informed consent: All the parents signed an informed consent form prior to intervention.

## Contribution of authors

BN designed the study and collected the data. MHK analyzed the data and drafted the manuscript. IAB collected the data and helped in manuscript drafting. MT revised the paper critically and helped in data analysis and manuscript drafting.

## Conflicts of interest

There are no conflicts of interest in terms of the present study.

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