IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

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Original Article

Comparison of the Therapeutic Effects of Bubble CPAP and Ventilator CPAP on Respiratory Distress Syndrome in Premature Neonates

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ABSTRACT

***Background*:** Respiratory distress syndrome is one of the main complications associated with low birth weight, and a main cause of mortality in premature neonates. The present study aimed to compare the efficacy of ventilator continuous positive airway pressure (CPAP) and bubble CPAP in the treatment of respiratory distress syndrome (RDS) in premature neonates.

***Methods*:** This randomized controlled clinical trial was conducted on 119 neonates diagnosed with RDS, with the gestational age of 28-34 weeks and birth weight of 1000-2200 grams, who were admitted in the neonatal intensive care unit (NICU). Infants were allocated to two groups of ventilator CPAP (VCPAP) and bubble CPAP (BCPAP) therapy.

***Results*:** Mean weight, gestational age, and one-minute Apgar score were not significantly different between the two groups. However, duration of treatment with mechanical ventilation in the BCPAP group was significantly lower compared to the VCPAP group. In addition, frequency of complications had no significant difference between the two groups.

Conclusion: In the treatment of RDS, duration of mechanical ventilation was lower in the BCPAP group compared to the VCPAP group in premature neonates.

Keywords: Bubble CPAP, Neonate, Oxygen therapy, Respiratory distress syndrome

Introduction

Low birth weight (LBW) is one of the main causes of neonatal mortality and morbidity. The World Health Organization (WHO) has estimated the prevalence of LBW to be approximately 10% in Iran (1). According to two studies performed in Yazd (a central province in Iran) in 2004 and 2008, the prevalence of LBW was 8.4% and 8.8%, respectively (2, 3).

Prematurity or intrauterine growth restriction (IUGR) are associated with the occurrence of LBW, which may lead to complications such as respiratory distress syndrome (RDS), broncho-pulmonary dysplasia, retinopathy of prematurity, intraventricular hemorrhage, air leak, hypo-glycemia, and infections (4, 5). RDS is among the main complications associated with LBW, as well as a major cause of mortality in premature neonates. RDS occurs due to surfactant inadequacy, and the treatment may involve continuous positive airway pressure (CPAP) (6).

CPAP is a non-invasive therapeutic method, which generates a positive dilating pressure during a respiratory cycle to prevent alveolar and small-airway collapse, especially during expiration (6). This positive pressure can be applied by ventilator CPAP (VCPAP) using a ventilator (7). Recently, applying positive pressure by bubbles has been considered by a method known as bubble CPAP (BCPAP) (8), which is more cost-efficient and easier to use compared to VCPAP.

Some studies have confirmed the efficacy of BCPAP (7, 8), while the others have demonstrated

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Please cite this paper as:
Noori Shadkam M, Movahedinia M, Noori Shadkam Z, Mehrparvar AM. Comparison of the Therapeutic Effects of Bubble CPAP and Ventilator CPAP on Respiratory Distress Syndrome in Premature Neonates. Iranian Journal of Neonatology. 2017 Sep: 8(3). DOI: 10.22038/ijn.2017.18835.1215

contradictory results (9, 10). For instance, Lee et al. reported a reduction in the ventilation and respiratory rate (in minutes) in BCPAP compared to VCPAP, with no difference in the O_2 saturation, thereby proposing BCPAP as an inexpensive, effective approach for the respiratory support of premature neonates (11). In another research, Bahman Bijari et al. reported a 24-hour survival rate of 100% and 77% for BCPAP and VCPAP, respectively (8). Moreover, findings of Tagare et al. show a success rate of 87% and 80% for BCPAP and VCPAP, respectively, and it was concluded that early BCPAP is an effective treatment method for moderate RDS (7). Meanwhile, Courtney et al. claimed that VCPAP and BCPAP are equally effective in the treatment of RDS (9).

The present study aimed to compare the efficacy of VCPAP and BCPAP in the treatment of RDS in premature neonates.

Methods

This randomized controlled trial was conducted on 119 neonates admitted to the neonatal intensive care unit (NICU) of Shahid Sadoughi Hospital in Yazd, Iran during March 2013-September 2015. Infants had a gestational age 28-34 weeks and weight of 1000-2200 grams. Indications of RDS in the neonates included tachypnea (respiratory rate of >60), grunting, nasal flaring, intercostal retractions, and need for FiO_2 (more than 21%). According to the Silverman-Anderson table, respiration score of the neonates at birth was within the range of 5-7.

Sample size was calculated to be 45 subjects per each group based on the previous studies in this regard (7). Considering the possibility of loss to follow-up, 55 neonates were assigned to each study group. Exclusion criteria of the study were as follows: 1) congenital anomalies (e.g., cardiac diseases, diaphragmatic hernia, esophageal atresia, cleft palate, cleft lip, gastroschisis, omphalocele, and gastrointestinal obstruction); 2) moderate-to-severe asphyxia (grade II or III); 3) cardiopulmonary dysfunction due to clinical sepsis; 4) hematocrit level of <35; 5) intracranial hemorrhage; 6) intraventricular hemorrhage (grade III and IV) and 7) laboratory indications of sepsis.

Neonates were randomly allocated to two groups of BCPAP therapy (device: Fisher & Paykel, New Zealand) and VCPAP therapy (device: Stephan, Germany). Randomization was performed using random number tables.

The present study could not be blinded since the treatment methods were obviously different. Chest X-ray and arterial blood gas analysis were performed immediately after initiating the treatment procedures. CPAP therapy continued until complete improvement or need for surfactant administration. It is notable that surfactant was administered to the neonates with CPAP pressure of 5-7 cmH_2O, inspiratory O_2 concentration of 40-70%, and O_2 saturation of <85%.

The criterion for the treatment response of the infants was no need for CPAP (i.e., CPAP pressure of <3 cmH_2O and FiO_2 of <40%). Recovery was defined as the absence of respiratory distress and no need for additional oxygen. Respiratory failure was considered in the case of increased respiratory score, pH of <7.2, PCO_2 of ≥60 mmHg, O_2 saturation of <85% at the FIO_2 of 40-70%, and CPAP pressure of 5-7 cmH_2O, which required mechanical ventilation.

The primary outcomes were the length of mechanical ventilation, CPAP, and oxygen therapy with hood, while the secondary outcomes were the length of hospitalization, weight at discharge, occurrence of complications, and death. Neonates with a suspicion of air leak initially underwent transillumination, followed by a chest X-ray in order to confirm the diagnosis.

To identify patent ductus arteriosus (PDA), echocardiography was performed on the infants (device: ZONARE, USA) at the end of the first week or upon the physician's suspicion. For the detection of intraventricular hemorrhage (IVH), brain ultrasound (Device: ZONARE, USA) was performed at 24-48 hours after birth, in the second week of birth (if the first test was normal) or at any time when IVH indications were present. All the infants were evaluated at the end of the first month of birth for the retinopathy of prematurity (ROP) by an ophthalmologist.

Data analysis was performed in SPSS version 18 using Chi-square and Fisher's exact test for qualitative variables and Student's t-test for quantitative variables. P-value of less than 0.05 was considered significant in all the statistical analyses.

Prior to the study, written informed consent was obtained from all the parents. The current research has been extracted from a residency thesis in pediatrics and approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences. In addition, the study has been registered in the Iranian Registry of Clinical Trials (www.irct.ir; IRCT2014032716870N2).

Results

In total, 119 neonates with RDS were enrolled in the study and randomly divided into two groups. Neonates in the first and second group

Table 1. Comparison of Demographic Characteristics between Study Groups

Variable (Mean±SD)	BCPAP (N=57)	VCPAP (N=53)	P-value
Gestational Age (week)	30.5±1.8	31±1.6	0.82
Birth Weight (g)	1460±420	1501±412	0.83
One-Minute Apgar Score	7.3±1.6	7.2±1.2	0.91

received treatment with VCPAP and BCPAP, respectively. Gestational age of the infants was 28-34 weeks, and they weighed 1000-2200 grams. Five patients in the BCPAP group and four patients in the VCPAP group died before completing the study and during treatment. Finally, 110 neonates remained in the research. No significant differences were observed between the study groups in terms of the gestational age, birth weight, and one-minute Apgar score (Table 1).

Male-to-female ratio of the neonates was 52.6% and 54.7% in the BCPAP and VCPAP groups, respectively, and the difference was not statistically significant in this regard (P=0.82). Frequency of delivery by caesarian section was 56.1% and 60.4% in the BCPAP and VCPAP groups, respectively, with no statistically significant difference in this regard (P=0.88). Table 2 compares the duration of respiratory support in the two study groups. Duration of mechanical ventilation in the BCPAP group was lower compared to the VCPAP group, and the difference was statistically significant in this regard (P=0.045).

Complications were observed in 26% and 25% of the neonates in the BCPAP and VCPAP groups, respectively, and the difference in this regard was not considered statistically significant (P=1). Among the observed complications, IVH, air leak, ROP, and bronchopulmonary dysplasia (BPD) were more frequent in the VCPAP group, while PDA was more common in the BCPAP group; however, no significant differences were observed between the groups in this regard.

In total, nine neonates (7.6%) died due to the RSD complications, five of whom were in the BCPAP group (two cases due to IVH and three cases due to sepsis), and four infants were in the VCPAP group (one case due to IVH, one case due to air leak and two due to sepsis). However, the differences in this regard were not considered statistically significant in the study groups (P=0.64).

According to the obtained results, mean cost of hospitalization in the BCPAP group was lower compared to the VCPAP group (P=0.705). Table 3 compares the length of hospitalization, weight at discharge, and RSD complications between the study groups.

Discussion

CPAP is a non-invasive method of respiratory treatment, which generates a positive dilating pressure during a respiratory cycle (6). In the present study, we compared the efficacy of two CPAP devices of BCPAP and VCPAP in the treatment of RDS in premature infants. BCPAP is known to be remarkably more cost-efficient and easier to use compared to VCPAP.

According to our findings, mean duration of mechanical ventilation in the BCPAP group was lower compared to the VCPAP group, and the difference in this regard was statistically significant. Duration of treatment with CPAP and oxygen therapy with oxyhood in the BCPAP group was lower compared to the VCPAP group, while

Table 2. Comparison of Respiratory Support Duration between Study Groups

Variable	BCPAP (N= 57)	VCPAP (N=53)	P-value
Duration of Mechanical Ventilation (hour)	35.2±11.4	46.3±9.1	0.045
Duration of Treatment with CPAP (day)	50.1±16.3	52.5±13.8	0.61
Duration of Oxygen Administration with Hood (day)	4.3±3.7	4.8±3.3	0.65

Table 3. Comparison of Length of Hospitalization, Weight at Discharge, and RSD Complication between Study Groups

Variables		BCPAP (N=57)	VCPAP (N=531)	P-value
Length of Hospitalization (day) (Mean±SD)		20.1±13.6	22.8±11.80	0.51
Weight at Discharge (day) (Mean±SD)		1695±386	1647±3520.55	0.55
Surfactant Therapy N (%)	Yes	31 (54)	29 (55)	
	No	26 (46)	24 (45)	0.95
RSD Complications N (%)	PDA	3 (5.2)	2 (3.8)	0.9
	Air Leak	3 (5.2)	4 (7.5)	0.7
	IVH	2 (3.5)	4 (7.5)	0.61
	BPD	1 (1.7)	2 (3.8)	0.45
	ROD	4 (7)	6 (11.3)	0.73
	No Complications	42 (74)	40 (75)	1

the difference in this regard was not statistically significant.

In a study conducted on the NICU patients in Iran in 2011, duration of mechanical ventilation in BCPAP was shorter compared to VCPAP, and the difference was not considered significant (8), which is consistent with the results of the current study. Furthermore, Tagare et al. (2010) reported similar findings regarding the duration of CPAP treatment by the two aforementioned methods (7). In another study, Mohamadizadeh et al. (2011) evaluated 44 neonates and found no significant difference between BCPAP and VCPAP in terms of the duration of treatment, mechanical ventilation, and oxygen therapy, which is in contrast to the results of the current research (12).

In another study in this regard, Mazella et al. (2001) examined neonates with RDS and gestational age of less than 36 weeks and demonstrated that the need for oxygen therapy and respiratory rate was significantly higher in the BCPAP group compared to the other group, while the duration of mechanical ventilation and CPAP therapy had no significant difference between the study groups (13).

In a similar study, Gupta et al. (2009) compared the efficacy and safety of BCPAP and infant flow driver CPAP after extubation in premature neonates. According to the findings, duration of CPAP therapy was significantly lower in the group receiving treatment with BCPAP (14). It is notable that in the mentioned study, the infants had a gestational age of less than 30 weeks and birth weight of less than 1500 grams. According to a study conducted in Oxford University in 2006, BCPAP is a beneficial, inexpensive approach to be used in developing countries (15). Seemingly, the therapeutic effects of BCPAP are attributed to applying a concurrent positive end-expiratory pressure and oscillation in the trachea (11).

With respect to the frequency of RSD complications, results of the current study showed a higher frequency of PDA in the BCPAP group, as well as the higher rates of IVH, air leak, ROP, and BPO in the VCPAP group. However, no statistically significant differences were observed in this regard.

Consistent with the present study, Bahman Bijari et al. reported the higher incidence of IVH in the VCPAP group and PDA in the BCPAP group (8). Moreover, nasal trauma was detected in 12% of the neonates, while this complication was not assessed in the current research. In another study, Mohamadizadeh et al. stated that the frequency of chronic lung diseases, IVH, and pneumothorax was higher in BCPAP compared to VCPAP, while the difference was not statistically significant in this regard (12).

In the current study, mean length of hospitalization in the BCPAP group was insignificantly shorter compared to the VCPAP group, while in the study by Bahman Bijari et al., this parameter was significantly lower in the BCPAP group (8). It is noteworthy that in the mentioned research, study population consisted of the neonates with birth weight of less than 1500 grams. On the other hand, Tagare et al. proposed contradictory results regarding the length of hospitalization, as the subjects in the BCPAP group were hospitalized for a longer period (7).

In the present study, we assessed the weight of neonates at the time of discharge and observed an insignificant difference between the two groups; to the best of our knowledge, this parameter has not been previously measured in the studies in this regard. Furthermore, cost of hospitalization in the BCPAP group in the current research was insignificantly lower compared to the VCPAP group, while in the study by Bahman Bijari et al., cost of hospitalization was significantly lower in the neonates receiving treatment with BCPAP (8).

The current research had some limitations. For instance, since we used well-known treatment methods, the individuals who assessed the outcomes could not be blinded to the procedures. Another limitation of the study was the small sample size, which might restrict the generalizability of the results.

Conclusion

According to the results, use of BCPAP in the treatment of RDS in premature neonates could reduce the duration of mechanical ventilation more significantly compared to VCPAP.

Conflicts of interests

None declared.

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