Randomized controlled trial of two methods of nasal continuous positive airway pressure (N-CPAP) in preterm infants with respiratory distress syndrome: underwater bubbly CPAP vs. Medijet system device

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SUMMARY: Hosseini MB, Heidarzadeh M, Balila M, Ghojazadeh M, Janani R, Safavi-nia S, Naghavi-Behzad M, Alikhah H. Randomized controlled trial of two methods of nasal continuous positive airway pressure (N-CPAP) in preterm infants with respiratory distress syndrome: underwater bubbly CPAP vs. Medijet system device. Turk J Pediatr 2012; 54: 632-640.

There has been an increasing interest in the application of non-invasive respiratory support in preterm infants, and different types of nasal continuous positive airway pressure (N-CPAP) devices are being used in Neonatal Intensive Care Units (NICUs). The objective of the present study was to compare the duration of CPAP need and possible complications of two methods of (N-CPAP) delivery: Bubble CPAP (B-CPAP) and Medijet (MJ) system device in preterm infants with respiratory distress syndrome (RDS). This prospective randomized clinical trial was performed on 161 preterm infants (28-37 weeks of gestational age) with RDS and eligible for CPAP therapy. The infants were inborn and admitted in a level III NICU of Al-Zahra Teaching Hospital (Tabriz, Iran) from April 2010 to September 2011. All infants were randomized in the first hour of life to B-CPAP or MJ system. Short binasal prongs were used in both groups and CPAP was set at the level of 5-6 cm H_2O. The primary outcome of this study was duration of CPAP need (hour). Other outcomes, such as complications of the two methods of N-CPAP, were evaluated using a checklist. Ninety infants were randomized to the MJ system, and 71 were randomized to B-CPAP. The mean gestational age and birth weight were similar in the two groups, as was the duration of CPAP need (44.3±20.64 vs. 49.2±21.2 hours, respectively; p=0.66). Moreover, the probability of complications, such as CPAP failure rate, pulmonary hemorrhage, pneumothorax, intraventricular hemorrhage, abdominal distention, necrotizing enterocolitis, and bronchopulmonary dysplasia, was the same between the two study groups (p>0.05). There was a trend of more hyperemia of the nose in the B-CPAP group in comparison to the MJ system group (10% versus 3.3%, respectively), but the difference was not significant (p=0.08). In conclusion, the MJ system is as effective as B-CPAP in the management of infants with RDS.

Key words: continuous positive airway pressure, mechanical ventilation, preterm infants, respiratory distress syndrome.

Nowadays, the worldwide increasing advances in neonatal intensive care units (NICUs) have caused a significant decrease in infant mortality[1]. Infant mortality has decreased from 26 in 1000 liveborn infants in 1960 to 6.9 in 2007 in the United States (US)[2]. The incidence of prematurity in the world has also increased, reaching 12.5% in some countries (in the US, from 7.9% in 2003 to 8.1% in 2004). Today, regarding the reduction of death of premature infants with the use of antenatal steroids and surfactant therapy, the important priorities

in neonatal care are reduction of morbidities such as chronic lung disease (CLD) and intraventricular hemorrhage (IVH), as well as reduction in the duration of hospitalization and costs. Development of non-invasive methods including nasal continuous positive airway pressure (N-CPAP) has led to improvements in the respiratory care of infants[3].

The acronym CPAP is defined as a positive pressure applied throughout the respiratory cycle to the airway of a spontaneously breathing infant[1]. The purpose is: improvement in oxygenation, increasing the total volume of the lungs, preventing collapse and atelectasis without creating too much stretch in the lungs, and improvement in ventilation/perfusion matching. There is a particular interest in delivering CPAP through the nasal passage because it decreases complications[4]. Early use of N-CPAP can decrease harm to the lungs and also the need for mechanical ventilation[5].

In the late 20th century, with the increasing interest in non-invasive respiratory support in preterm infants, different types of N-CPAP were used in NICUs[6]. In underwater bubble CPAP (B-CPAP), which is a form of continuous flow CPAP, blended gas flows to the infant after being heated and humidified. Typically, nasal prong cannulas such as the Flexi trunk or Hudson® prongs are secured in the infant's nares. The distal end of the expiratory tubing is immersed under either 0.25% acetic acid or sterile water to a specific depth to provide the approximate level of CPAP desired[7].

Variable-flow CPAP uses flow changes to generate the CPAP level. Special prongs and flow generators are used for this kind of CPAP[8]. Relatively high gas flows are needed[9]. The Medijet (MJ) system has a chamber (volume reservoir) in which the flow enters it via a large hole at high speed; the jet is indirectly running at 90° away from the baby. The baby is always breathing from this chamber. A pipe connected to the generator used for measuring pressure is located under water, and it simultaneously serves as a pressure relief valve[25]. The variable-flow driver systems have been shown to recruit lung volume very effectively and to decrease the work of breathing in low birth weight (LBW) infants[8,9]. In a randomized, controlled trial study comparing the rate of extubation failure, however, the variable-flow device did not result in fewer reintubations[10]. Nonetheless, in infants receiving variable-flow CPAP, the oxygen requirement and length of hospital stay were less than with conventional, continuous-flow CPAP. In a similar but smaller study, Mazzella et al.[11] found lower oxygen requirements and respiratory rates in infants randomized to the Infant Flow Driver (IFD), a form of variable-flow driver systems, compared with B-CPAP delivered by a single hypopharyngeal prong.

Gupta et al.[12] compared two methods of B-CPAP and IFD and concluded that the average time for respiratory support in B-CPAP is 50% less than in other groups. He also found that B-CPAP is as effective as IFD after extubation of premature infants[12].

In the last decade, besides using N-CPAP through ventilators, both B-CPAP and the MJ system have been used, but only a few studies[13] were found in which the two methods were compared. The objective of the present study was to compare the duration of CPAP therapy in neonates with respiratory distress syndrome (RDS) treated with B-CPAP vs. MJ system and to study the possible complications caused by these methods.

Material and Methods

This randomized clinical trial study was conducted on 161 premature infants with 28-37 weeks of gestation suffering from RDS and eligible for CPAP therapy, who were inborn and admitted in the level III NICU of Al-Zahra Teaching Hospital (Tabriz, Iran) between April 2010 and September 2011.

All participants' parents signed a written consent, and the study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences (Ref number 8923).

Inclusion criteria were: non-incubated preterm infants and gestational age 28-37 weeks with: early respiratory distress (Silverman–Anderson Retraction Score >5-6, age <12 hours (h), PCO_2 <65 mmHg or pH >7.2-7.25, and FiO_2 (fraction of inspired oxygen) >40%).

Exclusion criteria were: major congenital malformation, neuromuscular diseases, severe birth asphyxia, overwhelming infection, severe apnea, patent ductus arteriosus (PDA), and intubation at delivery.

Immediately after NICU admission, all infants were evaluated, and after randomization (by Rand list software), they underwent N-CPAP as either B-CPAP or MJ system. We used the Fisher and Paykel Bubble-CPAP (BC161, New Zealand, UK), which involves a source of gas flow (6-8 L/min), an air oxygen blender (Universal Blender Medin Medical Innovation GMBH, Germany), humidifier (MR850, Fisher & Paykel Health Care, New Zealand), and a respiratory circuit. We used nasal tubing (Flexi trunk) and nasal prong to deliver CPAP. Nasal prongs were positioned at least 2 mm from the septum to avoid pressure necrosis. The patients obtained 5-6 cm H_2O of CPAP.

The MJ systems (N-CPAP Generator 1010, Medin Medical Innovations GMBH, Germany) had a generator with two silicon tubes. The thick tube was connected to a flow meter after blending of air and oxygen (Universal Blender Medin Medical Innovation GMBH, Germany). The flow was approximately 8-10 L/min, which resulted in a pressure of approximately 5-6 cm H_20 at the nose level. The thin tube had to be connected to a pressure indicator. After choosing the proper size of nasal prong or nasal mask according to the size of the infant's nose, we guided the straps over both cheeks and through the holes in the tabs from below, and then secured them to the Velcro felt on the cap.

In both groups, the FiO_2 was adjusted to maintain the oxygen saturation within predefined limits for each infant. The unit guidelines for these limits in this population were 85% for the lower limit and 93% for the upper limit.

According to the European Consensus Guidelines on the Management of Neonatal Respiratory Distress Syndrome in Preterm Infants – 2010 update, if needed, the infant underwent intratracheal surfactant injection (poractant alfa 200 mg/kg) with methods of INSURE (i.e. INtubation SURfactant Extubation) (14).

The criteria for weaning was the same in both groups and included the absence of respiratory distress (minimal or no retractions and respiratory rate of 30-60 per minute) and presence of the following criteria: FiO_2 <0.30, PEEP ≤4 cm H_2O, PaO_2 >50 mmHg, and $PaCO_2$ <65 mmHg. CPAP failure was defined as one of the following signs: (i) persistent oxygen saturation <85% with FiO_2 >50%; (ii) pCO_2 >65 and pH <7.25; (iii) the need for CPAP >8 cm H_2O; or (iv) recurrent apnea with bradycardia.

The primary outcome of this study was duration of CPAP need (hour) defined as total time from starting of CPAP to the time of total weaning of N-CPAP. Other outcomes included: bronchopulmonary dysplasia (O_2 dependency for at least 28 postnatal days), pneumothorax, pulmonary hemorrhage, trauma to nose including: columella necrosis and hyperemia of nose, abdominal distention, feeding intolerance, time of complete enteral feeding, necrotizing enterocolitis (NEC), IVH grade ≥2, hospital stay, and CPAP failure.

Oxygen requirements, respiratory rate (RR), heart rate (HR), and O_2 saturation (by pulse oximetry) were monitored continuously and recorded every 4 h. Blood gases were determined on capillary blood every 12 h or at the discretion of the health care team. Blood pressure was measured by non-invasive methods every 6 h. All infants underwent an ultrasound cerebral scan (Sonosite) (by a radiologist who was blinded to the infant group) at enrolment and at least one time subsequently during the first week. Periventricular hemorrhage/IVH was classified as described by Papile et al.[15]. Total duration of time to achieve 21% of FiO_2 with N-CPAP (h) and need for surfactant therapy were also recorded.

The statistical analysis was performed by the Statistical Package for the Social Sciences (SPSS) software package version 16.0/win. Quantitative data were presented as mean ± standard deviation (SD) and frequency and percentage (%). The data gathered from the study were assessed using descriptive statistical methods, chi-square or Fisher's exact test among the qualitative variables. The test of the mean difference between stand-alone groups was used for assessing quantitative variables between the two groups, and repeated measure of ANOVA was used for assessing the changes in respiratory indicator between the two groups at different times. A p value of <0.05 was considered as statistically significant.

This study has been registered in the Iranian Registry Clinical Trail (IRCT.ir) (Irct ID: RCT138903174113N1).

Results

A total of 161 infants were enrolled in our study and randomly assigned to one of the two treatment groups. Table I summarizes the clinical data at the time of enrolment. Mean gestational age and birth weight were similar in the two groups. However, there was a significant difference between the two groups in the number of infants who were small for gestational age (SGA) using the Lubchenco curves (p=0.02) and weight grouping (<0.001). There were more extremely low birth weight (ELBW) infants in the MJ system group.

In the MJ system group, 44/90 (48.8%), 23/90 (25.6%) and 23/90 (25.6%) of the mothers received one, two or no dose of betamethasone, respectively. In the B-CPAP group, 30/71 (42.2%), 16/71 (22.5%) and 25/71 (35.2%) received one, two or no dose of steroids, and there was no significant difference (p=0.41).

In the MJ system group, 42/90 (46.7%), 6/90 (6.7%) and 42/90 (46.7%) of the infants received one, two or no dose of surfactant, respectively. In the B-CPAP group, 37/71 (52.9%), 3/71 (4.3%) and 30/71 (42.9%) received one, two or no dose of surfactant, respectively, and the difference was not significant (p=0.66). In general, 45% of our studied infants did not receive surfactant.

Primary (duration of CPAP need (h)) and other outcomes are summarized in Table II, and no significant differences were found in all these outcomes between the two groups. There was no case of severe nose trauma such as columella necrosis, but there was a trend of more hyperemia of the nose in the B-CPAP group in comparison to the MJ system group (10% versus 3.3%, respectively), but the difference was not significant (p=0.08).

Continuous positive airway pressure (CPAP) failure was relatively more common in the MJ system group than the B-CPAP group, but the difference was not significant (p=0.61). All CPAP failure cases in both groups were

Table I. Baseline Characteristics at Trial Entry of Infants Assigned to Bubbly CPAP (B-CPAP) and the Medijet (MJ) System

	MJ system (n=90)	B-CPAP (n=71)	P -value
Gestational age (GA) (wk)	29.92±5.73	29.98±5.22	0.94
GA (28-31 wk +6 days)	69(23.3%)	56(78.9%)	
GA (32-37 wk)	21(23.3%)	15(21.1%)	
Number SGA	16(17.8%)	4(5.6%)	0.02
Male	52(57.8%)	47(66.2%)	0.27
Female	38(42.2%)	24(33.8%)	
M/F	52/38	47/24	0.27
Body weight (g)	1551±558	1636±524	0.32
Weight (<1000 g)	14(15.6%)	1(1.4%)	
Weight (1000-1499 g)	40(44.4%)	38(53.3%)	<0.001
Weight (>1500 g)	36(40%)	68(42.2%)	
Type of delivery: C/S	69(78.4%)	41(61.2%)	0.01
Type of delivery: NVD	19(21.6%)	26(38.8%)	
Maternal steroid	44(48.8 %)	30(42.2 %)	0.41
Surfactant	42(46.7%)	37(52.9%)	0.66
Mean of 1st min Apgar	6±1	6±2	0.93
Mean of 5th min Apgar	8±1	8±1	
Saturated O_2 (%)	96±2.1	95.6±2.4	0.42
O_2 requirement	35.7±7.1	36.9±7.8	0.08
PCO_2 (mmHg)	45.9±13.6	49.8±12.2	0.033

SGA: Small for gestational age. NVD: Normal vaginal delivery. C/S: Cesarean section.

Table II. Outcomes of Infants Assigned to B-CPAP and MJ System N-CPAP

	MJ system (n=90)	Bubble N-CPAP (n=71)	P Value
* Duration of CPAP (h)	44.3±20.64 (8-140)	49.2±21.2 (8-128)	0.66
Duration to achieve 21%O_2 with N-CPAP(h)	71.32±4.4	81.6±6.2	0.61
O_2 need in 28 day	9(10%)	7(11.3%)	0.97
Apnea	3(3.3%)	7(9.9%)	0.08
Pneumothorax	2(2.2%)	1(1.4%)	0.7
Pulmonary hemorrhage	3(3.3%)	0 (0%)	0.12
Columella necrosis	0(0%)	0(0%)	
Hyperemia of nose	3(3.3%)	7(10%)	0.08
CPAP failure	8(8.9%)	8(11.3%)	0.61
Start of feeding	2.8±1.6	3.3±2.12	0.77
Complete enteral feed (d)	9.35±4.32	9.6±4	0.99
Abdominal distention	34(37.8%)	21(29.6%)	0.27
Feeding intolerance	20(22.7%)	11(16.2%)	0.28
Weight gain (g/d)	21.8±9.7	19.5±9.12	0.23
NEC	7(7.8%)	2(2.8%)	0.17
IVH ≥2	6(6.6%)	4(5.6%)	0.34
Hospital stay (d)	26.17±2	22.07±1.7	0.23
Mortality	3(3.3%)	1(1.4%)	0/33

*primary outcome
=MEAN ±SD
NEC: Necrotizing enterocolitis. IVH: Intraventricular hemorrhage.

intubated and received ventilator therapy according to the guideline of the Al-Zahra Teaching Hospital. Of 8 patients with CPAP failure in the MJ group, 5 of them were discharged from the hospital, 1 had CLD, and 2 infants died due to IVH and pulmonary hemorrhage. In the B-CPAP group, 8 patients had CPAP failure, all of whom were intubated, and 6 were discharged from the hospital. Causes of death in the two patients in this group were NEC and CLD, respectively.

Intraventricular hemorrhage (IVH) was assessed by portable ultrasonography (Sonosite M-Turbo). Our findings showed that 6 infants (6.6%) in the MJ system group and 4 infants (5.6%) in the B-CPAP group had IVH grade of ≥2 (p=0.34). Grade 3 IVH was seen only in the MJ system group, and it occurred in only 1 case.

A total of 70 infants in the MJ system group and 60 in the B-CPAP group were examined for retinopathy of prematurity (ROP) (dropout was related to family non-compliance after hospital discharge). In our study, we found only one case of ROP in each group, with a total frequency of 1.3%. The difference between the two groups was not statistically significant.

Screening for hearing loss was carried out with the method of AABR (Ambulatory Auditory Brainstem Response) before hospital discharge of the infants, and we did not find any case of abnormal response.

During the study, 4 infants (2.5%) died (3 in the MJ system group (3.3%) and 1 in the B-CPAP group (1.4%); p=0.63). The cause of death of the 2 infants in the MJ system group was proven to be sepsis; 1 of them had a maternal history of premature rupture of membranes (PROM), and the other had intrauterine growth restriction (IUGR) and was the product of a twin pregnancy. The main clinical picture in both of them was pulmonary hemorrhage, and they had positive blood cultures. Another infant in the MJ system group died due to advanced form of NEC despite surgical intervention and supportive care. In the B-CPAP group, with

regard to the infant who was a product of a twin pregnancy and had IUGR, death was possibly due to sepsis on the 13th day of life. Death occurred following a period of refractory apnea and a period of mechanical ventilation.

In our series of patients, the mean duration of hospitalization was 26.17±2 days in the MJ system group and 22.7±1.7 days in the B-CPAP group (p=0.23).

Nine of the infants suffered from NEC (7 in the MJ system group and 2 in the B-CPAP group). One of the infants in the B-CPAP group and 3 of the infants in the MJ system group had an advanced form of NEC and received surgical interventions; the follow-up showed all of them recovered with supportive treatment without any complication except for 1 infant in the MJ group.

Analysis of the trend of FiO_2 by ANOVA test showed that the changes in FiO_2 in the MJ system (p<0.001) and B-CPAP groups was significant (p<0.001), but the difference between the two groups was not statistically significant (p=0.22) (Fig. 1).There was no significant difference between the two groups in achieving FiO_2 of 21% under N-CPAP (p=0.66).

Changes in the RR in the MJ system group and B-CPAP group was significant (p<0.02), and N-CPAP led to a marked reduction in the work of breathing, but the difference between the two groups was not significant (p=0.72).

According to the ANOVA test, the SpO_2 changes were not significant between the two groups or within each group (p=0.05).

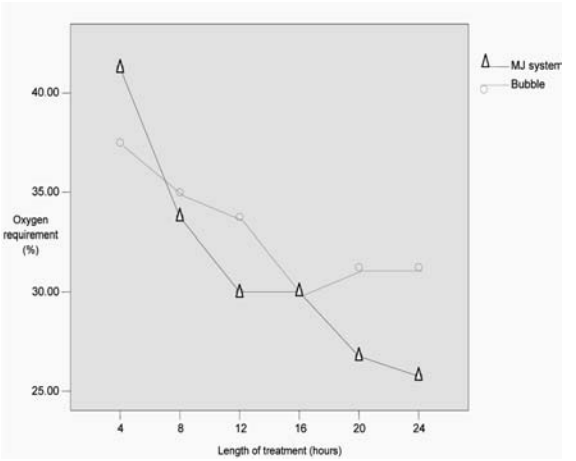

Fig. 1. Averaged curves of changes in fraction of inspired oxygen (FiO_2) during the first 24 h of treatment using the MJ system or B-CPAP. The difference between the two groups was not statistically significant (p=0.22).

Discussion

This study was designed to compare the effectiveness and complications of two methods of N-CPAP. We hypothesized that the patients supported by the MJ system need a shorter duration of respiratory support and have fewer complications especially in nasal trauma. In our study, use of the MJ system resulted in a finding similar to the B-CPAP group in mean duration of CPAP (h), duration to achieve 21% FiO_2 with N-CPAP (h), and oxygen need in 28 days.

To our knowledge, no research was found in which the MJ system and B-CPAP were compared. In our study, total duration of CPAP need was not significantly different between the two groups (p=0.66). No similar research was found in the literature, but in the study of Mazzella et al.[11], the duration of receiving CPAP in the IFD group (another form of variable-flow CPAP) was less than in B-CPAP (49.3±31 vs. 56.5±29.7 h, respectively). The IFD system was not used in our NICU, but the MJ system worked as a form of variable-flow CPAP. The mean duration of B-CPAP use in our study (49.2±21.2 h) was similar to use in the B-CPAP group (56.5±29.7 h) in the Mazzella et al.[11] study.

In another study, the median duration of CPAP support was 50% shorter in the infants on B-CPAP in comparison to IFD CPAP. To mention other studies, the research of Gupta et al.[12] was conducted on preterm infants at 24 to 29 weeks' gestation or with a birth weight of 600 to 1500 g, who were ventilated at birth for RDS and were smaller than our patients. They stated that this difference might be due to the putative advantages of bubbling, which is thought to contribute to improved gas exchange and better airway patency and lung volume recruitment with less atelectatic lung injury.

There was only one research that compared the IFD and MJ system devices. Gutiérrez Laso et al.[16] studied preterm infants requiring N-CPAP for respiratory distress at birth. The mean gestational age was 29.4 weeks and the mean birth weight was 1340 g. They found

that 6 h after initiation of N-CPAP, FiO_2, CO_2 and the respiratory effort decreased in both groups, but the difference between the two groups was not statistically significant.

Use of CPAP mainly results in an increase in functional residual capacity and an improvement in lung compliance. Our study suggested that, in view of the reduction in the need of FiO_2 in both B-CPAP and MJ system groups, B-CPAP and the MJ system may have had beneficial effects on lung mechanics via different mechanisms. Delivering mechanical oscillatory vibrations of the B-CPAP that simulate waveforms produced by high-frequency ventilation (HFV) is crucial in this form of N-CPAP[17,18]. It should be noted that B-CPAP has very low N-CPAP pressure stability, because there is no pressure regulation. The MJ system has a chamber (volume reservoir) where the jet is indirectly run at 90° away from the baby. The baby is always breathing from this chamber, so the flow never goes directly into the baby. The flow is smooth for the baby and can effectively decrease the work of breathing and FiO_2.

Preterm infants who had received antenatal steroids and surfactant therapy after birth were not excluded. Such treatments may significantly influence lung recruitment and consequently interfere with the quality of the data or the interpretation of the results.

In our study, complications such as apnea, pulmonary hemorrhage, nose trauma, feeding intolerance, NEC, IVH grade ≥2, and mortality rate were the same between the two groups.

Frequency of oxygen dependence at least for 28 days of life (BPD) was the same in both groups (11% and 10% in the B-CPAP and MJ system groups, respectively).We did not determine mild, moderate or severe forms of BPD in either group.

Avery[19] studied 1625 infants with a birth weight of 700-1500 g in Colombia, and only 5% of infants under B-CPAP had suffered from CLD[19]. In the "Columbia Approach", in which B-CPAP is used early in the course of respiratory distress in both premature and term-gestation infants, the incidence of CLD can effectively be lowered. The same approach was also chosen in this study, but intensity of BPD was not determined in our study[20].

The prevalence of NEC in Mazella et al.'s study[11] was 5.6%, and it was the same in both the IFD and N-CPAP groups[12]. Aly et al.[21] carried out a study on 343 very low birth weight (VLBW) infants who were under early N-CPAP treatment, and prevalence of NEC was 7% and the risk of NEC in VLBW premature infants was not increased with the use of early N-CPAP[21]. They used a water-seal CPAP unit on arrival to the NICU using short nasal prongs (Hudson Respiratory Care, Temecula, CA). Because of the greater prevalence of abdominal distention and more NEC in the MJ system group and despite the use of orogastric tube, it seems there is more pushing of air in to the gastrointestinal tract, which requires further research.

In our study, hyperemia of the nose was seen in 3/90 (3.3%) in the MJ system group and in 7/71 (10%) in the B-CPAP group, and the difference was not significant. We used nasal mask and prong alternatively every 6 h in the MJ system group, but there was only nasal prong in the B-CPAP group. A close supervision program was planned for both groups. Larger and heavier prong adapter size and unavailability of nasal masks for B-CPAP patients may have a role in the greater prevalence of nasal trauma. All cases of hyperemia of the nose recovered after a few days of conservative interventions. We had less nose trauma in our MJ system group in comparison to the MJ group in the study of Gutiérrez Laso et al.[16], in which four infants in the MJ group had significant nasal lesions (MJ: 4/34, 11.8%).

In the study of Bahman-Bijari et al.[22] in Afzalipour Hospital of Kerman, Iran, 50 infants between 1000-2000 g in two groups of B-CPAP and CPAP with ventilator were analyzed for duration of treatment, therapeutic response and CPAP complications. Nasal trauma was seen in 12% of cases in both groups. The prevalence of nasal trauma with B-CPAP was similar to that of our study (7/71, 10%)[22].

In the analysis of Fischer et al[23]. on 989 infants under treatment with N-CPAP with an average gestational age of 34 weeks and mean birth weight of 2142 g, the occurrence of nose trauma was 42.5%. They graded nasal trauma as stage I, II and III, and most of the patients had stage I (88.3%). The risk of nose trauma was higher in infants <32 weeks of age and

1500 g of weight and who had received CPAP for more than 5 days[23]. Persistent visible scars were present in two cases of their cohort. We did not grade nasal trauma, but found only hyperemia of the nose (stage I) in our patients.

The frequency of pneumothorax in the MJ system group of our study was 2/90 (2.2%), and we did not find a significant difference when compared to the B-CPAP group (p=0.7). In the study of Gutiérrez Laso et al.[16], who also used the MJ system, air leaks occurred in 2/34 patients (5.8%). The lower frequency of air leak in our study may be due to the use of limiting CPAP pressure to 5-6 cm H_2O, which incurs a low risk of serious complications, or use of surfactant therapy[24].

In our study, we found the total prevalence of IVH grade ≥2 was 6.2% in the MJ group, and grade 3 was determined in 1.2% of them. In the B-CPAP group, 6.2% of infants had grade 2 IVH.

In the study of Bahman-Bijari et al.[22], they found IVH was less in the B-CPAP group than the CPAP by ventilator (1/25 vs. 3/25). We did not follow these patients in our research in the two groups.

The small sample size of this study does limit its applicability. A multicenter randomized controlled trial is needed to further confirm these findings. In conclusion, the MJ system is as effective as B-CPAP in the management of infants with RDS. Patients in the MJ system group had a lower rate of nasal trauma, but the difference was not significant.

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