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Original Article

Analytical Study of Different Modes of Continuous Positive Airway Pressure (CPAP) in Management of Respiratory Distress Syndrome (RDS) in Preterm Neonates

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Abstract

Background: Respiratory distress syndrome (RDS), is the single most important cause of morbidity and mortality in preterm infants. In infants with progressive respiratory insufficiency, intermittent positive pressure ventilation (IPPV) with surfactant has been the usual treatment, but it is invasive, potentially resulting in airway and lung injury. Continuous positive airway pressure (CPAP) has been used for the prevention and treatment of respiratory distress syndrome, as well as for the prevention of apnoea, and in weaning from IPPV.

Objective: To evaluate the effect of different types of CPAP in treatment of preterm neonates with respiratory distress syndrome in Al-Azhar (Assiut) university hospital neonatal intensive care unit (NICU).

Patients and methods: This was a prospective study, conducted at Al-Azhar (Assiut) university hospital NICU. The study included 60 preterm neonates with respiratory distress syndrome divided into 3 groups: (1st group); 20 cases on nasal CPAP; (2nd group); 20 cases on nasopharyngeal CPAP and (3rd group); 20 cases on mask CPAP from March 2021 to November 2021.

Results: The results of our study showed significant difference between the three groups regarding complications, nasal irritation and problems in fixation as it occur in (10%, 10%, 85%) respectively of cases in mask group and (90%, 85%, 85%) respectively in nasal group and (90%, 0%,0%) respectively in nasopharyngeal group with p value < 0.001 in all. There was also a significant difference between the three groups regarding to response to treatment with P value < 0.04**.**

Conclusions: CPAP is one of the effective treatments of RDS leading to significant improvement of outcome, reducing hospital stay and the need for invasive mechanical ventilation with its harmful adverse effects and thus the case fatality rate of RDS cases and so the overall mortality rate of the NICU.

Key words: Respiratory distress syndrome, CPAP, neonates, NICU, preterm.

Introduction

Neonatal respiratory distress syndrome (RDS) is the most common cause of respiratory failure in the first days after birth, results from tendency of the alveoli and terminal bronchioles to collapse because of the absence of lung surfactant and immature state of alveolarization of the lung acini"[1].

Respiratory distress syndrome is inversely related to gestational age of the infant [2]. So, remains a dominant clinical problem encountered among preterm infants [3].

The incidence of complications in the survivors of RDS remains significant because more of the sickest, most immature infants are surviving [3].

CPAP is now used as a substitute for mechanical ventilation to provide respiratory support for many babies with RDS, and some can be managed on CPAP without receiving surfactant treatment [4].

CPAP therapy uses machines specifically designed to deliver a flow of air at a constant pressure. This constant stream of air opens and keeps the upper airway unobstructed during inhalation and exhalation. Some CPAP machines have other features as well, such as heated humidifiers [5].

Nasal CPAP: Nasal prongs or nasal mask is the most common modality of treatment [6].

Nasal CPAP is frequently used in infants, though its use is controversial. Studies have shown nasal CPAP reduces ventilator time but an increased occurrence of pneumothorax was also prevalent [7].

Nasopharyngeal CPAP: Is administered by a tube that is placed through the person's nose and ends in the nasopharynx. [6]

Face mask CPAP: A full face mask over the mouth and nose is another approach for people who breathe out of their mouths when they sleep [6].

The aim of this study is to evaluate the effect of different types of CPAP in treatment of preterm neonates with

respiratory distress syndrome in Al-Azhar (Assiut) university hospital NICU.

Methods

This was Prospective study conducted at Al-Azhar (Assiut) university hospital NICU from March 2021 to November 2021**.**

Inclusion criteria: The study included all preterm neonates with gestational age from 34 week to less than 37 week at Al-Azhar (Assiut) university hospital NICU with respiratory distress syndrome presented by at least two of the following symptoms:-tachypnea; retraction; nasal flaring; grunting; cyanosis; who need oxygen above 40% & Pco2 above 7 kpa in arterial blood gases or 7.5 kpa in capillary blood gases. The study included 60 preterm neonates with respiratory distress syndrome divided into 3 groups: (1^{st})group 20 cases on nasal CPAP; (2^{nd}) group 20 cases on nasopharyngeal CPAP ; and (3^{rd}) group 20 cases on mask CPAP. Data were collected for type of CPAP used, gestational age, age when randomized, actual weight, duration of CPAP, level of PEEP, blood gas at the time of randomization, need for sedation, clinical improvement, CPAP complication (blocked tube, air leak ….etc), nasal irritation, problems of CPAP fixation, whether the patient was already on CPAP while being transported to our unit. Patients were randomized as soon as we received the order to transfer a baby to our hospital.

Exclusion criteria: Preterm neonates less than 34 weeks, preterm neonates with diseases other than respiratory distress syndrome, full term neonates, when there was either increasing respiratory insufficiency with a need for intubation or a FiO2 of less than 30% for more than 4 hours and infant more than 28days.

All neonates enrolled in this study were subjected to:

Full History

1) Personal history: (name, age, sex, address and order among siblings).

2) History of present illness: (onset, course, duration, associations and related symptoms).

3) Past history: For 1st 28days.

4) Family history: Thorough history about other members affected by the same disease from either sides of the patient's family.

5) Perinatal history:

A- Prenatal history: pregnancy condition including (drug intake, smoking, seizures in pregnancy, hospitalization in early pregnancy, severe anemia frequency of prenatal visits, prior fetal death and birth interval).

B- Natal history: Labour and delivery (spontaneous or induced) onset and duration of labour, methods of delivery (spontaneous vaginal delivery SVD or cesarean section CS), signs of fetal distress, problems during pregnancy or delivery, medicines given to the mother e.g. pethidine.

C- Postnatal history: APGAR score and Down score, any resuscitation needed, any abnormalities detected, birth weight and head circumference, estimated gestational age and vitamin K given.

6) Vaccination history: at 1st 28days of life.

Examination:

- General examination: Down score, Apgar score, height, weight, head circumference, complexion and any visible anomalies.
- Systemic examination: as Chest, cardiac, abdominal and CNS examination.
- Investigations: the following Investigation were done according to the presentation:
  - CBC, CRP, RBG and Blood film.
  - Blood gas analysis.
  - Chest X-Ray.
  - Echocardiography.
  - Chest ultrasound.

Ethical approval

The present study was conducted in accordance with international ethical standards and applicable local registry rules. An approval of the study was gained from the academic and ethical committee of Al-Azhar Assiut Faculty of Medicine, Al-Azhar University. All

participants' caregivers received a written consent form. The informed consent was clear and indicated the purpose of the study, and their freedom to participate or withdraw at any time without any obligation. Furthermore, participants' confidentiality and anonymity were assured by assigning each participant with a code number for the purpose of analysis only. The study was not based on any incentives or rewards for the participants. The study was conducted in accordance with Helsinki standards as revised in 2013.

Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 24. Quantitative data were expressed as mean ±SD. Qualitative data were expressed as frequency and percentage. Mean (average): the central value of a discrete set of numbers, specifically the sum of values divided by the number of values. Standard deviation (SD): is the measure of dispersion of a set of values. A low SD indicates that the values tend to be close to the mean of the set, while a high SD indicate that the values are spread out over a wider range. P value was considered significant if P value less than or equal to 0.05 after consulting a statistician.

Results

In this study we found that there was no statistical significant difference between studied groups as regard sex, gestational age and weight. (Table 1)

Our study showed highly statistical significant difference between studied groups as regard problem fixation. There was no problem fixation in nasal and naso-pharyngeal group while all Mask group patients (100%) had problem fixation.

This study showed no statistical significant difference (p-value > 0.05) between studied groups as regard response. Regarding description of response in all studied patients, 30 patients (50%) were improved and the other 30 patients (50%) were mechanically ventilated.

There was no statistical significant relation between response and (sex, weight and PCO2) (Table 3) . There was statistically significant relation between response and (gestational age, level of PEEP, duration of ventilation, pH and HCO3) (Table 4). In the present study there was highly statistical significant difference (p-value <0.001) between studied groups as regard complications and nasal irritation. In mask group there were 2 patients (10%) with complications and 18 patients (90%) had no complications while in nasal group and naso-pharyngeal group all patients (100%) had complications. (Table 5) (Figure 2)

There was no nasal irritation in Mask group and nasopharyngeal group while in all nasal group patients (100%) had nasal irritation. (Figures1,3)

Discussion

Respiratory distress syndrome in the perinatal period is common among preterm infants, particularly among those born at <30 weeks of gestation. The American Academy of Pediatrics has endorsed the use of continuous positive airway pressure (CPAP) among preterm infants with respiratory distress syndrome, based on lower rates of the combined outcome of bronchopulmonary dysplasia (BPD) or death [8].

CPAP failure, defined as the need for tracheal intubation and mechanical ventilation, is common among preterm infants <30 weeks of gestation, with failure rates approaching 45–50% in large clinical trials.

In developing countries and resource-limited facilities in which intubation and mechanical ventilation is not available, CPAP failure is associated with greater mortality [9].

Thus, preventing CPAP failure remains a high priority among health care providers caring for preterm infants. These observations led to the design and development of a novel, low-cost, CPAP system-Seattle-PAP [10].

Nasal continuous positive airway pressure (NCPAP) is a simple, low cost

and non- invasive method of ventilating a sick newborn. Bubble CPAP is the most commonly used modality for delivery of NCPAP. Traditionally, short bi-nasal prongs have remained the standard of care for delivery of NCPAP. The limitations of delivering NCPAP with prongs include mechanical difficulties in maintaining the nasal prongs, poor tolerance of the infant to the apparatus, difficulties in positioning the neonate, columella injury and septal deformities [11].

Nasal masks are increasing being used for delivering CPAP in recent times due to their ease of application. A randomized trial in neonates <31 weeks gestation comparing nasal mask with binasal prongs showed less intubation rate within 72 hours for the treatment of respiratory distress syndrome (RDS) or in post extubation setting with nasal mask [12].

A recent randomized controlled trial (RCT) from India reported a 6% reduction in the oxygen requirement at 2 hours of CPAP initiation with nasal mask as compared to nasal prongs. Nasal trauma has been reported with the use of both nasal masks and prongs and occurs equally with each interface. There is need for more evidence before nasal masks can replace short binasal prongs [13].

The aim of this study is to evaluate the effect of different types of CPAP in treatment of preterm neonates with respiratory distress syndrome in Al-Azhar (Assiut) University hospital NICU.

In this study we found that there was no statistical significant difference between studied groups as regard sex, gestational age and weight

Regarding to gestational age Abd-Allah et al [14] found that preterm cases were more than full term ones in all studied groups with no significant variation in the mean of GA per weeks. The results were in agreement with two studies by Rezzonico et al and Kawaza et al [15,16] whom observed preterm age group predominance among all treated groups.

The results are explained by the fact that preterm neonates were more susceptible to RDS because of relative surfactant deficiency.

The findings of Sai et al [17] are in agreement with our results as they showed that Differences in baseline characteristics were not statistically significant

Kieran et al [18] found that the groups were well matched for gestational age, birth weight, gender, mode of delivery, age at randomization, and duration of ventilation before randomization.

Say et al [19] found that Mean GA was 29.3 ± 1.6 and 29.1 ± 2.0 weeks and mean birth weight 1,225 ± 257 and 1,282 ± 312 g in NP and NM infants, respectively (i.e. values did not differ between groups; p = 0.55 and p = 0.22, respectively). The other baseline characteristics and prenatal risk factors were also similar between the two groups

Goel et al [20] showed that the baseline demographic characteristics (sex, gestational age, weight) of enrolled infants were similar

Backes et al [21] reported that treatment effect heterogeneity by gestational age, birth weight, or exposure to antenatal corticosteroids was not observed

In Abd-Allah et al [14] study, RD cases showed male predominance for all studied groups. This was in agreement with many studies reported predominance of male gender and also reported 1.6 ratios for males to females of total cases [22,15] .It may be related to different hormonal profile which affects surfactant synthesis intrauterine.

In the present study we found that there was no statistical significant difference between studied groups as regard duration of treatment. In mask group the mean duration was 4.4 ± 1.05 days, in nasal group the mean duration was 4.8 ± 1.44 days while in naso-pharyngeal group the mean duration was 4.2 ± 1.20 days.

Similar results were reported by Kieran et al [18] who found that the groups were

well matched for duration of ventilation before randomization

In contrast to our study Say et al [19] found that the median duration of NCPAP was significantly lower in NM infants than in NP infants (4 (1–5) vs. 2 (1–3) h; $p < 0.01$)

Also Ettrmal et al [22] showed that there was statistically significant difference in duration of treatment between the studied groups, which was significantly lower in NHFV group than NCPAP group.

Our study showed that there was no statistical significant difference between studied groups as regard level of PEEP. In mask group it was (6) in 8 patients (40%) and (7) in 12 patients (60%), in nasal group it was (6) in 6 patients (30%) and (7) in 14 patients (70%) while in naso-pharyngeal group it was (6) in 12 patients (60%) and (7) in 8 patients (40%).

Say et al [19] found that alterations in PEEP over time in both groups during the first 24 h of life were similar that was correlated with our study.

In our study, there was no statistical significant difference between studied groups as regard pH and HCO3 but there was statistically significant difference between studied groups as regard PCO2.

Kieran et al [18] found that the median FIO2 at randomization was not different between the groups

Say et al [19] showed that the median NCPAP was 5 (5–7) cmH2O in NP infants and 5 (5–7) cmH2O in NM infants, and did not differ between the groups ($p = 0.81$). The median FiO2 was 34.3 (30–39) in NP infants and 34.5 (33–39) in NM infants and was similar in the 2 groups ($p = 0.9$).

Mazzella et al [23] found a significantly lower oxygen requirement and respiratory rate in infants randomized to short NP than to CPAP delivered via nasopharyngeal prong. They did not assess the requirement for intubation beyond 48 hour from randomization.

Kakkilaya et al [24] found that there were no differences between the 23–26 weeks' and 27–29 weeks' GA categories

in the time to CPAP failure, median FiO2, CPAP level, A-a DO2, a/A PO2, and PaCO2.

In Ettrmal et al [22] study there was statistically non-significant difference between the studied groups regarding oxygen supply after treatment. This was in accordance with Malakian et al [25] who concluded that NHFOV did not decrease the need for mechanical ventilation compared with NCPAP overall in the first 72 hours of life; the rates of the primary outcome did not differ significantly between the NHFOV (6.5%) and NCPAP (14.1%) groups (P = 0.13). This was also in agreement with Zhu et al [26] who conducted a study in 18 tertiary neonatal intensive care units in China. A total of 302 preterm infants born at a gestational age (GA) of 26 weeks +0/7D –33 weeks +6/7D weeks with a diagnosis of RDS. They concluded that NHFOV was not superior to NCPAP with regard to the primary outcome when applied as the primary respiratory support for RDS in infants between 26+0/7 and 33+6/7 weeks of GA. This was in disagreement with Li et al [27] who involved 463 patients. The meta-analysis estimated a lower risk of intubation (relative risk = 0.50, 95% confidence interval of 0.36 to 0.70); NHFOV significantly reduced risk for intubation compared with NCPAP/BP-CPAP.

This study showed no statistical significant difference (p-value > 0.05) between studied groups as regard response. Regarding description of response in all studied patients, 30 patients (50%) were improved and the other 30 patients (50%) were mechanically ventilated.

There was no statistical significant relation between response and (sex, weight and PCO2). There was statistically significant relation between response and (gestational age, level of PEEP, duration of ventilation, pH and HCO3).

Kieran et al [18] reported previously that NCPAP was more effective at preventing

intubation and ventilation within 72 h of starting therapy when given via NM as opposed to via NP.

In Say et al [19] study, they found that both interfaces are equally effective at preventing intubation, but that applying NM necessitated a shorter duration of NCPAP. In their study, the infants were treated with NCPAP both as the primary treatment of respiratory distress and as an aid to extubation, and almost twice as many infants required intubation when compared our study. We thought that these unusual reduced rates of MV requirement in the first 72 h of life, i.e. 17.3% (NP) and 16.2% (NM) in our study could be related to the less invasive surfactant administration technique and that these low rates resulted in statistical insignificance regarding the different interfaces.

In the present study there was highly statistical significant difference (p-value < 0.001) between studied groups as regard complications and nasal irritation. In mask group there were 2 patients (10%) with complications and 18 patients (90%) had no complications while in nasal group and naso-pharyngeal group all patients (100%) had complications. There was no nasal irritation in Mask group and nasopharyngeal group while in all nasal group patients (100%) had nasal irritation.

In a case series reported by Robertson et al [28] the incidence of nasal trauma resulting from nasal prong with the IFD was 20% in a group of VLBW infants. This is lower than our value, which may partly be because we included redness as a sign of trauma.

Say et al [19] found that the incidence of moderate and severe BPD was significantly higher in the NP group than in the NM group (n = 11 or 14.6% and n = 2 or 2.7%, respectively; p < 0.01), but overall BPD rates did not differ between groups.

Iyer et al [29] reported a reduced combined outcome of death and/or BPD by 17% in infants with established RDS

who received early surfactant and noninvasive MV.

In randomized, controlled trials conducted by Rego et al [30] no significant differences in the frequency of skin injury (excoriation, bleeding or erythma) were found when comparing different nasal interface groups. Similar to previous findings [19] did not observe a significant difference in skin breakdown rates according to nasal interface, but the rate diminished to 13.5%, lower than reported in the literature [31] .

Regarding Goel et al [20] CPAP failure was seen in 13% infants on nasal mask and in 25% infants on nasal prongs, but failed to reach statistical significance (P=0.15). Incidence of pulmonary interstitial emphysema was significantly lesser in infants on nasal mask as compared to nasal prongs (P=0.03), although higher flows were required in mask group which was statistically significant [6.2 (0.7) vs 5.9 (0.4) L/min, P= 0.008]. There was a significant lower incidence of overall nasal trauma in mask group as compared to prongs.

A study by Kieran et al [18] compared mask vs prongs using IFD, and found that in terms of NCPAP failure, nasal mask was superior than prongs which was statistically significant (28% vs 52%). Our overall CPAP failure rate was comparable to the previously done studies by [32, 33] .

Ettrmal et al [22] study showed statistically non-significant difference between the studied groups regarding occurrence of nasal injury. This was in agreement with [30] who showed insignificant difference between the studied groups regarding traumatization of nasal skin and mucosa (P=0.260).

Our study showed highly statistical significant difference between studied groups as regard problem fixation. There was no problem fixation in nasal and naso-pharyngeal group while all Mask group patients (100%) had problem fixation.

We concluded that CPAP is an effective treatment of respiratory distress syndrome leading to significant improvement of outcome of admitted neonates. There is no statistical significant difference between studied groups as regard response. Mask type CPAP has the least complications.

Conclusions

CPAP is one of effective treatment of RDS leading to significant improvement of outcome reducing hospital stay, need for invasive mechanical ventilation with its harmful adverse effects and thus the case fatality rate of RDS cases and so the overall mortality rate of the NICU. We recommend early treatment of preterm babies with RDS with different types of CPAP and further studies on large geographical scale and on larger sample size to emphasize our conclusion.

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Author's contributions

All of authors shared equally in this work and have seen and agreed to the submitted version of the manuscript.

Conflict of interest

The authors declare that they have no competing interests

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Table (1): Comparisons between studied groups as regard demographic data.

Item		CPAP						P-value
		Mask (n = 20)		Nasal (n = 20)		Naso-pharyngeal (n = 20)		
Sex	**Male**	8	40%	14	70%	12	60%	0.150 NS
	Female	12	60%	6	30%	8	40%	
Gestational age	**34 weeks**	12	60%	6	30%	12	60%	0.141 NS
	35 weeks	4	20%	8	40%	2	10%	
	36 weeks	4	20%	6	30%	6	30%	
Weight (kg)	**Mean**	2.23		2.24		2.17		0.966 NS
	±SD	0.38		0.44		0.34		
Duration (days)	**Mean**	4.4		4.8		4.2		0.423 NS
	±SD	1.05		1.44		1.20		

NS: p-value > 0.05 is considered non-significant.
CPAP: continuous positive airway pressure, Kg: kilogram, SD: standard deviation.

Table (2): Comparisons between studied groups as regard level of PEEP.

Item		CPAP			P-value
		Mask (n = 20)	**Nasal (n = 20)**	**Naso-pharyngeal (n = 20)**	
PEEP CmH2O	**(6)**	8 40%	6 30%	12 60%	0.150 NS
	(7)	12 60%	14 70%	8 40%	

NS: p-value > 0.05 is considered non-significant.
CPAP: continuous positive airway pressure, CmH2o: centimeter water

Table (3): Comparisons between studied groups as regard ABG results.

Item		CPAP			P-value
		Mask (n = 20)	**Nasal (n = 20)**	**Naso-pharyngeal (n = 20)**	
pH	**Mean**	7.29	7.35	7.34	0.0.051 NS
	±SD	0.10	0.11	0.12	
PCO_2	**Mean**	35.5	44.7	44.0	0.007 S
	±SD	9.4	9.1	10.6	
HCO_3	**Mean**	16.7	20.1	17.9	0.191 NS
	±SD	4.2	6.6	5.8	

S: p-value < 0.05 is considered significant. NS: p-value > 0.05 is considered non-significant.
CPAP: continuous positive airway pressure, ABG: arterial blood gases,

Table (4): Comparisons between studied groups as regard response.

Item		CPAP						P-value
		Mask (n = 20)		Nasal (n = 20)		Naso-pharyngeal (n = 20)		
Response	**Improved**	8	40%	10	50%	12	60%	0.04 S
	MV	12	60%	10	50%	8	40%	

NS: p-value <0.05 is considered significant.
CPAP: continuous positive airway pressure, MV: mechanical ventilation,

Table (5): Comparisons between studied groups as regard complications.

Item		CPAP						P-value
		Mask (n = 20)		Nasal (n = 20)		Naso-pharyngeal (n = 20)		
Complications	No	18	90%	2	10%	2	10%	< 0.001 HS
	Yes	2	10%	18	90%	18	90%	
Nasal irritation	No	18	90%	3	15%	20	100%	< 0.001 HS
	Yes	2	10%	17	85%	0	0%	
Problem fixation	No	3	15%	3	15%	20	100%	< 0.001 HS
	Yes	17	85%	17	85%	0	0%	

HS: p-value < 0.001 is considered highly significant.
CPAP: continuous positive airway pressure,

Table (6): Description of response in all studied patients.

Item		All studied patients (n = 60)	
Response	**Improved**	30	50%
	MV	30	50%

MV: mechanical ventilation,

Table (7): Relation between response and other studied data in all studied patients.

Item		Response				P-value
		Improved (n = 30)		MV (n = 30)		
Sex	**Male**	18	60%	16	53.3%	0.602 NS
	Female	12	40%	14	46.7%	
Gestational age	**34 weeks**	8	26.7%	20	66.7%	0.006 S
	35 weeks	10	33.3%	6	20%	
	36 weeks	12	40%	4	13.3%	
Weight (kg)	**Mean**	2.3		2.1		0.214 NS
	±SD	0.4		0.3		
Duration (days)	**Mean**	4.0		4.9		0.003 S
	±SD	0.8		1.4		
pH	**Mean**	7.36		7.29		0.007 S
	±SD	0.11		0.1		
PCO2	**Mean**	42.1		40.7		0.591 NS
	±SD	7.2		13.0		
HCO3	**Mean**	19.7		16.7		0.039 S
	±SD	5.5		5.7		

S: p-value < 0.05 is considered significant. NS: p-value > 0.05 is considered non-significant.
MV: mechanical ventilation, PEEP: positive end expiratory pressure, kg: kilogram

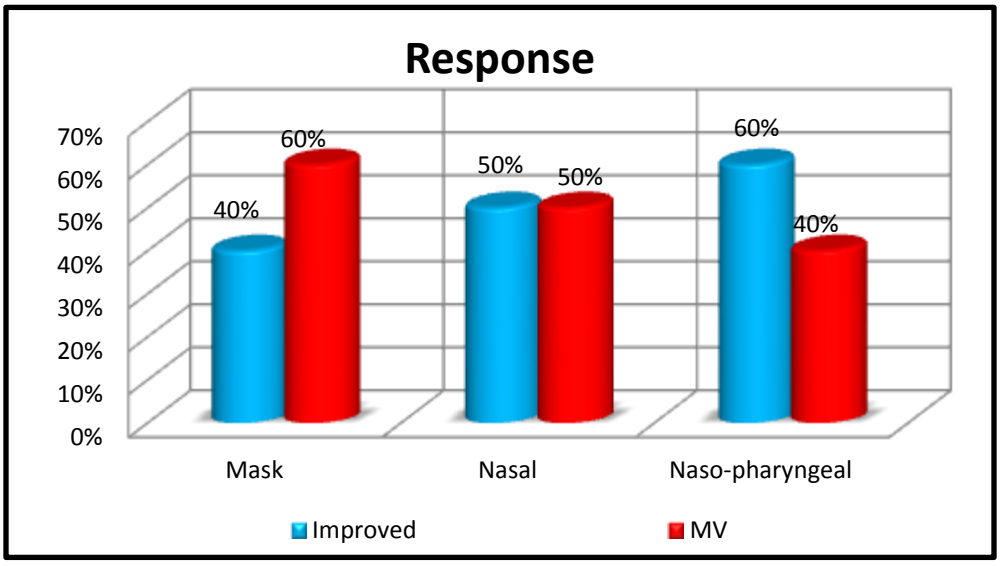

Figure (1): Comparisons between studied groups of preterm neonates with respiratory distress syndrome regarding to response.

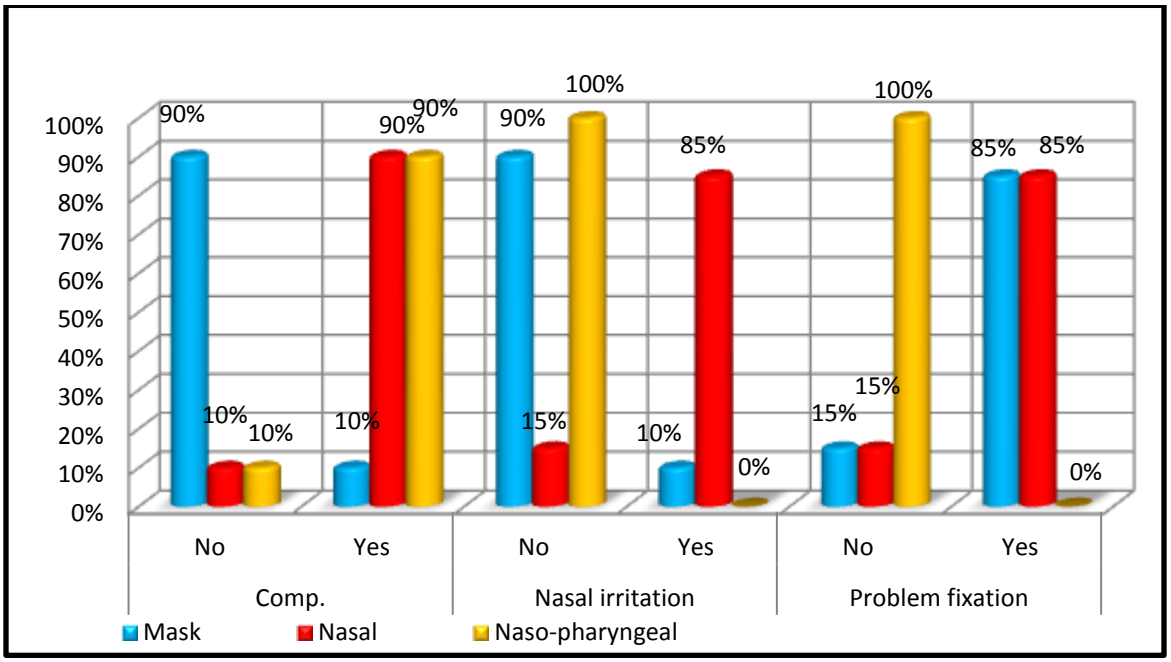

Figure (2): Comparisons between studied groups of preterm neonates with respiratory distress syndrome regarding to complications.

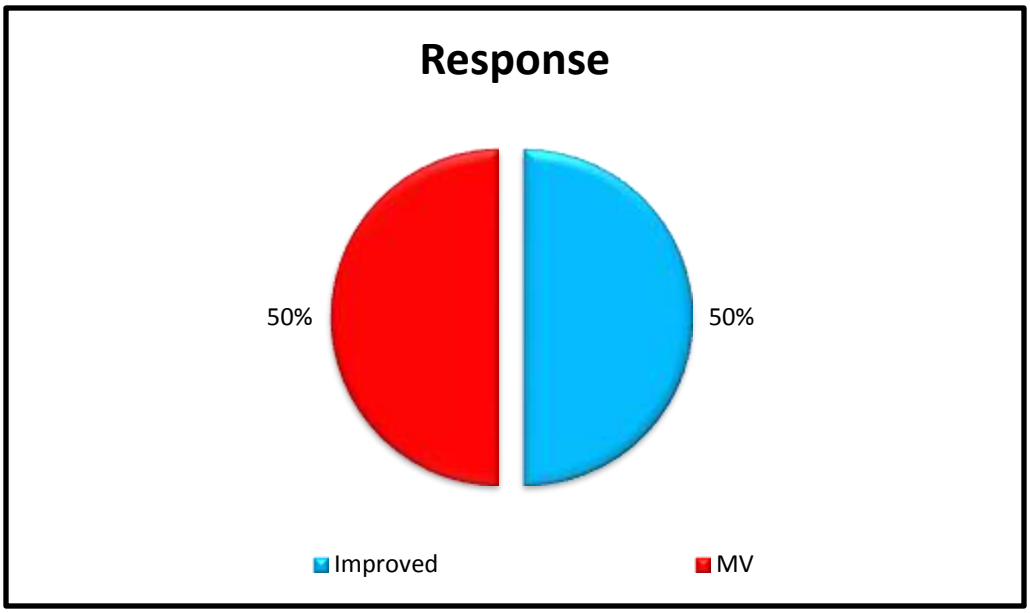

Figure (3): Description of response to different modes of CPAP in all studied preterm neonates with respiratory distress syndrome.

Citation: Mostafa M. Ali; Abdelmeguid M. Bayoumi; Mohammed M. Younis; Khaled H. Awad. "Analytical Study of Different Modes of Continuous Positive Airway Pressure (CPAP) in Management of Respiratory Distress Syndrome (RDS) in Preterm Neonates". *Annals of Neonatology Journal* 2022; 4(2): 25-46 doi: 10.21608/anj.2022.122114.1047