Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

The Early use of CPAP in Neonatal Pneumonia: Randomized Control Trial.

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Received: January 2018
Accepted: January 2018

ABSTRACT

Background: Aim- To assess clinical resolution of neonatal pneumonia by early use of CPAP. Study design- Randomized control trial. **Methods:** Neonates with a gestational age of >35 weeks having tachypnea (RR≥ 60/min) and respiratory distress were included in the study. The neonates were subjected to a radiological examination for confirmation of pneumonia. Further a sepsis screen was performed, if the screen was positive, the patient was enrolled for inclusion in the study. The randomization allocation was done and the babies allotted to the study (CPAP) group or the control group. Babies in study group were put on CPAP soon after randomization allocation and the babies in the control group were managed as per the unit protocol. **Results:** It has shown that the early use of CPAP in addition to standard treatment results in early resolution of clinical pneumonia & significant reduce the duration of oxygen therapy. Further it lowered the need for mechanical ventilation. However there was no difference in the duration of hospital stay in the two groups. CPAP was well tolerated by the neonates (both late preterm and term) with few complications. No baby's condition gave concern that there could be a significant air leak. **Conclusion:** In our study, the early use of CPAP in addition to standard treatment results in early resolution of clinical pneumonia & significant reduce the duration of oxygen therapy. Further it lowered the need for mechanical ventilation. CPAP was well tolerated by the newborn (both late preterm and term) with few complications.

Keywords: CPAP, Neonate, Neonatal Pneumonia.

INTRODUCTION

Respiratory distress is one of the commonest disorders encountered within the first 48-72 hours of life. It occurs in 0.96 to 12 % of live births and is responsible for about 20% of neonatal mortality.[1] Respiratory pathology is the commonest (32-54%) autopsy finding among early neonatal deaths.[2-4] The spectrum of respiratory distress in neonates includes pneumonia, transient tachypnea of the newborn, hyaline membrane disease, meconium aspiration syndrome and other miscellaneous causes. Intrauterine and early onset pneumonia was found at autopsy in 10-38% of stillborn and 20-63% of live born babies who subsequently died (with all but one of six studies in the range of 20-32%).[5] Case fatality rates are higher for intrauterine or early onset pneumonia than for late onset neonatal pneumonia and higher among low birth weight newborns.[6-8]

Respiratory distress in newborns presents with tachypnea, inspiratory retractions and expiratory grunting. During grunting the glottis is partially closed, which increases the transpulmonary pressure and prevents atelectasis.[9] Based on this principle, CPAP ventilation delivered through an endotracheal tube was first used in 1971 to treat cases of HMD successfully.[10] CPAP increases FRC and improvement in lung compliance.

One of the pathogenetic mechanisms of lung infection is the clogging of alveoli by the bacteria and the debris, thus blocking normal gas exchange and function. In addition, this debris, the exuded fluid and other factors all act to inactivate surfactant, and to limit its function. Thus, many of the pulmonary consequences of pneumonia mimic RDS, with areas of collapse and other areas of over-expansion.

The use of CPAP in pneumonia may prevent respiratory failure and improve outcome. In medical literature there are evidence based guidelines for the use of CPAP in neonatal respiratory failure. Till now there are no evidence based guide lines in early use of CPAP in neonatal pneumonia.

Aims & Objectives

1. To assess the role of CPAP in resolution of respiratory distress in neonatal pneumonia.

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MATERIALS AND METHODS

Setting/patients

The study was conducted in the Department of Neonatology, IPGMER- SSKM Hospital from Jan 2015 to April 2016. Infants (>35wks) were within 48 hours of life with clinical & radiological features of pneumonia. Infants with MAS, CHD, major congenital malformation, severe birth asphyxia, and hydrops were excluded.

Sample Size

Since there were few studies on neonatal pneumonia in the babies>35 weeks of gestation, it was not feasible to estimate the exact incidence of pneumonia. A large number of babies with respiratory distress turn out with other causes of respiratory distress. The use of CPAP in babies with pneumonia has not been studied. Hence it was fill that a sample of convenience. We propose to include 25 neonates in each arm of the study.

Study Protocol

Neonates with a gestational age of >35 weeks as assessed by the modified Ballard score were eligible for enrolment in the study. The babies having tachypnea (RR≥ 60/min) and/or respiratory distress defined as grunting, nasal flaring or chest retraction were included in the study. An informed signed consent from the parents was obtained for permission / acceptance to enroll in the study. The neonates were subjected to a radiological examination for confirmation of pneumonia. Further a sepsis screen was performed (TLC, I: E ratio, microESR and CRP) and if the screen was positive, the patient was enrolled in the study.

The randomization allocation was done and the babies allotted to the study (CPAP) group or the control group (conventional management). Babies in study group were put on CPAP soon after randomization allocation and the babies in the control group respiratory distress managed by high flow nasal cannula (flow 5litre)

Assessment during study: All the babies were followed up till resolution of pneumonia or death. After the initial radiological examination for enrolling confirmed cases of pneumonia, the neonates were subjected to further radiological studies. The clinical course was assessed by the Downe's score recorded 2 hourly on a scale of 0-10. The rest of the management of the babies was done as per unit protocol for management of pneumonia

Oxygen therapy: On the basis of objective evidence of hypoxemia, neonates were given oxygen. As per the unit's standard policy, the neonates with pneumonia in control group were given oxygen via high flow nasal cannula for improvement of oxygenation.

CPAP System: In our study, we used continuous flow devices (Bubble CPAP and Ventilator-derived) & interfaces were short nasal prongs (Binasal) and nasal mask.

Protocol in the CPAP group: An initial setting of CPAP was PEEP 5cm H2O & FIO2 adjusted to maintain SpO2 88-93%. Further adjustment in the CPAP settings was done according to the clinical and blood gas parameters to keep them within normal limits. Changes in CPAP settings were done based on blood gas PaO2 and PaCO2 values. Maximum support that was tired before labeling as 'failure' and switching on to mechanical ventilation was PEEP of 7 cm of H2O and FIO2 of 0.7

Written, informed consent was obtained from parents. Ethical approval for the study was obtained from the institution research ethical committee.

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean □ SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

During study period, 55 neonates were eligible. Two neonates were not entered into the study because their families didn't agree to participate in the study. Three newborn were subsequently excluded: one had congenital cystic adenomatoid malformation of the lung; two infants had congenital heart disease. A total of 50 enrolled newborn infants completed the study. Respiratory distress was diagnosed at a mean age of 21 hours (0- 48 hours)

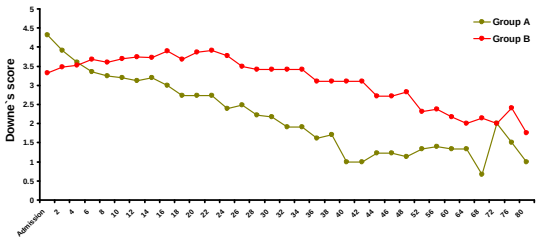
Out of 50, only seventeen neonates with pneumonia were delivered at home, while the remaining were born at SSKM hospitals. Thirty eight percent neonates with pneumonia were full term, rest were late preterm (≥35 up to 37 weeks). Three neonates were VLBW. Thirty five neonates were born to mothers with high risk factors for pneumonia/ sepsis. In 29 cases (58%) there was only one risk factor, and in six cases (12%) there were two or more risk factors. The single most common risk factor was prolonged rupture of membranes (20 cases). Out of the thirty five mothers of neonates with high risk factors for pneumonia, only five had received antibiotics perinatally. Out of 50 cases of pneumonia, blood culture was positive in 14 cases (8 in study group, 6 in control group). Most isolates (71.42 percent) were Gram-negative bacteria (E. coli 21.42%; Klebsiella 21.42%; Pseudomonas 21.42%). The remaining isolates (35.71 percent) were Gram-positive bacteria (Streptococcus pneumoniae 21.42%; Staph. aureus 14.28%).

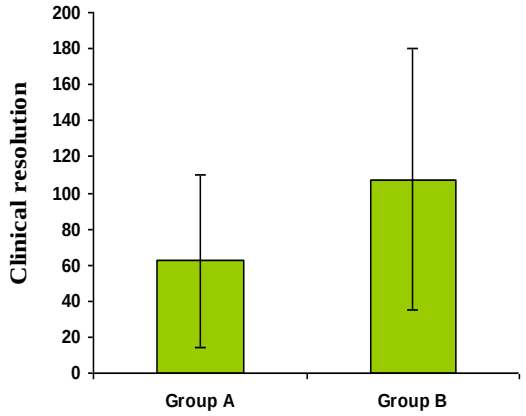
The most common x –ray abnormality identified was bilateral patchy alveolar densities, noted in 80% of

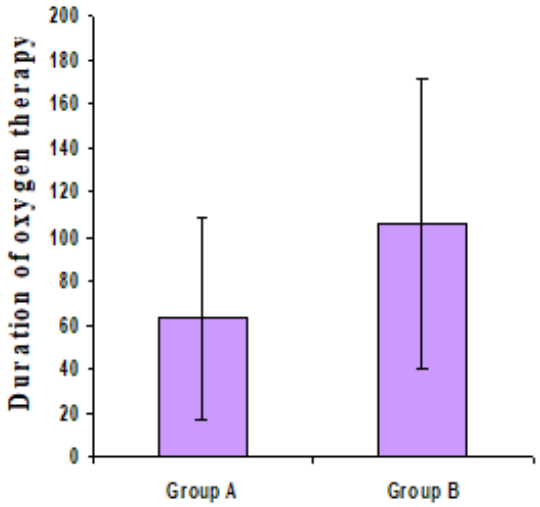
cases. Ten percent patients had characteristically extensive, dense alveolar changes, hyperinflation was observed in 8% cases.

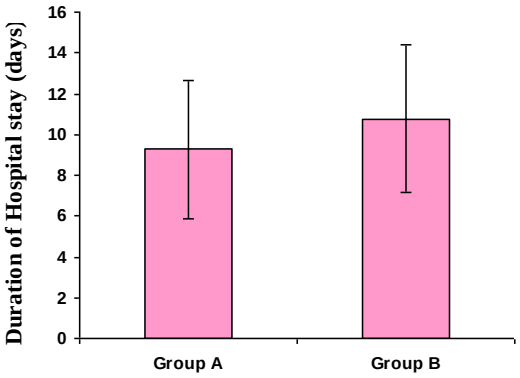
Table 1: Comparison of clinical resolution, duration of oxygen therapy, requirement of mechanical ventilation &hospital stays (days)

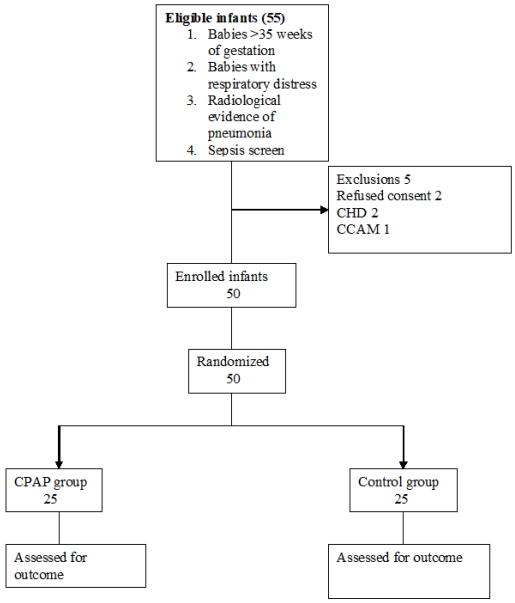
	Group A	Group B	P value
Clinical resolution	62.50±47.83	107.24±72.62	0.017*
Duration of oxygen therapy	63.04±46.36	105.76±66.19	0.011*
Mechanical ventilation	3(12%)	9(36%)	0.047*
Duration of Hospital stay (days)	9.28±3.39	10.76±3.61	0.142











It has shown that the early use of CPAP in addition to standard treatment results in early resolution of clinical pneumonia & significant reduce the duration of oxygen therapy. Further it lowered the need for mechanical ventilation. However there was no difference in the duration of hospital stay in the two groups.

CPAP was well tolerated by the neonates (both late preterm and term) with few complications. No baby's condition gave concern that there could be a significant air leak.

DISCUSSION

This study is, to our knowledge, the first randomized controlled trial investigating the value of early use of CPAP in neonatal pneumonia. It has shown that the early use of CPAP in addition to standard treatment results in early resolution of clinical pneumonia & significant reduce the duration of oxygen therapy. Another interesting observation in our study was that the early use of CPAP in neonatal pneumonia lowers the need for mechanical ventilation. The number of babies who required mechanical ventilation in the

CPAP group vs. the control group was 3 vs. 9. This was a statistically significant difference (p= 0.047). There is established evidence that CPAP given for RDS in neonates significantly reduces the need for mechanical ventilation.[11]

In the present study, 34% of the neonates were delivered at home while the remaining in our hospital. Thirty five (70%) mothers of neonates with respiratory distress had predisposing factors for pneumonia. Isaacs D et al,[12] in their study found that 78% of the neonates who developed pneumonia had a risk factor for pneumonia present. Webber et al found that twenty seven cases (77%) had risk factors for the early onset neonatal pneumonia.[9]

Diagnosis of pneumonia is frustratingly incomplete, with most large studies failing to identify a causative organism in 33 to 45% of patients.[13-15] Diagnosis by blood culture is highly specific, but the sensitivity of blood cultures for bacterial pneumonia is 25%. In our study, bacterial etiology of pneumonia was established in 14 neonates (28%) by blood culture. This was lower than that reported earlier by Webber et al (46%) and Mathur et al (47.5%).[8,16] The most common isolate was Group B streptococci (69%) identified by Webber. We isolated Klebsiella sp in 21.42% of case and our findings are consistent with the earlier studies which suggest increasing incidence of Klebsiella sp and Pseudomonas. Earlier studies on neonatal pneumonia have included neonates with only radiological findings and have not considered blood culture positivity in diagnosis of neonatal pneumonia. Webber et al.[8] however, had classified cases as 'definitive pneumonia' if respiratory pathogen was isolated from blood and 'probable pneumonia' if blood culture failed to show a pathogen, in the presence of a positive chest x- ray. In the present study the incidence of definitive pneumonia' was (28%).

Mortality rates in early onset pneumonia in our study were 10% (1 in CPAP group & 4 in control group). The case fatality rates for early onset pneumonia were 29% reported by Webber et al. All of them were seen in preterm infants. The mortality rates for perinatally acquired pneumonia varies and has been estimated to be 20 percent, with a higher mortality rate of 50 percent for postnatally acquired pneumonia.[18] In one recent review of perinatally acquired infection, the overall mortality was 10 percent.[19] This decline was attributed to increased use of perinatal antibiotics. In the present study, only five mothers (10%) received antibiotics perinatally. This dramatic reduction in the mortality rates was attributed to the early use of CPAP.

CONCLUSION

In our study, the early use of CPAP in addition to standard treatment results in early resolution of clinical pneumonia & significant reduce the duration of oxygen therapy. Further it lowered the need for mechanical ventilation. CPAP was well tolerated by the newborn (both late preterm and term) with few complications. However there was no difference in the duration of hospital stay in the two groups, we feel that this study was not large enough to confidently demonstrate any difference in length of hospital stay. A Large multi-centre study would be needed to investigate whether CPAP is of value in reducing the duration of hospital stay and mortality in neonatal pneumonia.

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How to cite this article: Munian D, Biswas RK, Mukherjee R. The Early use of CPAP in Neonatal Pneumonia: Randomized Control Trial. Ann. Int. Med. Den. Res. 2018; 4(2):PE06-PE10.

Source of Support: Nil, **Conflict of Interest:** None declared