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Role of early labour room CPAP in preterms 28 to 32weeks

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Abstract

Respiratory distress syndrome (RDS) is one of the most common causes of mortality and morbidity in preterm neonates. CPAP, Surfactant and mechanical ventilation have been the main stay management techniques in RDS. The present research aims to study the usefulness of early delivery room CPAP in preterms and its outcome.

Methods: The study was a randomized control clinical trial with 109 neonates. Neonates born between 28 0/7 to 32 6/7 with evidence of RDS were randomized to receive either delivery room CPAP or delayed CPAP.These groups are compared for predefined primary and secondary outcomes.

Results: Mean Birth weight of cases is 1.24 ± 0.17 and in controls is 1.21 ± 0.19.(P=0.489)The Meangestational age of cases is 29.81 ± 1.56 and in controls is 29.81±1.64 (p=1.0). In this study 23(42.59%) preterms among the cases and 29(52.73%) in controls were present on CPAP for 48-72 hrs. Only 11(20.37%) among cases had CPAP requirement beyond 72 hrs (p=0.55). 16(29.63%) cases required mechanical ventilation, Whereas 28(50.91) preterms in the controls needed mechanical ventilation (p=0.0235). 30 neonates were discharged within 14 days among cases and 16 neonates among control groups. 8 neonates stayed in nicu between 15 – 21 days and 15 neonates in control group. 1 neonate stayed beyond 21 days from cases group and 2 neonates from control group (p=0.0231). 15(27.78%) preterms died due to various causes in the study group and 20(36.36%)preterms died in control group(p=0.337).

Conclusions: Early administration of CPAP in the delivery room in preterm neonates developing respiratory distress decreases the need for mechanical ventilation. Early administration of CPAP helps in early discharge from hospital and early recovery. There is no difference in mortality between the two groups indicating there is no significant impact of early labour room CPAP on mortality

Keywords: CPAP, Preterms

Introduction

Respiratory Distress Syndrome (RDS) is a clinical syndrome characterized by respiratory failure in a preterm neonate.

The immature lung in RDS is deficient in surfactant and is prone to atelectasis, which in turn leads to lung inflammation and poor gas exchange. Limited facilities exist at rural hospitals for the management of newborn infants with respiratory distress syndrome (RDS). Furthermore, the secondary and tertiary hospitals are under severe strain to accept all the referrals from rural hospitals. Many of these infants require intubation and

ventilation with a resuscitation bag which must be sustained for hours until the transport team arrives. Not only lung damage is inflicted by the prolonged ventilation, but transferring the infant by helicopter and ambulance is expensive.

Before the introduction of mechanical ventilation and Continuous Positive Airway Pressure (CPAP) in the 1960's and 1970's, the only therapy for respiratory failure in the preterm newborn was oxygen and fluids.

CPAP refers to the application of positive pressure to the airway of a spontaneously breathing infant throughout the respiratory cycle. The first clinical use of CPAP was reported by Gregory et al in a landmark report in 1971. They described the use of CPAP via endotracheal tube or a head box in preterm infants with respiratory distress syndrome (RDS).[1] shortly after this, Kattwinkel reported successful use of nasal prongs to provide CPAP in these infants.[2]

CPAP, often thought to be the 'missing link' between supplemental oxygen and mechanical ventilation, is gaining immense popularity in neonatal intensive care units. Being technically simple, inexpensive and effective, it has become the primary mode of respiratory support in preterm low birth weight (LBW) infants. If used early and judiciously in infants with respiratory distress, CPAP can save many lives and reduce upward referrals.[3] It could well be a boon for babies born in resource restricted countries.There are many trials in which efficacy of CPAP was proven in preterm neonates <28 weeks of gestational age and there is not much data available to prove the efficacy in preterms from 28 – 32 weeks so this study was done

Aims

1. To study the usefulness of Early delivery room CPAP in preterm (<32 weeks).
2. To study the requirement of oxygen, ventilator support in 2 groups.
3. To study the incidence of complications like Sepsis in 2 groups.

Objectives

- **PRIMARY OBJECTIVE:** To know the morbidity & mortality patterns in babies <32 weeks with early CPAP and those without early CPAP.

- **SECONDARY OBJECTIVE**: To know the requirement of oxygen, duration of the stay and requirement of advanced life supportive measures in babies with early CPAP and in babies without early CPAP.

PATIENTS AND METHODS

SOURCE OF DATA:

- Neonates with respiratory distress admitted in neonatal intensive care unit and neonates developing respiratory distress immediately after birth.

INCLUSION CRITERIA:

- All preterm neonates with gestational age 28 weeks to 32 weeks.
- All preterm neonates admitted in NICU with respiratory distress less than 6 hours with respiratory distress.
- All preterm neonates developing respiratory distress immediately after birth in delivery room

EXCLUSION CRITERIA:

- Preterm less than 28 weeks and more than 32 weeks.
- Preterms admitted with respiratory distress after 6 hours of life.
- Neonates with congenital malformations.
- Neonates requiring mechanical ventilation at the time of admission and at birth

TYPE OF STUDY:

• Facility based interventional study (Randomised control study)

DURATION OF STUDY:

• May 2014 to june 2015 (12 months)

METHOD OF COLLECTION OF DATA:

The study population included preterm neonates admitted to the NICU with respiratory distress within 6 hours of life and in preterm neonates developing respiratory distress immediately after birth in delivery room. They were categorized into case and control groups. Cases included neonates with respiratory distress who were started on CPAP in the labour room within 15 minutes of life. Control group included neonates with respiratory distress who were started on CPAP after 15 minutes to 6 hours of life.

Both the groups were monitored till they are discharged and the need for mechanical ventilation was noted. Clinical diagnosis was made based on time of onset of respiratory distress and clinical examination and respiratory scoring (Silverman Anderson score). Then chest X-ray and routine investigations were done in all neonates. The usefulness of these investigations in aiding the diagnosis was noted. Duration of CPAP between the study and control groups are noted. These neonates were examined daily till they were in hospital.

STATISTICAL ANALYSIS:

Data entry was done in MICROSOFT EXCEL and analysis was done using descriptive statistics, student t test (unpaired) and chi square test($p<0.05$) by EPI info 7 statistical software

RESULTS AND OBSERVATIONS

The present interventional study was conducted in the neonatal intensive care unit (NICU) at a Government hospital for a period of 1 year.A total of 3034 babies were admitted to NICU during the study period, out of which 1551 were LBW babies. Of which babies with gestational age 28-32 weeks were 421 babies were included in the study after exclusion, out of which 54 babies were included in the study group and 55 in the control group.

TABLE 1:Distribution according to sex among cases and controls

SEX	**CASES**	**CONTROLS**
MALE	30(55.55%)	33(60%)
FEMALE	24(44.45%)	22(40%)
Total	54(100%)	46(100%)

The above table shows the sex distribution of babies in the study& control groups.In the present study it was observed that there were 30(55.55%) male babies in the cases and 33(60%) in controls whereas there were 24(44.44%) female babies in cases and 22(40%) in controls. there was a slight male predominance in the present study.

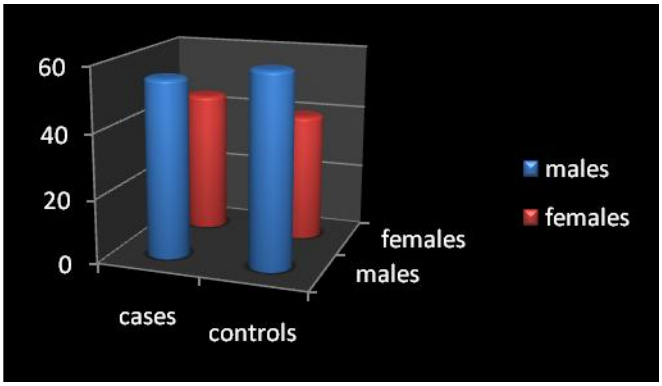

FIGURE 1 : SEX DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 2: <u>Distribution according to birth weight among cases and Controls.</u>

BIRTH WEIGHT(Gms)	**CASES**	**CONTROLS**
<1000	5(9.25%)	9(16.36%)
1000-1250	25(46.30%)	22(40%)
>1250	24(44.45%)	24(43.64%)
TOTAL	54(100%)	55(100%)
MEAN ± SD	1.24 ± 0.17	1.21 ± 0.19
t = 0.6930 , df = 107 ,p = 0.489		

This table shows the weight distribution of babies in the study & control groups. From the above table it was observed that there were 5(9.25%) preterm Extremely Low birth Weight (ELBW) i.e. under 1000 grams in cases and 9(16.36%) in controls. Most of the babies in the study & control group fell under the weight group of 1000-1250 gms constituting 25(46.30%) in cases and 22(40%) in control group. There were 24(44.45%) babies more than 1250 gms in cases and 24(43.64%) in controls.Mean and Standard Deviation (SD) in Birth weight of cases is 1.24 ± 0.17 and in controls is 1.21 ± 0.19 respectively.There was no statistically significant difference between the two groups

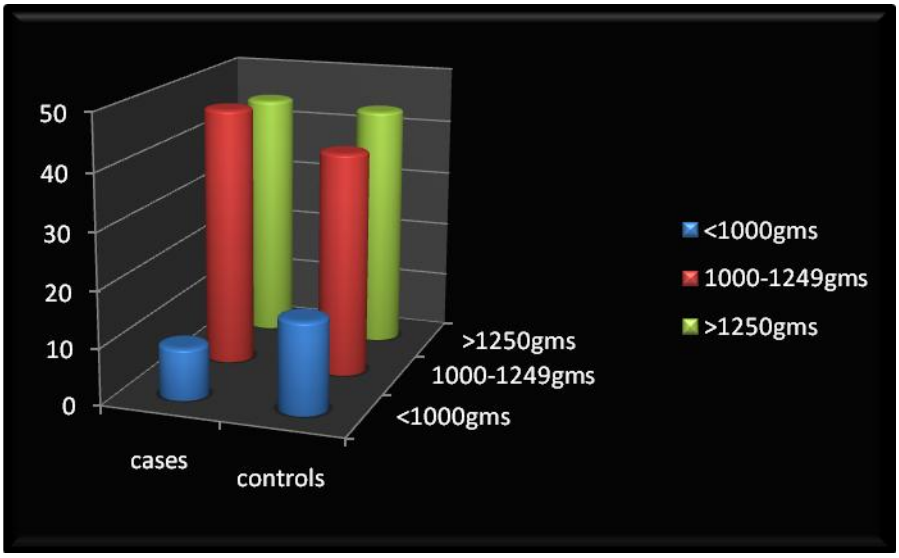

FIGURE 2 : BIRTH WEIGHT DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 3: Distribution according to gestational age among cases and controls

GESTATIONAL AGE(WEEKS)	CASES	CONTROLS
28	19(35.19%)	21(38.18%)
30	21(38.89%)	18(32.72%)
32	14(25.92%)	16(29.10%)
TOTAL	54(100%)	55(100%)
MEAN ± SD	29.81 ± 1.56	29.81±1.64
t = 0.000 , df = 107 , p = 1.000		

The above table shows the frequency distribution of babies according to the gestational age in the study and control groups. It was observed that among preterms of gestational age of 30 weeks cases constituted 21(38.89%) neonates and controls were 18(32.72%)neonates. 21(38.18%) preterms were of 28 weeks in controls constituting the majority. 14(25.92%) preterms in cases and 16(29.10%) in controls were 32 weeks of gestation. Mean and Standard Deviation (SD) in gestational age of cases is 29.81 ± 1.56 and in controls is 29.81±1.64 respectively.

There was no statistically significant difference between the two groups

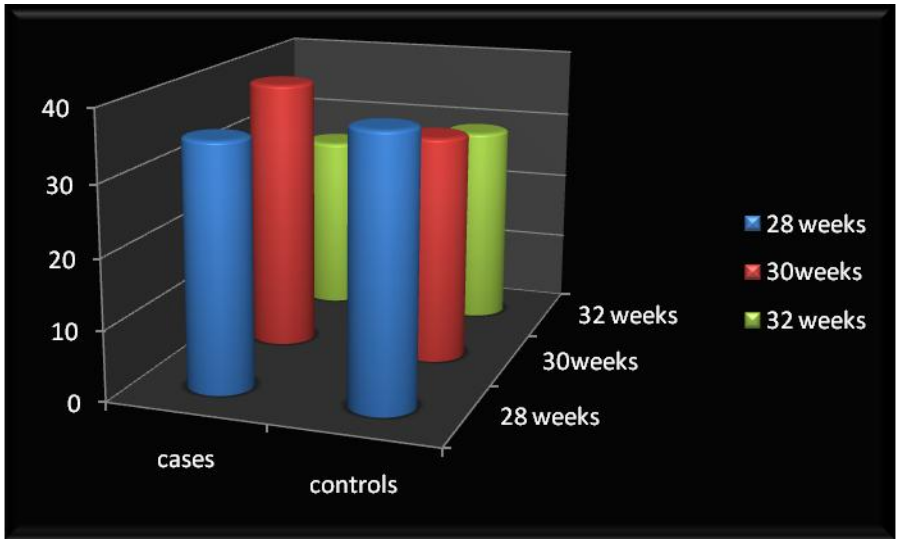

FIGURE 3: GESTATIONAL AGE DISTRIBUTION AMONG CASES AND COONTRLS

TABLE 4: Distribution according to respiratory rate among cases and controls

RR(respiratory rate)	CASES	CONTROLS
60-80	44(81.48%)	40(72.72%)
>80	10(18.52%)	15(27.27%)
TOTAL	54(100%)	55(100%)

Respiratory rate is taken as an important parameter for initiation of CPAP in the babies. 44(81.48%) of the preterms among the cases had the respiratory rate between 60-80 / minute. Only 10(18.52%) among the cases had their respiratory rate more than 80 per minute.

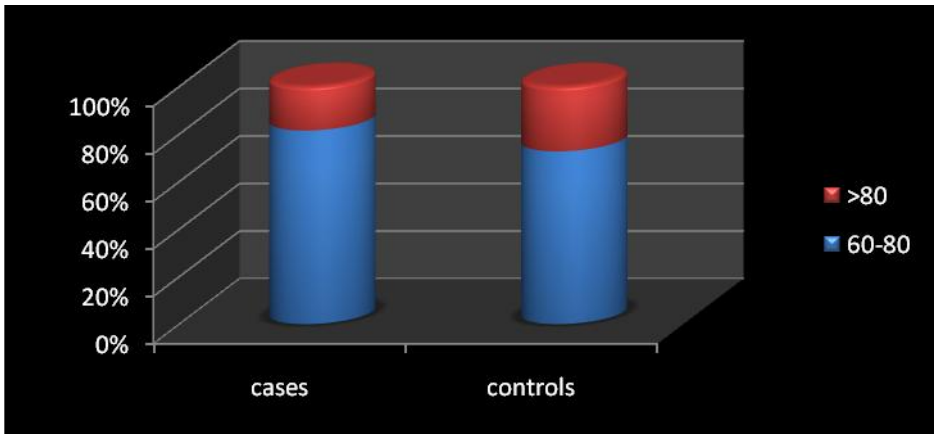

FIGURE 4 : RESPIRATORY RATE DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 5 : Distribution according to respiratory score among cases and controls

RESP SCORE	CASES	CONTROLS
5	20(37.03%)	9(16.36%)
6	26(48.16%)	40(72.73%)
7	8(14.81%)	6(10.91%)
TOTAL	54(100%)	55(100%)

Babies in study and control groupsare classified based on Siverman – Anderson respiratory distress score.

Majority of preterms had respiratory score of 6 in 26(48.15%) of cases in 40(72.73%) of controls. 20(37.03%) preterm in cases has respiratory score 5. Only 6(10.91%) preterms had respiratory score more than 7. Indicating the need of CPAP and its use in preventing the repiraorty distress in pre term babies.

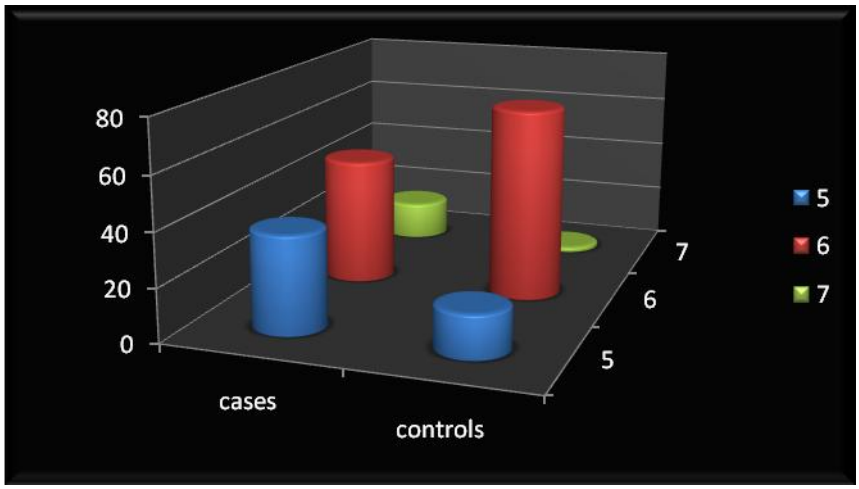

FIGURE 5 :RESPIRATORY SCORE DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 6: : Distribution according to maternal risk factors among cases and controls

MATERNAL RISK FACTORS	CASES	CONTROLS	TOTAL
PIH	22	17	39
POLY/OLIGOHYDROMNIOS	6	4	10
TWINS	6	8	14
Chi square value = 0.9358 , df 2 , p = 0.6263			

In this study 57.75% of all neonates including both the groups had maternal risk factors. PIH was seen in 35.7% of the population. Polyhydramnios was seen in 9.1% of the population and 12.8% were multiple gestation. High incidence of preterm deliveries were seen in mothers with PIH.

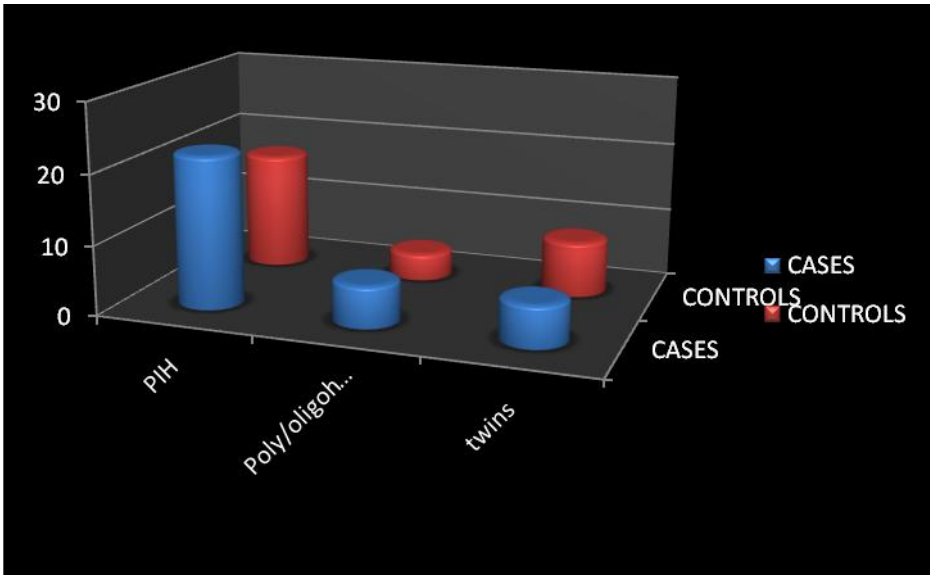

FIGURE 6: MATERNAL RISK FACTORS DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 7: <u>Distribution according to duration of CPAP among cases and controls</u>

DURATION OF CPAP(hours)	**CASES**	**CONTROLS**
24-48	20(37.04%)	16(29.09%)
48-72	23(42.59%)	29(52.73%)
>72	11(20.37%)	10(18.18%)
TOTAL	54(!00%)	55(100%)
MEAN ± SD	56.98 ± 17.03	58.78 ± 14.24
t = 0.5993 , df = 107 , p =0.5503		

In this study 23(42.59%) preterms among the cases and 29(52.73%) in controls were present on CPAP for 48-72 hrs. Only 11(20.37%) among cases had CPAP requirement beyond 72 hrs.There was no statistically significant difference regarding the time spent on CPAP between the two groups

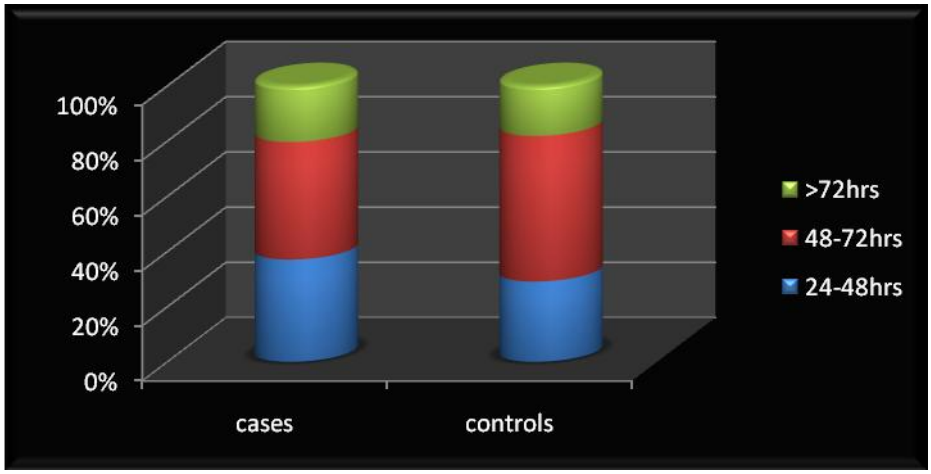

FIGURE 7 : DURATION OF CPAP DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 8: Distribution according to need for mechanical ventilation among cases and controls

NEED FOR MECH. VENTILATION	CASES	CONTROLS
YES	16(29.63%)	28(50.91%)
NO	38(70.37%)	27(49.09%)
TOTAL	54(100%)	55(100%)
Chi square value = 5.1255 , df 1 , p = 0.0235		

From the above table it is observed that 16(29.63%) cases required mechanical ventilation. Whereas 28(50.91) preterms in the controls needed mechanical ventilation. Indicating early initiation of cpap in the premature babies at delivery room will reduce the need of the mechanical ventilation and prolonged hospital stay on mechanical ventilation.There was a statistically significant difference between the two groups($p<0.05$)

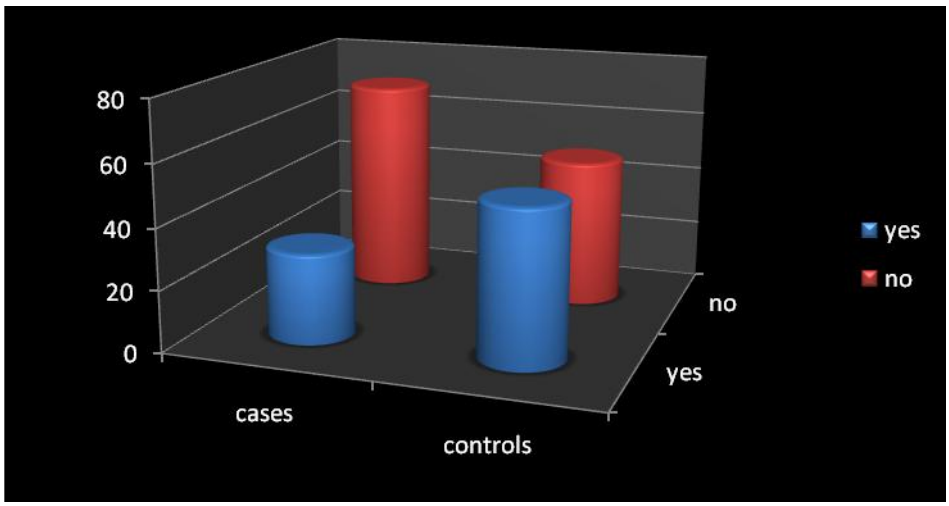

FIGURE 8 : NEED FOR MECHANICAL VENTILATION DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 9: Distribution according to duration of stay in nicu among cases and controls

DURATION OF STAY(DAYS)	CASES	CONTROLS
1-14	30	16
15-21	8	15
>21	1	2
MEAN ± SD	12.95 ± 3.22	14.82 ± 3.61
t = 2.3224 , df = 70 , p =0.0231		

The duration of stay in NICU in neonates with early CPAP was significantly less when compared to the control group. 30 neonates were discharged with in 14 days among cases and 16 neonates among control groups. 8 neonates stayed in nicu between 15 – 21 days and 15 neonates in control group. 1 neonate stayed beyond 21 days from cases group and 2 neonates from control group.

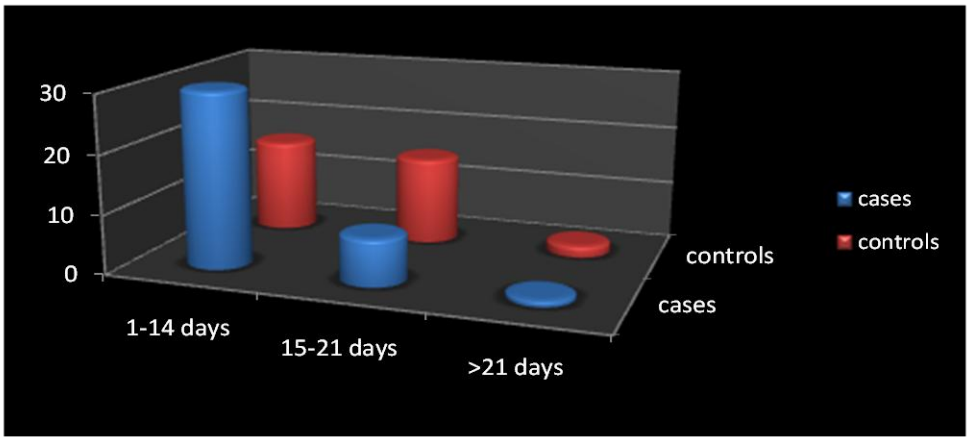

FIGURE 9: DURATION OF STAY IN NICU DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 10 : Distribution according to mortality among cases and controls

	CASES	CONTROLS
SURVIVAL	39(72.22%)	35(63.64%)
DEATHS	15(27.78%)	20(36.36%)
TOTAL	54(100%)	55(100%)
Chi square value = 0.9214 , df 1 , p = 0.3370		

In the present study 15(27.78%) preterms died due to various causes in the study group and 20(36.36%)preterms died in control group. There was no statistically significant difference between the two groups. Thus early initiation of CPAP does not have any impact on mortality

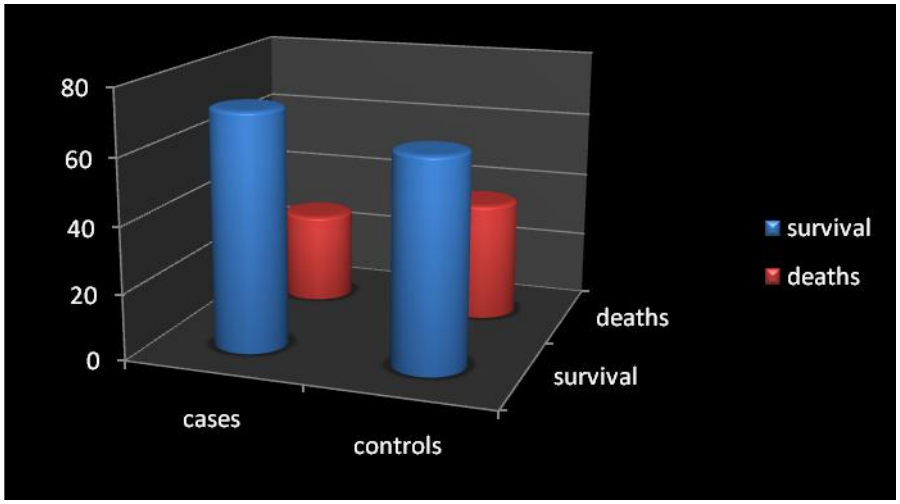

FIGURE 10 : MORTALITY DISTRIBUTION AMONG CASES AND CONTROLS

TABLE 11 :<u>Distribution according to sepsis among cases and controls</u>

COMPLICATIONS	**CASES**	**CONTROLS**
SEPSIS	10(18.52%)	11(20%)
NO SEPSIS	44(81.48%)	44(80%)
TOTAL	54(100%)	55(100%)
Chi square value = 0.0384 , df 1 ,0.8445		

In this study , sepsis was the most common complication accounting to 18.52% in the study group and 20% in the control group.There was no statistical difference between the two groups indicating the occurance of sepsis has nothing to do with timing of initiation of CPAP

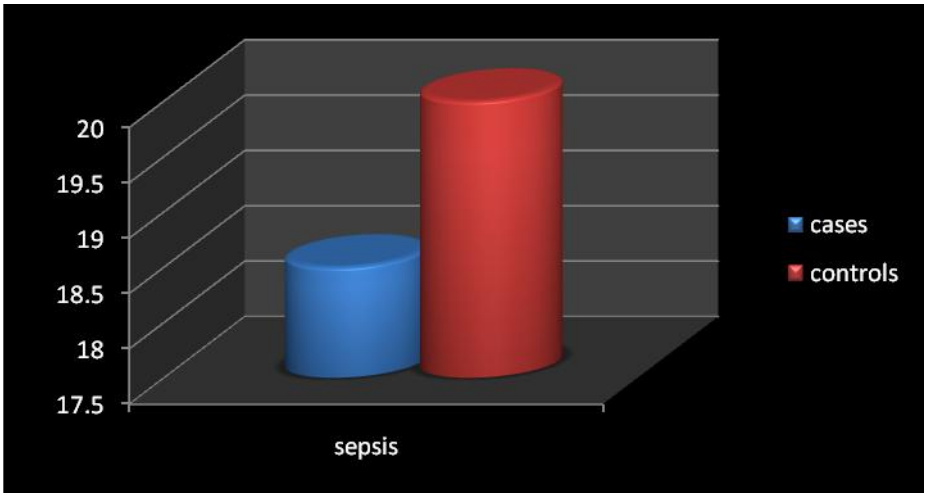

FIGURE 11 : COMPLICATIONS DISTRIBUTION AMONG CASES AND CONTROLS

DISCUSSION

CPAP has been used primarily to treat surfactant deficiency in preterm infants for many years [1] .Particular interest in CPAP focuses on its potential role to reduce ventilator-induced lung injury and BPD. The mechanisms responsible for the possible effects of CPAP to decrease BPD have not yet been evaluated. One postulated mechanism is the avoidance of aggressive initiation of intermittent positive pressure ventilation with high tidal volumes and inadvertent hyperventilation/under ventilation that occurs in ventilated infants [21].CPAP also protects the airway from mechanical injury and bacterial colonisation related to the endotracheal tube. CPAP putatively increases both functional residual capacity and endogenous respiratory drive leading to decreased delivery room intubations, reintubations and days on mechanical ventilation [38,].CPAP has been associated with decreased BPD in several clinical reports [3,15,39,40].Multivariate regression analysis has shown intubation and mechanical ventilation of preterm infants to be the single most important predictor of subsequent BPD.

The controversy of early vs delayed CPAP continues as many of the trials favouring early CPAP were carried out in the larger infants prior to routine use of antenatal steroids and postnatal surfactant.[3] The evidence suggesting decreased mechanical ventilation and increased exogenous surfactant use with early CPAP and brief ventilation in ELBW is from one small randomized clinical trial.[41] There are no studies as yet comparing the role of early surfactant administration with brief ventilation and extubation to nasal CPAP vs selective surfactant use with continued mechanical ventilation for ELBW preterm infants at risk for RDS. Additional randomized trials are needed and are underway.[42]

There are practical concerns regarding the implementation of early CPAP in the delivery room. Preterm infants allowed to breathe spontaneously with nasal prongs will not 'pink up' as rapidly and PCO2 values will be higher than tolerated by most clinicians previously. The decision point of when to intervene is imprecise and depends on experience and constant vigilance. Secondly, the safety of permissive hypercapnia has to be accepted.[43] Although high PCO2 levels may decrease lung injury[44] safe upper values for PCO2 have not been determined for preterm infants. Long-term follow-up of infants treated with permissive hypercapnia are now being reported and appear to be safe.[45] thirdly, the prolonged use of CPAP delivered by nasal

prongs can lead to nasal septal erosions and abnormal head moulding that can complicate clinical outcome.

In the present study neonates admitted to the NICU with respiratory distress within 6 hours of life were categorised into case and control groups. Cases included neonates with respiratory distress who were started on CPAP in the labour room within 15 minutes. Control group included neonates with respiratory distress who were started on CPAP after 15 minutes to 6 hours of life. Both the groups were monitored and the need for mechanical ventilator was noted. Clinical diagnosis wasmade based on time of onset of respiratory distress and clinical examination andrespiratory scoring (Silverman Anderson score).. A total of 3034 babies were admitted to NICU during the study period from may 2014 to June 2015, out of which 1551 were LBW babies. Of which babies with gestational age 28-32 weeks were 421 babies were included in the study after exclusion, out of which 54 babies were included in the study group and 55 in the control group.

In the present study, there is no statistically significant difference in study vs control group (mean ± SD 1.24 ± 0.17 vs 1.21 ± 0.19) in relation with Birth weight (p >0.05). Similar results obtained in the study conducted by Mohammed H. Bahbaha et al[46] i.e. With (mean ±SD 1.23 ± 0.16 vs 1.23 ± 0.13) in the study and control groups. The results were also comparable with the study done by Ammari et al. (2005) which reported that 78% of spontaneously breathing preterm babies with RDS and birth weight <1240 g could be managed with CPAP alone.

In the present study comparing the study group and the control group (mean ± SD 29.81 ± 1.56 vs 29.81 ± 1.64) there is no significant difference(p >0.05) between the two groups in relation with gestational age. The results in the present study were comparable with the results obtained in the study conducted by Mohammed H. Bahbaha et al[46] which shows the (mean ± SD 32.10 ± 1.88 vs 32.10 ± 1.88) respectively.

When it comes to the risk factors that are leading to the pre mature delivery 57.75% babies associated with maternal risk factors, of which PIH found to be predominant risk factor with 35.7% followed by hydromnios , multiple gestation(9%). High incidence of preterm deliveries were seen in mothers with PIH. This is comparable with the Mohammed H. Bahbaha, Hanaa A et al,[46] study with 17.5% babies associated with maternal risk factor being PIH. multiple gestation occurred in 10% , hypertension occurred in 7.5%.Regarding MRF, there was no significant difference between the two groups (P>0.05). This was in agreement with Covarrubias et al. [47].

In the present study among 109 infants assigned to study group (n=54) and control group (n=55),the need for mechanical ventilation is significantly lower in study group(29.63% vs 50.91%)[RR 0.62 ,95% CI(0.40-0.96)] p = 0.023 as compared to the results obtained in the study conducted by Booth et al.(2006) which showed the use of early CPAP led to a decrease in the need for mechanical ventilation (MV) [48].

Similar results were reported in larger infants (1000–1499g) from the group in SouthAuckland, New Zealand24 after starting nasal CPAP. When compared to historical controls, the number of infants ventilated (65 vs 14%), Ho JJ, Henderson, Davis (2002) showed the early use of CPAP decreased the use of subsequent positive pressure ventilation.[26] similar results were also seen in a study conducted by Millet V et al[49] on early continous positive pressure in the labour room showed the need for subsequent ventilation was reduced to 40% of population

Regarding the grade of respiratory distress, there was no statistically significant difference between the studied groups (P > 0.05) .This was in contrast to Subramaniam et al.[50] who concluded that if a preterm infant has good respiratory effort, but has

respiratory distress/apnea, the infant may be trialed on nCPAP rather than intubated immediately.

The duration of stay in NICU in neonates with early CPAP was significantly less when compared to the control group. 30 neonates were discharged within 14 days among cases and 16 neonates among control groups.8 neonates stayed in nicu between 15 – 21 days and 15 neonates in control group.1 neonate stayed beyond 21 days from cases group and 2 neonates from control group. The results were statistically significant(P <0.05). Upadhyay and colleagues stated that mechanically ventilated patients usually have more severe clinical states and need more time for weaning as they are exposed to more complications. This increases their number of days on assisted ventilation. This is also prominent if conventional mechanical ventilation follows a trial of nCPAP that was unsuccessful [51]

In this study, sepsis was the most common complication accounting to 18.5% in the study group and 20% in the control group. In the study done by Mohammed H. Bahbaha, Hanaa A. El-araby et al,[46] sepsis occurred in 12% of the nCPAP patients followed by mechanical ventilation. Mahmoud et al found that noninvasive ventilatory support can reduce the adverse effects associated with intubation and mechanical ventilation, such as BPD, sepsis, and trauma to the upper airways [52]

we found that early bubble CPAP when begun in the delivery room was safe, inexpensive and an effective way to avoid intubations in the deliveryroom. There is growing evidence indicates that early CPAP from birth is feasible and safe in preterm infants. nCPAP improves oxygenation in the few hours of the life .The use of CPAP was able to help in the establishment and maintenance of functional residual capacity (Gregory et al. 1971). As respiratory insufficiency may be a component of multiorgan dysfunction, preterm and term infants receiving surfactant-replacement therapy should be managed in facilities with technical and clinical expertise to administer surfactant and provide multisystem support.

SUMMARY

- Continuous positive airway pressure (CPAP) is a simple, inexpensive and gentle mode of respiratory support in preterm low birth weight (LBW) infants
- Early institution of CPAP was very successful in ameliorating RDS in newborns born less than 32 weeks, reduced the need for mechanical ventilation,helps in speedy recovery and early discharge from NICU
- In India and other developing countries starting nCPAP services in the special care newborns units with good level II care may be a better option than mechanical ventilation. This would improve the quality of care and also decrease the uptransfers to already over burdened level III NICUs in the medical colleges. Antenatal corticosteroids for women who deliver preterm babies, along with early use of CPAP and early use of surfactant in select cases would help in further reducing the need for mechanical ventilation especially in preterm infants with respiratory distress and incomplete steroid coverage, gestation 0.30), white out on the chest x-ray, where the risk of CPAP failure is very high

CONCLUSIONS

- The need for mechanical ventilation is 29.63% in study group and 50.91% in control group and this shows the early administration of CPAP in the delivery room in preterm neonates developing respiratory distress decreases the need for mechanical ventilation there by reducing the financial burden and

also complications related to invasive ventilation

- The duration of stay in NICU in neonates with early CPAP was significantly less when compared to the control group. This indicates early administration of CPAP helps in early discharge from hospital and early recovery
- There is no difference in mortality between the two groups indicating there is no significant impact of early labour room CPAP on mortality
- PIH accounts to be the major reason for cause of preterms in our study
- There is no difference in development of sepsis between the two groups
- There is slight decrease in duration of stay on CPAP among cases on whom we initiated CPAP immediately after developing respiratory distress in the delivery room when compared with control groups

LIMITATIONS OF THE PRESENT STUDY

- Early CPAP with rescue surfactant is the best approach to deal with respiratory distress syndrome in preterm neonates.As there is no uniformity in the govt supply of surfactant to our NICU we could not include the surfactant in our present study
- We couldn't follow up the babies to determine the long term complications of cpap
- As the study population is small the results obtained cannot be projected for the entire population hence further studies are needed with large size of the sample

REFERENCES

1. Gregory GA, Kitterman JA, Phibbs RH, et al: Treatment of idiopathic respiratory distress syndrome with continuous positive airway pressure. N Engl J Med1971;284:333-40
2. Kattwinkel J, Nearman HS, Fanaroff AA, Katona PG, Klaus MH. Apnea ofprematurity. Comparative therapeutic effects of cutaneous stimulation and nasalcontinuous positive airway pressure. J Pediatr 1975;86:588-92
3. Ho JJ, Subramaniam P, Henderson-Smart DJ, DavisPG. Continuous distending pressure for respiratory distress in preterm infants. Cochrane Database Syst Rev 2002: CD002271.
4. Koyamaibole L, Kodo J, Qovu DJ, Colquhoun S, Duke T. An evaluation of bubble-CPAP in a neonatal unit in a developing country: Effective respiratory support that can be applied by nurses. J Trop Peadr.2005 Dec; 205;52(4):249-253.
5. Narendran V, Donovan F, Hoath B, Akinbi T, Steichen j, Jobe H. Early bubble CPAP and outcomes in ELBW preterm infants. J Perinatology. 2003 May;23(3):195-199
6. Polin RA, Sahni R. Continuous positive airway pressure: old questions and new controversies. J Neonatal Perinatal Med 2008;1: 1-10.
7. Prophylactic or early selective surfactant combined with nCPAP in very preterm infants. Sandri F, Plavka R, Ancora G, Simeoni U, Stranak Z, Martinelli S, Pediatrics 2010;125:e1402-9. Epub 2010 May 3.
8. Ammari A, Suri M, Milisavljevic V, Sahni R, Bateman D, Sanocka U, et al. Variables associated with the early failure of nasal CPAP in very low birth weight infants. J Pediatr. 2005;147:341-7.
9. Henderson-Smart DJ, Subramaniam P, Davis PG. Continuous positive airway pressure versus theophylline for apnea in

preterm infants. Cochrane Database Syst Rev 2001: CD001072.

10. Pillow JJ, Hillman N, Moss TJ, Polglase G, Bold G, Beaumont C, *et al*. Bubble continuous positive airway pressure enhances lung volume and gas exchange inpreterm lambs. Am J Respir Crit Care Med. 2007;176:63-9.
11. Davis PG, Morley CJ. Non-invasive respiratory support: An alternative to mechanical ventilation in preterm infants. *In:* Bancalari E (ed). The Newborn Lung. Neonatology questions and new controversies. 1st edn. Philadelphia: Saunders 2008: p. 361-76.
12. Buzzella B, Claure N, D'Ugard C, Bancalari E. A randomized controlled trial of two nasal continuous positive airway pressure levels after extubation in preterm infants. J Pediatr. 2014;164:46-51.
13. Jardine LA, Inglis GD, Davies MW. Strategies for the withdrawal of nasal continuous positive airway pressure INDIAN PEDIATRICS 327 VOLUME 52__APRIL 15, 2015GUPTA, *et al.* CPAP IN PRETERM NEONATES (NCPAP) in preterm infants. Cochrane Database Syst Rev. 2011;2:CD006979
14. Gittermann MK, Fusch C, GittermannAR, Regazzoni BM, Moessinger AC. Earlynasal continuous positive airway pressure treatment reduces need for intubationin very low birth infants. Eur J Pediatr 1997;156:384-8
15. Poets CF, Sens B. Changes in intubation rates and outcome of VLBW -a populationbased study. Pediatrics 1996;98:24-7
16. Aly H, Massaro an,Patel K , El-mohandes AA(2005)Is it safer to intubate premature infants in the delivery room?pediatrics 115:1660-1665.
17. Davis PG, Henderson-Smart DJ. Nasal continuous positive airways pressure immediately after extubation for preventing morbidity in preterm infants. CochraneDatabase Syst Rev. 2003;2:CD000143.
18. Waldemer.A.Carlo. Apnea .Nelson textbook of paediatrics 20thedison, chapter 10.2.pg no 850
19. Goldsmith JP. Continuous positive airway pressure and conventional mechanical ventilation in the treatment of meconium aspiration syndrome. J Perinatol. 2008;28:S49-55.
20. Priya B, Murki S. CPAP for Meconium Aspiration Syndrome: Predictors of Failure. *In*: Thakre R, Pejaver RK. editors. Proceedings of VI Annual Convention of Neonatology Chapter of Indian Academy of Pediatrics: IAP Neocon 2013 Abstracts. Ahmedabad, India: IAP Neonatal Chapter India; 2013. p.12.
21. Ho JJ, Subramaniam P, Henderson-Smart DJ, Davis PG.Continuous distending pressure for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev. 2002;2:CD002271.
22. Buckmaster AG, Arnolda GR, Wright IM, Henderson- Smart DJ. CPAP use in babies with respiratory distress in Australian special care nurseries. J Paediatr Child Health. 2007;43:376-82.
23. Kiran S, Murki S, Pratap OT, Kandraju H, Reddy A. Nasal continuous positive airway pressure therapy in a nontertiary neonatal unit: Reduced need for up-transfers.Indian J Pediatr. 2014 Jun 21. [Epub ahead of print].
24. Finer NN, Carlo WA, Duara S, et al. Delivery room continuous positive airway pressure/positive end-expiratory pressure in extremely low birth weight infants: a feasibility trial. Pediatrics 2004;114:651–57.
25. Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet JM, Carlin JB; COIN Trial Investigators.Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med 2008;358:700-8.

26. Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev 2002:CD002975.
27. Early CPAP versus surfactant in extremely preterm infants. SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network, Finer NN, Carlo WA, Walsh MC, Rich W, et al. N Engl J Med 2010;362:1970-9.
28. Norendran V Donovan F Hoath B Akinbi T Steichen J,Jobe H.Early bubble CPAP and outcomes in ELBW preterm infants. J Perinatology 2003 may-23(3):195-199
29. Courtney SE, Kahn DJ, Singh R, Habib RH. Bubble and ventilator-derived nasal continuous positive airway pressure in premature infants: work of breathing and gas exchange. J Perinatol. 2010 April;15:1-7
30. Ancora G, Maranella E, Grandi S, Pierantoni L, Guglielmi M, Faldella G. Role of bilevel positive airway pressure in the management of preterm newborns who have received surfactant.Acta Paediatr. 2010;99:1807-11.
31. Lista G, Castoldi F, Fontana P, Daniele I, Cavigioli F, Rossi S, *et al*. Nasal continuous positive airway pressure (CPAP) versus bi-level nasal CPAP in preterm babies with respiratory distress syndrome: A randomised control trial. Arch Dis Child Fetal Neonatal Ed. 2010;95:F85-9.
32. 65. O'Brien K, Campbell C, Brown L, Wenger L, Shah V.Infant flow biphasic nasal continuous positive airway pressure (BP- NCPAP) *vs* infant flow NCPAP for the facilitation of extubation in infants' <1,250 grams: A randomized controlled trial. BMC Pediatr. 2012;12:43-51.
33. Sea-PAP. A Lifesaving Innovation for Infant Respiratory Distress. Available from: *http://www.seattlechildrens.org/research/developmental-therapeutics/labsprograms/neonatal-respiratory-support-technologies-team/sea- PAP/* Accessed June 25, 2014.
34. Diblasi RM, Zignego JC, Smith CV, Hansen TN, Richardson CP. Effective gas exchange in paralyzed juvenile rabbits using simple, inexpensive respiratorysupport devices. Pediatr Res. 2010;68:526-30
35. Thomas CW, Meinzen-Derr J, Hoath SB, Narendran V. Neurodevelopmental outcomes of extremely low birth weight infants ventilated with continuous positive airway pressure *vs* mechanical ventilation. Indian J Pediatr. 2012;79:218-23.
36. Vaucher YE, Peralta-Carcelen M, Finer NN, Carlo WA, Gantz MG, Walsh MC; SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Neurodevelopmental outcomes in the early CPAP and pulse oximetry trial. N Engl J Med. 2012;367:2495-50
37. Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, et al; American Heart Association. Neonatal resuscitation: 2010 American heart association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Pediatrics. 2010;126: e1400–13.
38. Davis PG, Henderson-Smart DJ. Nasal continous positive airway pressureimmediately after extubation for preventing morbidity in preterm infants. TheCochrane Library, Issue 2. Oxford: Update Software Ltd., 2002.
39. Kamper J, Wulff K, Larsen C, Lindequist S. Early treatment with nasal continuous positive airway pressure in very low-birth weight infants. Acta PaediatrScand 1993;82:193–7.
40. Lundstrom KE, Griesen G. Early treatment with nasal-CPAP. Acta PaediatrScand 1993;82:856.

41. Verder H, Albertsen P, Ebbesen F, et al. Nasal continuous positive airwaypressure and early surfactant therapy for respiratory distress syndrome in newborns
of less than 30 weeks gestation. Pediatrics 1999;103(2):E25.
42. Merran AT (IFDAS study group). Early nasal continuous positive airway pressure
with prophylactic surfactant for neonates at risk of RDS. The IFDAS multi-centerrandomized trial. Pediatr Res 2002;51(4):379A.
43. Mariani G, Cifuentes J, Carlo WA. Randomised trial of permissive hypercapnia in
preterm infants. Pediatrics 1999;104:1082–8.
44. Shibata K, Cregg N, Engelberts D, Takeuchi A, Fedorko L, Kavanagh BP. Hypercapnic acidosis may attenuate acute lung injury by inhibition of endogenousxanthine oxidase. Am J Respir Crit Care Med 1998;158: 1578–84.
45. Sanocka U, Durkin M, Chiroboga C, Kuban K, Hinton V, VanMarter L, BellingerD. Variations in respiratory management of VLBW infants: Effects on long term outcomes. Pediatr Res 2002;51(4):289A.
46.Mohammed H. Bahbah , Hanna A. El-araby , Mohammed A. Khedr, Early nasal continous positive airway pressure compared with mechanical ventilation in very low birth weight neonates, Menoufia Medical Journal 204,27:711-716
47. Covarrubias LO, Aguirre GE, Chapuz JR, May AI, Velázquez JD, Eguiluz ME Maternal factors associated to prematurity. Ginecol Obstet Mex 2008; 76:526–536
48. Booth C, Premkumar M H, Yannoulis A. et al.(2006). Sustainable use of continuous postitve airway pressure during the first week after delivery in extremely preterm infants. Arch Dis Childhood. July 13;
49.Millet V , Lacroze V , Bartoli JM, Samperiz S , Leclaire M , Unal D.Early continous positive pressure in labour room NCBI journal 1997 jan 4(1):15-20
50. Subramaniam P, Henderson-Smart DJ, Davis PG. Prophylactic nasal continuous
positive airways pressure for preventing morbidity and mortality in very preterm infants. Cochrane Database Syst Rev 2005; 3:CD001243.)
51. Upadhyay A, Deorari AK. Continuous positive airway pressure – a gentler approach to ventilation. Indian Pediatr 2004; 41:459–469.
52. Mahmoud RA, Roehr CC, Schmalisch G. Current methods of non-invasive ventilatory support for neonates. Paediatr Respir Rev 2011; 12:196–205.