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Original Research Article

Antenatal Corticosteroid Therapy Prevents Preterm Birth Related Complications

Behera Narendra[1], Behera Jayanti Prava[2], Dash Nishanta Nilotpala[3]
[1]Asso. Professor, Dept. Of Paediatrics , M.K.C.G. Medical College and Hospital, Brahmapur, Odisha, India
[2]Asso. Professor, Dept. of Pharmacology, M.K.C.G. Medical College and Hospital, Brahmapur, Odisha, India
[3]Paediatric Specialist, CHC, Jatni, Khurda, Odisha, India

***Corresponding author**
Behera Jayanti Prava
Email: pravabeherajayanti@yahoo.co.in

Abstract: Preterm birth complications, is a major killer of under 5 children. We are far behind to achieve Millennium Development Goal 4 (MDG 4), targeted to reduce under-five mortality rate by two-third. In 2015, WHO strongly recommends antenatal corticosteroid single or double dose during preterm labour to prevent preterm related complications. Data on antenatal corticosteroid use, and outcomes including safety were absent in nearly all countries. This study aimed to assess the effectiveness of antenatal corticosteroid on prevention of preterm birth related complications. Also to assess the risk factors associated and outcome of antenatal corticosteroid therapy in terms of mortality/ morbidity in preterm infants. This cross sectional, prospective and hospital based observational study conducted during December 2015 to November 2016 in the Special new born care unit of a tertiary care hospital, Odisha, India and approved by the Institutional Ethics Committee. 200 preterm babies including both inborn and out born categories, admitted in to the SNCU level II were enrolled in this study. The demographic data like mother's age, baby's gestational age , normal age, sex, birth weight, regular antenatal check up and the detailed data about the antenatal corticosteroid therapy, were recorded from hospital record and asking questions to the parents/guardians. The role of antenatal corticosteroid on preterm related complications like RDS, NEC, IVH, PDA and Sepsis as well as treatment outcome were evaluated. The data were analyzed by a statistical software Graph pad prism ver. 7 by a computer by Chi-square test with odd's ratio. Out born cases, male sex, 28-32wks of gestational age (54.5%), low birth weight ranges from 1000-1500 gms, mothers with age group of 20-25yrs (54.2%) , mothers without antenatal check up were more associated to risk of complications and mortality. There is significant reduction of percentage of complications and death % with ANS treated group than without ANS group.
Keywords: Inj. Dexamethasone, Antenatal check up, preterm labour, neonatal mortality

INTRODUCTION

Preterm birth complications are the leading cause of death in children under 5 years which accounts 45% of death during the neonatal period. Every year, an estimated 15 million babies are born preterm (before 37 completed weeks of gestation), and this number is rising. The complications, related to preterm birth are responsible for nearly 1 million under 5 deaths in 2015. More than three-quarters of premature babies can be saved with feasible, cost-effective perinatal care for every mother and baby, provision of antenatal steroid injections to pregnant women at risk of preterm labour, kangaroo mother care and antibiotics to treat newborn infections [1]. A study reported that preterm birth complications killed more than 300 000 Indian children under 5 in 2013. India was among the five countries having the highest mortality rate in under 5 with 1.3 million deaths [2]. Since 1990, the world has reduced number of child deaths by more than one half with a remarkable progress. But falls short of the Millennium Development Goal 4 (MDG 4), which has a target to reduce two-thirds of under-five mortality rate. In 2015, an estimated 5.9 million under 5 children will still die, equivalent to 11 every minute. This underscores that child survival and needs to be an ongoing priority when we think beyond the MDGs [3, 4]. WHO strongly recommends antenatal Inj dexamethasone single or double dose during preterm labour to prevent preterm related complications. The practice of giving antenatal corticosteroid is not

adequate in developing countries. Data on antenatal corticosteroid coverage, use, and outcomes including safety were absent in nearly all countries as per the report of a multi country analysis study [5].

On this back ground, this study was conducted to assess the efficacy of antenatal corticosteroid (ANS) to prevent the preterm birth complications, to evaluate the management outcome and to identify various demographic risk factors associated with preterm infants.

AIMS AND OBJECTIVES

To assess the effectiveness of antenatal corticosteroid on prevention of preterm birth related complications like RDS (Respiratory Distress Syndrome), IVH (Intraventricular Hemorrhage), NEC (Necrotizing Enterocolitis), PDA (Patent Ductus Arteriosus) and Septaecemia. Also to assess the demographic risk factors associated and outcome of antenatal corticosteroid therapy in terms of mortality/ morbidity in preterm infants.

MATERIALS AND METHODS

Study setting

The present study was conducted in the SNCU (Special new born care unit), Dept. of Paediatrics, M.K.C.G Medical College *and Hospital*, Berhampur and included all hospitalized preterm newborns. The study protocol was approved by the Institutional Ethics Committee (IEC).

Study design

This was a cross sectional, prospective and hospital based observational study.

Study duration

December 2015 to November 2016

Study subjects

200 preterm babies including both inborn and out born categories who had been admitted in to the SNCU level II of MKCG Medical College Hospital were enrolled in this study.

Inclusion criteria

The patients with gestational age less than 37 wks, both in born and out born babies,0 - 28 days of age , both male and female sexes were selected for this study. Only the newborns, whose parents/guardians agreed to give their consent in an (ICF) informed consent from, were included.

Exclusion criteria

The term IUGR ,term / post term babies (≥ 37 wks gestation),Congenital malformations / Syndromic babies , HIE(hypoxemic ischemic encephalopathy) cases and mothers contraindicated for antenatal corticosteroid therapy (e.g. hepatic lesions, TB, peptic ulcer, on immunosuppressive therapy) were excluded from the study.

Study procedure

The demographic data like mother's age, baby's gestational age , normal age, sex, birth weight, regular antenatal check up and the detailed data about the antenatal corticosteroid therapy, were recorded in an appropriate case record form (CRF). The data were collected from hospital record and asking questions to the parents/guardians of the newborns. The outcome in terms of complications like RDS, NEC, IVH, PDA and Sepsis were evaluated at the time of hospitalization. The babies were managed with medical and supportive care in SNCU and followed up daily during the hospital stay. At every week up to the end of the 3rd wk of hospitalization, the outcome of management was evaluated in terms of cured or referred or death.

STATISTICS

The data were analyzed by a statistical software Graph pad prism ver. 7 by a computer. The categorical demographic data were expressed in percentage. The data regarding preventive effects of ANS against different complications and outcomes in terms of morbidity and mortality were compared between ANS receiver and ANS non receiver by Chi-square test.

RESULTS

It is depicted from the table no.1 that the gestational age distribution among the preterm babies between >28 wks to 34 wks and maximum within 28-32wks i.e 54.5.5%followed by 33-37wks (34.5%). So the gestational age between 28-32 wks (very preterm) showed more risk for preterm delivery. The preterm babies were maximum presented within the birth weight of 1000 - 1500gm (42 %) followed by 15-2000gm in 25% and very less with > 2000gm i.e only 10.5%. Therefore, the birth weight 1000 -1500gm (very low birth weight) carries more risk for preterm related complications. Mother's age group 20-25 years were more presented with premature babies (54%) followed by 26-30 years (30%) whereas at 31-35 years age group only with 16 % cases. So mothers age within the range of 20-25 years showing risk of preterm delivery. Regular antenatal check up was conducted in 84% of cases.

Table 1: Demographic Risk Factors of Preterm Babies Admitted to SNCU (N=200)

Characteristics	Number	Percentage (%)
Gestational age (wks)		
<28wks	22	11
28-32wks	109	**54.5**
33 -37wks	69	34.5
Birth Weight (gms)		
<1000	45	22.5
1000-1500	84	**42**
1501-2000	50	25
2001-2500	21	10.5
Mother 's Age (yrs)		
20-25	108	**54**
26-30	60	30
31-35	32	16
Antenatal Check up		
YES	172	86
NO	28	14

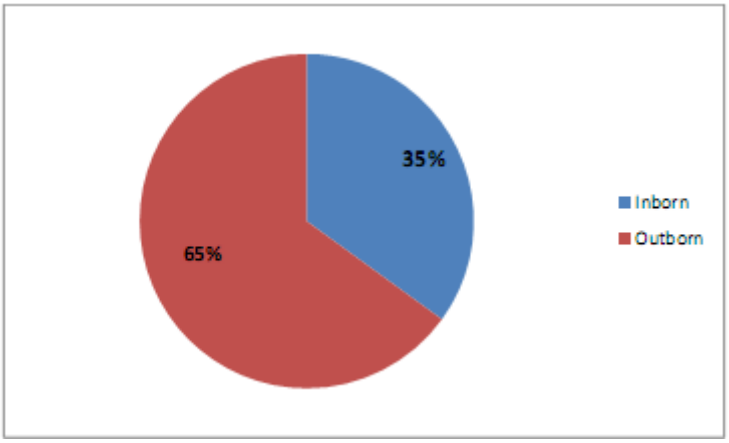

Fig-1:Distribution of Inborn and Out born Preterm Infants in the SNCU (N=200)

It was observed in the fig. No1 that maximum percentage of patients contributed by out born cases (65%) compared with inborn cases i.e only 35%. In this study, outborn neonates showed an association with preterm related complications.

Table 2: Distribution of preterm babies according to antenatal corticosteroid received by mother

Antenatal corticosteroid received (Inj. Dexamethasone 6mg IM)	Inborn	Outborn
Yes	70	0
No	0	130*****

N=200, Chi-square test,* indicates 'P' value <0.001 (without antenatal corticosteroid compared with antenatal corticosteroid)

I t is observed in this study 100% of inborn cases received antenatal corticosteroid whereas 100% of outborn cases not received the corticosteroid. The out born cases were significantly associated with not received antenatal corticosteroid.

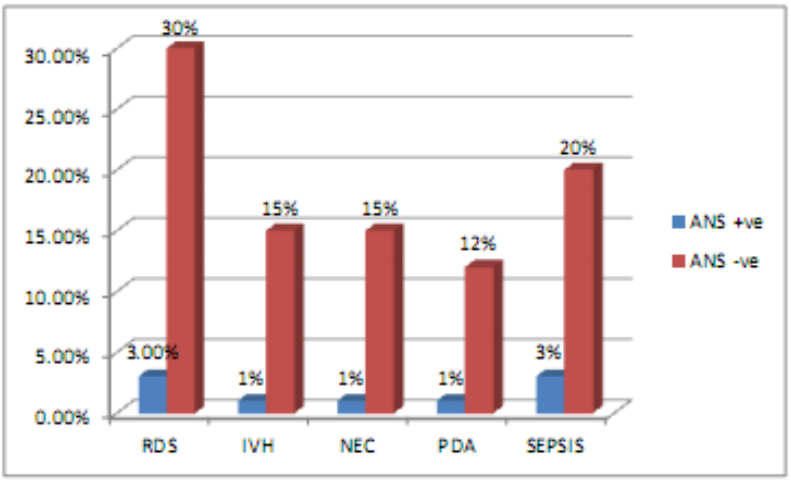

Fig-2: Occurrence of Complications in Preterm Infant (n=275)

Chi-square test , p<0.001 (ANS positive Vs ANS –Ve), ANS(Antenatal corticosteroid)

It is clearly depicted in figure no.1 that the different types of complications like RDS,IVH, NEC,PDA and sepsis were significantly more presented with the babies who were not exposed to antenatal corticosteroids in comparison to those patients without antenatal corticosteroids. RDs presented with more percentage of cases (30%) followed by sepsis (20%), IVH (15%) , NEC(15%) and PDA(12%).

Table 3: Outcome in preterm infants with ANS Vs without ANS at Weekly Interval

Outcome of preterm infants		Cured (127)	Referred (9)	Death (64)
1st wk.	Steroid received	36(51.4%)*	1(1.4%)	6(8.5%)
	Not received	23(17.6%)	5(3.8%)*	42(30.7%)*
2nd wk.	Steroid received	22(31.4%)	1(1.4%)	2(2.8%)
	Not received	39(30%)	2(1.5%)	13(9.2%)
3rd wk	Steroid received	2(2.8%)	0	0
	Not received	5(3.8%)	0	1(0.76%)

n=200, data expressed in percentage, Chi-square test, p<0.001(steroid recieved Vs not recieved)

In the present study, it is observed that maximum percentage of cases got cured (51.4%), in ANS received patients whereas maximum death (30.7%) occurred in the patient who were not exposed to ANS in the 1st wk of life.

Table 4: Outcome of antenatal steroid therapy in preterm newborn

Effect of antenatal steroid therapy							
	Cured	Not cured	Total	95% CI	RR	P value	Significant
No steroid	67	63	130	0.50-0.73	0.60		
Steroid	60	10	70				
	127	73	200			<0.0001	Yes
Chi-Square test							

N=200, data expressed in number, 'p' value <0.0001(Steroid Vs No steroid)

The above Table No.4, showed significantly more percentage of cured in steroid group (received ANS) than that of non steroid group (not received ANS).

DISCUSSION

In this present study, 70 (35%) cases delivered in this hospital were taken as inborn and 130 (65%) cases who delivered outside of this institution, taken as out born (fig.1). This study result reflected that out born

cases were more vulnerable to complications and mortality. It is as per other study, reported that most commonly referred cases were respiratory distress, perinatal asphyxia , prematurity and meconium stained liquor which lead to different preterm related complications due to delay in transport to the hospital leading to death [7, 11]. It was observed that maximum percentage (42%) of preterm babies were very low birth weight ranges from 1000-1500 gms (Table No.1) which is similar to other studies [6]. This study showed that maximum number of preterm were in 28-32wks of gestational age (54.5%). This was in comparison with studies done by [1]. The preterm mortality, morbidity and complications were higher in this age group. It was observed that male preterm (57.1%) outweighed females (42.8%) [1, 7]. Male preponderance may be due the more importance given to male child in the family. In our study, majority of mothers were within the age group of 20-25yrs (54.2%). This was in comparison with other studies [1, 8]. Table No.2 showed 100% inborn preterm babies received antenatal corticosteroids where as 100% out born babies not received ANS. This was in variance with a study [9] which showed <10% coverage of ANS in low income countries.This study reported that cases without ANS showed more complications and maximum percentage with RDS [12]. There is significantly lesser percentage of complications such as RDS, IVH, NEC, PDA and Sepsis in preterm infants whose mothers received ANS than the babies who had not received ANS (Fig No.2) [13]. Trials have also shown that antenatal corticosteroid therapy improves circulatory stability in preterm neonates, resulting in lower rates of intraventricular hemorrhage (IVH) and necrotizing enterocolitis compared with unexposed preterm neonates [10]. Antenatal steroids stimulate development of type 1 and type 2 pneumocytes which leads to structural and biochemical changes improving both lung mechanics and gas exchange. Type 2 pneumocytes increases surfactant production by producing surfactant proteins and enzymes required for phospholipid synthesis. Other effects of antenatal corticosteroids are induction of pulmonary beta-receptors, which cause surfactant release and absorption of alveolar fluid and induction of foetal lung antioxidant enzymes, and upregulation of gene expression for the epithelial Na+ channel, which is important for absorption of lung fluid after birth [10]. In the present study Table 3 showed, the outcome of antenatal corticosteroid in terms of cured /referred / death during 1st, 2nd and 3rd wks of follow up period. Maximum percentage of cases cured was observed in preterm infants whose mothers received ANS and maximum death occurred in preterm infants whose mother not received ANS during 1st wk of treatment. This is in comparison with studies which reported earlier cure and lesser duration of hospital stay in those preterm whose mothers were exposed to ANS [6]. There is significantly more percentage of cure among steroid receivers than non receivers with RR (0.60), 95% CI (0.50-0.73) and p <0.0001. Similar studies reported 80% cure rate in those received ANS and 68% in not received ANS [1].

CONCLUSION

The complications like Respiratory Distress Syndrome (RDS), Necrotizing Enterocolitis (NEC), Intra ventricular Haemorrhage (IVH), congenital heart disease (CHD) and septicaemia were commonly associated with preterm infants. This study result reflected that out born cases were more suffered from complications than inborn cases. Because all the mothers of inborn cases routinely received antenatal corticosteroid during preterm labour whereas all the mothers of out born cases not received the same. As antenatal corticosteroid is not a practise by doctors in peripheral hospitals and for home delivery by TBA (Trained Birth Attendant).In this study antenatal corticosteroid produced significantly lesser number of complications like RDS, NEC, IVH, PDA and sepsis. The percentage of patients cured was also significantly more with corticosteroid group in comparison to without corticosteroid.

It is concluded from our study result that antenatal corticosteroid therapy can prevent complications so also morbidity and mortalities in preterm infants. Though other studies reported the efficacy of antenatal corticosteroids in prevention of preterm related complications and 'WHO' recommended the use of antenatal corticosteroids in all preterm labour to prevent preterm related complication, in our study it was observed that ANS is only practised in tertiary care centre, not in peripheral hospitals. Therefore, it can be suggested that use of antenatal corticosteroid should be implemented in MCH programme, included in the EDL and training programme should conducted to train the heath personals for its use in our state.

LIMITATIONS OF THE STDUY

This is a short term cross sectional study with small sample size conducted in a tertiary care centre. The study result did not show any comparison between the outcome of ANS in early preterm and late preterm.

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