ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

ASSOCIATION OF NEONATAL HYPERBILIRUBINEMIA WITH USE OF OXYTOCIN FOR AUGUMENTATION OF LABOUR

KEY WORDS:
Hyperbilirubinemia, Oxytocin, Phototherapy

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ABSTRACT

Introduction: Neonatal Hyperbilirubinemia is a common manifestation among the new borns. Jaundice is one of the most common condition that requires medical attention in new borns 50% of full term and 80% of preterm nenonates develop hyperbilirubinemia due to one or other reasons. There are many studies suggesting that administration of oxytocin to augument labour causes neonatal hyperbilirubinemia.

Objective: To compare the incidence of occurrence of hyperbilirubinemia in neonates born to antenatal women with and without oxytocin augumentation during labour.

Materials And Methods : 100 patients were taken for this prospective study. All are women admitted in the labour ward at GGH, Kadapa with spontaneous onset of labour in latent or active phase of labour with gestational age of 38 weeks to 40 weeks 6 days. All women under the study are divided into 2 groups. 50 women fulfilling all inclusion and exclusion criteria who had administered oxytocin administration were considered as control group. Total bilurubin levels were measured on Day 1 by collecting 10ml of cord blood at delivery and on Day 3 and Day 5 by heel prick using spectophotometry. Data was analysed in MS excel sheet. Statistical analysis was done through unpaired one tailed 't' test.

Results : Average total bilirubin was 4.79 on Day 1, 8.7 on Day 3 & 5.75 on Day 5 in the study group and 3.88 on Day 1, 5.66 on Day 3 and 3.43 on Day 5 for the control group. 14 babies admitted in NICU with a mean of 3.5 days stay at NICU. 10 babies received phototherapy in the study group compared to 4 babies admitted in NICU with a mean stay of 2.75 days with 4 babies receiving phototherapy in control group.

Conclusion: The findings in this study depict that oxytocin administration for augumentation of labour resulted in increased bilurubin levels in the new born and raised rate of NICU admissions and increased mean stay at NICU, increased need for phototherapy. Since all the common causes of neonatal hyperbilirubinemia in an otherwise normal pregnancy were ruled out, the results may be attributed to oxytocin administration.

INTRODUCTION

Neonatal Hyperbilirubinemia is a common manifestation among the new borns. 50% of full term and 80% of preterm develop NNJ on account of increased production of bilirubin (less life span of RBC and high Heamoglobin), decreased hepatic uptake of bilirubin in plasma, defective bilirubin concentration, defective bilirubin excretion and increased enterohepatic circulation, increased enterohepatic circulation. Causes of NNJ in 1st 24 hours include 1. Hemolytic disorders 2. TORCH (Congenital infection).

2nd day – 3rd week: 1. Physiological (Disappear after the 1st week)
2. Breast milk jaundice
3. Sepsis
4. Cephalhematoma
5. Hemolytic disorders

Persistence after 3rd week : 1. Breast milk Jaundice
2. Hypothyroidism
3. Pyloricstenosis
4. Cholestasis

Neonatal Hyperbilirubinemia is generally mild and appears after 48 hours and peaks after 4-5 days of birth in term nenonates and generally less than 12-15 mg/dl. It is deeper and appear earlier in preterm but never before 24 hours. Hyperbilirubinemia is exaggerated in cases of cephalhematoma, Intraverticularhaemorrhage, Hypothyrodism, Hypoxia, Congenital Heart Disease, TORCH Infections.

Oxytocin is a hormone produced endogenously in the supraoptic and paraventricular nucleus of the hypothalamus and stored in the posterior pituitary and released in the blood circulation. It predominantly affects the uterine smooth muscles and causes contraction of the uterine musculature. Its action is physiological. In small doses oxytocin has vasodilatory properties and might cause transient hypotension and tachycardia. But in high concentrations, due to activation of vasopressin receptors, it has weak antidiuretic property and pressor activity. In case of delayed progress of labour due to inadequate uterine contractions, synthetic oxytocin may be supplemented from outside to aid the uterine contraction and subsequent vaginal delivery. Synthetic oxytocin can be administered from outside to enhance the action of endogenous oxytocin.

There are many factors that lead to the development of Hyperbilirubinemia in a neonate like ABO incompatibility, gestational age, preeclampsia, certain drugs used by mother and oxytocin administration.

Many theories have been proposed to explain hyperbilirubinemia in neonates caused due to oxytocin administration to mother. Most plausible explanation for this is the possibility that administering oxytocin stimulates uterine contractions with redistribution of the blood between placenta and the fetus. More specifically increased red cell mass of the infant would result in more bilirubin production from degradation of these RBCs. Short life span of RBC more Hb concentration. Other minor fascinating reasons may be probable effect of oxytocin on RBC directly causing premature removal from the circulation, stimulation of haemoxygenase activity and increased heme breakdown, inhibition of glucoronyl transferase, interference with normal hepatic maturation process. Though the validity of these reasons is under question, they may be considered for studies.

The neonatal hyperbilirubinemia practice guidelines published in 2004 by the American Academy of Paediatrics (AAP) expresses the paediatric community's concern regarding bilirubin-induced neurological pathology. Serum bilirubin levels at birth - normally 1.8-2.8mg/dl. Between the 3rd and 4th day the bilirubin levels in mature infants increases to 5-10mg/dl. It is clinically manifested with bilirubin level of

more than 5 mg/dl and is harmless. But in some cases may lead to neurotoxicity in severe condition, therefore early detection and treatment of neonatal hyperbilirubinemia is crucial in the prevention of bilirubin induced encephalo pathy.

Though medical education and research is pushing its limits, study on administering oxytocin effects on neonate needs to be vast and the effects need to be segregated and the proper pathophysiology needs to be established with reproducible results. Oxytocin is the most commonly used drug in obstetric practice, and is on the WHO list of essential medicines. Neonatal hyperbilirubinemia may have adverse effects later on in the life.

OBJECTIVES

1. To compare the incidence of Neonatal Hyperbilirubinemia in neonates born to mothers with and without oxytocin augumentation in labour.
2. To study the neonatal outcome parameters like APGAR scores NICU admission and stay, need for phototherapy.

MATERIAL AND METHODS

Place Of Study:

After getting institutional ethics committee approval, this study has been started and conducted in the department of obstetrics and gynaecology, Government General Hospital, Kadapa.

Type of Study :

Prospective comparative observational study.

Strength Of The Study :

130 women (65 women in the control group and 65 women in study group) were included after proper informed consent. As the labour progressed, some women in both groups were dropped due to appearance of various exclusion criteria (15 in study group and 15 in control group) were excluded. 50 in each group were finally included in study.

Duration of Study:

April 2020 to September 2020 (6 Months).

Inclusion Criteria:

Primigravida with normal BMI, with uncomplicated low risk term pregnancy (≥ 38 weeks) with spontaneous onset of labour needing augumentation of labour, delivered vaginally were included in the study.

Exclusion Criteria :

1. Rh negative pregnancy.
2. GDM/Overt diabetes complicating pregnancy.
3. Antepatum Haemorrhage.
4. Evidence of Placental insufficiency.
5. Oligohydramnios.
6. Fetal Growth Restriction.
7. Polyhydramnios.
8. Hypo / Hyperthyroidism.
9. Any other drugs other than Iron Folic Acid Supplementation.
10. Meconium stained liquor.
11. Instrumental vaginal delivery.
12. Babies with congenital anamolies / infections.
13. Cephalhematoma.
14. Birth weight < 2.5 kg.
15. APGAR < 6.

Around 15 women in each group were excluded after recruitment.

Sample Design:

Women admitted in the labour room with spontaneous onset of labour, in latent or active phase of 1st stage of labour at Government General Hospital, Kadapa carrying pregnancy with period of gestation 38 weeks and above.50 women fulfilling all inclusion and exclusion criteria were considered for the study. Similarly 50 women with same criteria were considered as control group.

Method Of Collection Of Data :

Preliminary data like demographic information, antenatal history, clinical findings of each visit and investigation reports of all women were collected from Antenatal card. Date and indication of admission to hospital were noted. Findings of intrapartum FHR monitoring by CTG or stethoscope were recorded and partogram was maintained. After delivery, perinatal outcomes were studied in detail and recorded. Total bilirubin levels were measured on day 1 by collecting 10ml of cord blood at delivery and on day 3 and 5 by heel prick. Total Bilirubin was calculated by spectrophotometry. Any maternal complication was also noted.

PARAMETERS AND PROCEDURES:

Maternal

1. Maternal demographic and obstetric data: Age, Parity, Gestational age
2. Labour events: FHR tracing by CTG, Partogram, Colour of liquor, Oxytocin administration.
3. Postpartum – any complications like PPH, mortality.

Baby

APGAR score at 1 and 5 minutes, Birth weight ,Features of birth asphyxia, Total bilirubin levels (Day 1,3,5), Admission to NICU ,Number of days stay in NICU and Phototherapy details.

Study Tools:

Case Record Form, Antenatal OPD Ticket, CTG Paper and Machine Partograph, Sphygmomanometer, Weighing machine, Measuring tape.

Study Procedure:

It was a prospective comparative observational study. After approval from the Ethics Committee of the Institution, Informed written consents were taken from all women recruited for and willing to participate in this study. Women considered for this study were primigravida carrying pregnancy with period of gestation 38 weeks and above. Women admitted in labour room with spontaneous onset of labour in either latent or active phase of first stage of labour. Admission Cardiotocography was done in all cases. Partograph was plotted in all the cases and progression of labour was followed up in all the cases. Internal examination was performed every 4 hours in case of spontaneous rupture of membranes and 2 hourly in case of artificial rupture of membranes. Women in whom meconium stained liquor was noted were excluded from the study. Ringer Lactate was used for intrapartum fluid administration. Cases without satisfactory progress of the labour due to inadequate uterine contractions were administered oxytocin to augment labour. Protocol used was a low dose oxytocin labour augmentation protocol starting with a dose of 5 units in case of primi. No. of uterine contractions, duration of the uterine contraction and intensity of the uterine contractions, maternal pulse, fetal heart rate were noted. Dose of oxytocin was slowly stepped up in case of inadequacy of uterine contractions. Final dose of oxytocin used and the duration of the augmentation was noted.

Drip rate	Observation time	Fetal Heart rate	Maternal Vitals	No. and intensity of uterine contractions	Remarks
8 drops / min	30 minutes				
16 drops / min	15 minues				
32 drops / min	Maximum dose given				

The above given chart was maintained to check for the maternal and fetal parameters during labour. All labor events including intrapartum FHR monitoring by intermittent

auscultation by stethoscope or continuous electronic fetal monitoring was done and persistent fetal bradycardia, when observed, was noted. Labour was followed up until the delivery and cases with normal vaginal delivery without any instrumentation were included. Cases, where babies were born with cord around the neck , cephalhematoma, features of birth asphyxia, congenital anomalies, low birth weight were excluded from the study to reduce the chances of results being because of the above said reasons. All the newborns were attended by a neonatologist and all the details were duly noted. After delivery maternal outcomes were noted Perinatal outcomes like birth weight, APGAR score, NICU admissions, indication for admission, No. of days of admission were noted. Total bilirubin in the neonates on day 1, 3 and 5 were noted. 50 women were considered in the control group with similar inclusion and exclusion criteria where labour was not augmented with oxytocin. All the above mentioned parameters were noted in the babies born to these mothers and compared to the results of the women in the study group.

RESULTS AND DISCUSSION

Table2: Maternal Demographic and Obstetric Variables:
This table shows the maternal age, BMI and gestational age distribution.

Variables		Study group (Oxytocin administered) n=50	Control n=50
Age	< 20 Years	29	21
	21-25 Years	22	28
BMI	18.5-25	50	50
Gest Age	38-39^{+6} weeks	30	40
	> 40 WEEKS	20	10

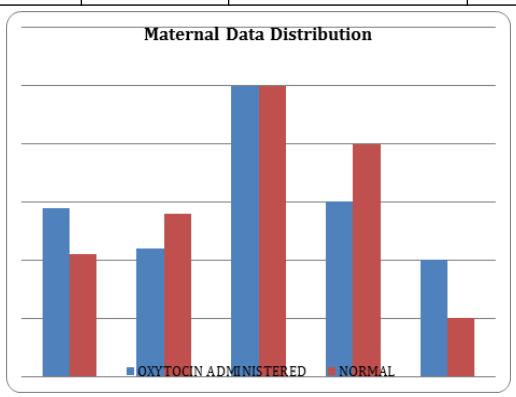

Fig.I

Table 3 : Birth Weight

Birth Weight (in Gms)	Study Group (Oxytocin Administered) n = 50	Control N=50
2500-2750	20	19
2750-3000	22	18
3000 and above	8	8

Table 4 : Neonatal Outcome Variables Distribution:
This table shows APGAR scores, NICU admissions, No. of days of stay and Mean bilirubin levels in both study and control group.

Variables		Study Group (Oxytocin Administered) n = 50	Control group N = 50	Mean Difference	p-Value
NICU Admission	No. of Patients	16	4		
	Mean Days	3.53 ± 1.47	2.75 ± 0.5	0.7	<0.05*
Phototherapy Given	No. of Patients	10	4		
Total Bilirubin	Day 1	4.99 ± 1.20	3.68 ± 0.95	1.31	P<0.05*
	Day 3	8.90 ± 3.62	5.68 ± 2.96	3.22	P<0.05*
	Day 5	5.75 ± 1.71	3.74 ± 1.57	2.01	P<0.05*
APGAR Score	6-8	13	8		
	>8	37	42		

(Statistically significant*)

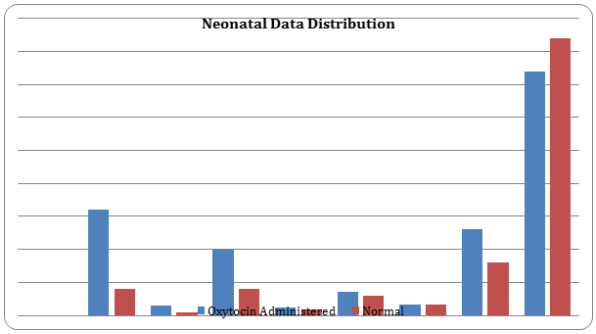

Fig.2

Oxytocin has been an integral and important part of managing labour in our country since a long time now. Risks like transient intra uterine fetal compromise, birth asphyxia and increased operative interventions are well studied and documented. Uncommon conditions that may be associated with oxytocin administration in the mother during labour is hyperbilirubinemia in the neonates. Though this hyperbilirubinemia is well within the physiological limits, there is a theoretical risk and a few studies suggesting that the oxytocin administered do cause it and it has been verified in our study as well with increased mean bilirubin levels, NICU admissions and mean stay, increased rates of need for phototherapy in women where oxytocin was used for augmentation of labour.

This is a prospective observational comparative study and women between 18-25 years were considered in the study. In total 100 women were considered in the study and they were divided equally into 2 groups, 50 women were considered in the study group where labour was augmented with Oxytocin and 50 women were considered in the control group where labour was not augmented with Oxytocin. In both groups most women had a BMI of 21.

32 women had a gestation age of 39 weeks, 13 women had a gestation age of 38 weeks, and only 5 women had a gestation age of more than 40 in the control group. Similarly, 21 women had a gestation age of 39 weeks, 14 women had a gestation of 38 weeks, and 15 women had a gestation age of more than 40 in the study group.

In the study group 20 cases had birth weight between 2500-2750 gm, 22 cases had birth weight between 2750-3000 gm, and 8 cases had birth weight above 3000 gm. In the control group, 19 cases had birth weight between 2500-2750 gm, 18 cases had birth weight 2750-3000 gm, 13 cases had birth weight above 3000 gm.

Average total bilirubin was 3.68 on day 1, 5.68 on day 3, and 3.74 on day 5 for the control group. For the study group, average total bilirubin was 4.99 on day 1, 8.9 on day 3, and 5.75 on day 5. The results show a significant increase in the total bilirubin levels in the oxytocin induced compared to control group on all three days($p<0.05$). These results are comparable to the results in the study by Patil S et al, Singhi et al. In the study group, 13 cases had an APGAR score 6-8, and 37 cases had an APGAR score greater than 8. In the control group, 8 cases had an APGAR score 6- 8, and 42 cases had an APGAR score greater than 8.

15 cases were admitted to NICU in the study group, of which 11

babies received phototherapy. 4 cases were admitted to NICU in the control group, and all of them received phototherapy. Mean stay in NICU was 3.5 days in study group against 2.75 days in control group, and the difference is statistically significant.

CONCLUSION

The findings in our study show that oxytocin administration during labour for augmentation results in increased total bilirubin levels in the neonates. Since oxytocin is the most commonly used drug in the obstetric practice for quite some time now and neonatal hyperbilirubinemia is associated with adverse effects later in life, we suggest extreme caution when administering oxytocin for augmentation of labour, to give best possible perinatal outcome.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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