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Original Research Article

Effect of dexamethasone on fetal heart rate variability, by non-invasive non-stress test tracing in preterm labour

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ABSTRACT

Background: To analyse the effects of antenatal dexamethasone on fetal heart rate variability (fHRV), when administered to mothers between 30-37 weeks of gestation, at risk of preterm delivery and corroborate presenting maternal symptoms with mode of delivery and perinatal outcomes.
Method: Prospective observational study conducted for 1 Year among pregnant women with gestation between 30 completed weeks to 36 weeks 6 days, with symptoms suggesting risk of preterm delivery. The sample size calculated was 52. Dexamethasone phosphate, 24 mg in 4 divided doses, was administered as intramuscular injections 12 hours apart. NST tracings were taken at three points-before first dose, one hour after first dose and one hour after the fourth dose. Chi-square test and Paired t test was applied, $p<0.05$ was considered statistically significant.
Results: Strong correlation was found between antenatal dexamethasone administration and fHRV ($p<0.05$) which increased after administration of the first dose of dexamethasone compared to its value prior to administration. There was a further increase after the fourth dose.
Conclusions: Dexamethasone is associated with increase in fHRV evident on non-stress test recordings, without significant decrease in baseline fetal heart rate.

Keywords: Antenatal, Dexamethasone, fHRV, Non stress test, Preterm labour

INTRODUCTION

Globally, preterm birth has emerged as a serious public health problem, and is a leading cause of perinatal mortality and morbidity The well-known approaches to prevent premature birth and its associated complications include bed rest, tocolysis, antibiotics, and antenatal steroids administration to the mother.[1] The best treatment effects of antenatal steroid administration are observed when the delivery occurs within 7 days from the full steroid dose completion, with respiratory distress syndrome (RDS) risk reducing by 50%.[2] Antenatal corticosteroid administration has been proved to be beneficial for lung maturation of the fetus, when administered 24 hours prior to preterm delivery, with significant effects when given between 24 and 34 weeks of gestation.[3] When mothers receive corticosteroids, neonates have reduced severity, frequency, or both, of RDS, intracranial haemorrhage, necrotising enterocolitis and death, compared to neonates of mothers who did not receive corticosteroids prior to preterm delivery.[4] However, antenatal corticosteroid administration may alter fHRV.[5] Betamethasone and dexamethasone are the two preferred corticosteroids for antenatal administration in order to potentiate the maturation of fetal organs. Though there are no differences in perinatal death or variations in biophysical activity, trials have concluded that there is a decreased incidence of intraventricular haemorrhage (IVH) when dexamethasone is used, as compared to betamethasone.[6] The approved regimen of treatment recommends four 6-mg intramuscular doses of dexamethasone, each given at an interval of 12 hours.[4] However, corticosteroids should not be administered in late preterm labour, once chorio-amnionitis is clinically

diagnosed. Maternal side effects of dexamethasone injection include increased risk of infections and down regulation of hypothalamo-pituitary-adrenal axis.[7] Hence, more than two courses of antenatal corticosteroids are not recommended at present.[4] The ideal therapeutic window for delivery after corticosteroid administration is 2-7 days, but as per one study, only 20-40% women actually deliver within that period.[8]

Non stress test (NST) is a non invasive test done to monitor fetal heart rate and thus assess fetal wellbeing. Tracing of NST includes baseline fetal heart rate, presence of acceleration, deceleration, fHRV and uterine tone with fetal movement count. Baseline fHRV is determined in a 10-min window, excluding accelerations and decelerations. Baseline FHR variability is defined as fluctuations in baseline FHR that are irregular in amplitude and frequency. Fluctuations are visually quantitated as the amplitude of peak-to-trough in beats per minute.[9] Using this definition, baseline FHR variability is categorized as-absent: undetectable, minimal: greater than undetectable, but less than/ equal to 5 beats per min, moderate: 6-25 beats per min and marked: greater than 25 beats per min.

This study analysed effects of antenatal dexamethasone on fHRV in NST when administered to mothers between 30-37 weeks of gestation, at risk of preterm delivery and corroborate presenting maternal symptoms with mode of delivery and perinatal outcomes in preterm labour.

METHODS

The study was a prospective observational study conducted for one year from 1st January to 31st December 2019 among pregnant women with gestational age between 30 completed weeks to 36 weeks 6 days, admitted in the maternity ward of college of medicine and JNM hospital, Kalyani, West Bengal, India. Antenatal mothers with symptoms suggesting risk of preterm delivery and presenting with symptoms like decreased fetal movement, leaking per vagina, bleeding per vagina, and lower abdominal pain in latent phase of labour were included. Pregnant women with active labour contractions whose immediate delivery was inevitable and had already received corticosteroid injections excluded from study.

For calculating sample size, G* 3.1.9.2 for Windows was used (released in 2014). These data were put in the G*Power package. The data collected was entered in MS excel 2010. The data was analysed by IBM SPSS® version 22.0. Chi-square test was used to compare the proportions. Paired t test was applied to the numerical data. The data was summarized with tables and appropriate diagrams. Two tailed significance tests with p=0.05 or less was considered to be statistically significant.

Institutional ethical clearance (Office of institutional ethics committee reg no. ECR/674/Inst/2014/RR-17 college of medicine and JNM hospital) was taken prior to the study. Informed consent of pregnant mothers, with gestational age between 30 weeks to 36 weeks 6 days at risk of preterm delivery to participate in the study was obtained. The 24 mg of dexamethasone was administered in 4 equal doses of 6 mg, each 12 hours apart, as per the treatment protocol of the hospital. NST tracings were taken at three points in time-one before administration of dexamethasone, 2nd after one hour of administration of the first dose of dexamethasone, and the third after one hour of administration of the fourth dose of dexamethasone.

RESULTS

The 52 antenatal mothers were enrolled and participated during the study period fulfilling the criteria. The minimum, maximum, mean and standard deviation of different variables calculated during the study was tabulated (Table 1). It was found during the study that preterm labour was most commonly found in primigravida (Table 2). Majority (28.5%) of the participants presented at 34 completed weeks (Figure 1). Lower abdominal pain was the most common complaint on admission (Table 3) and majority of the patients had a closed cervical OS on admission (Figure 2). The 86.5% of the patients progressed in labour and delivered vaginally (Figure 3), out of which 55.2% were preterm vaginal births (Table 4). 63.8% babies cried at birth, roomed in and fed well with no RD (Table 5). It was observed that there is strong correlation between subsequent intramuscular doses of antenatal dexamethasone administration and fHRV obtained on NST recordings in pregnant women at risk of preterm delivery (Table 6). fHRV was significantly different in the pairs of "pre dexamethasone and post 1st dose of dexamethasone", "pre-dexamethasone and post 4th dose dexamethasone", as well as "post 1st dose and post 4th dose dexamethasone". fHRV has increased in all the three pairs (Table 7). Hence, it is calculated that fHRV increased after administration of the first dose of dexamethasone compared to its value prior to dexamethasone administration. There was a further increase in fHRV after the fourth dose of dexamethasone compared to its value after the first dose. Comparing the SNCU admitted babies with the causes the cause of admission and fHRV (Table 8) it was seen heart rate variability has no significant (p=0.98) difference.

Table 1: Descriptive statistics of variables.

Variables	N	Minimum	Maximum	Mean	SD
Age (Years)	52	16	34	24.23	4.549
Pulse	52	68	112	85.19	8.395
Systolic blood pressure	52	98	154	118.92	10.155
Diastolic blood pressure	52	66	98	78.92	6.305

Continued.

Variables	N	Minimum	Maximum	Mean	SD
Fundal height	52	30	36	34.23	1.843
Foetal heart rate (FHR)	52	110	152	135.25	8.051
Pre dexa FHR	52	110	145	133.77	7.643
Post 1st dose dexa FHR	52	110	155	134.42	9.323
Post 4th dose dexa FHR	47	120	150	135.85	7.754
Pre dexa acceleration (acc)	52	1	4	2.52	0.727
Post 1st dose dexa acc	52	0	5	3.10	1.176
Post 4th dose dexa acc	47	2	6	3.96	1.301
Pre dexa deceleration (dec)	52	0	1	0.02	0.139
Post 1st dose dexa dec	52	0	1	0.06	0.235
Post 4th dose dexa dec	47	0	2	0.11	0.375
Pre dexa fHRV	52	3	16	8.33	3.240
Post 1st dose dexa fHRV	52	6	30	13.75	5.137
Post 4th dose dexa fHRV	47	5	35	17.15	5.905
Change in fHRV post 1st dose dexa	52	0	15	5.25	3.265
Change in fHRV post 4th dose dexa	47	-10	10	3.55	3.735
Valid N (list wise)	47				

Table 2: Distribution of participants according to order of pregnancy.

Gravida	N	Percent (%)
G1	29	55.8
G2	16	30.8
G3	6	11.5
G4	0	0.0
G5	1	1.9
Total	52	100.0

Table 3: Distribution of the participants according to presenting complaints.

Complaints	N	Percent (%)
Lower abdominal pain	23	43.7
Lower abdominal pain with decreased foetal movement	4	7.6
Decreased foetal movement	9	17.2
Decreased liquor	1	1.9
Bleeding per vagina	3	5.7
Leakage per vagina	8	15.3
Lower abdominal pain with bleeding per vagina	3	5.7
Lower abdominal pain with leakage per vagina	1	1.9
Total	52	100.0

Table 4: Delivery outcome.

Delivery outcome	N	Percent (%)
Preterm caesarean section (CS)	6	11.4
Preterm vaginal delivery	29	55.2
Term caesarean section (CS)	2	3.8
Term vaginal delivery	15	28.6
Total	52	100.0

Table 5: Condition of baby at birth.

Conditions	N	Percent (%)
Cried at birth, rooming in, feeding well	33	63.8
Required sick neonatal care unit (SNCU) admission	19	36.2
Total	52	100

Table 6: Paired sample correlations between dexamethasone and fetal heart rate variability.

Variables		N	Correlation	Sig.
Pair 1	Pre-dexamethasone fHRV and post 1st dose fHRV	52	0.765	0.000
Pair 2	Pre_dexa_Fhrv and Post_4th dose_fhrv	47	0.773	0.000
Pair 3	Post_1st dose_FHRV and post_4th dose_fhrv	47	0.775	0.000

Table 7: Paired sample test between dexamethasone dose and fetal heart rate variability.

Paired sample test		Paired differences			
		Mean	S. D.	Std. error mean	95% CI of difference Lower
Pair 1	Pre-dexamethasone fHRV-post 1st dose fHRV	-5.423	3.380	0.469	-6.364
Pair 2	Pre-dexamethasone fHRV- post-4th dose fHRV	-8.894	4.066	0.593	-10.087
Pair 3	Post 1st dose fHRV-post 4th dose fHRV	-3.553	3.735	.545	-4.650

Table 8: Sick neonatal care unit admission and fHRV.

Serial No.	fHRV changes after dexamethasone	Cause of SNCU admission
1	Increased after both 1st and 4th dose	Low birth weight
2	Increased after both 1st and 4th dose	Transient tachypnea of new born
3	Increased after first dose, unaltered after 4th dose	Low birth weight
4	Increased after both 1st and 4th dose	Low birth weight
5	Increased after both 1st and 4th dose	Meconium aspiration
6	Increased after both 1st and 4th dose	Low birth weight
7	Increased after 1st dose, unaltered after 4th dose	Transient tachypnea of new born
8	Increased after both 1st and 4th dose	Perinatal asphyxia
9	Increased after both 1st and 4th dose	Congenital malformation
10	Increased after both 1st and 4th dose	For observation (delayed cry)
11	Increased after both 1st and 4th dose	Low birth weight
12	Increased after both 1st and 4th dose	Low birth weight
13	Increased after both 1st and 4th dose	Transient tachypnea of new born
14	Increased after both 1st and 4th dose	Perinatal asphyxia
15	Increased after both 1st and 4th dose	Low birth weight
16	Increased after both 1st and 4th dose	Congenital malformation
17	Increased after both 1st and 4th dose	Meconium aspiration
18	Increased after both 1st and 4th dose	Low birth weight
19	Increased after both 1st and 4th dose	Transient tachypnea of new born

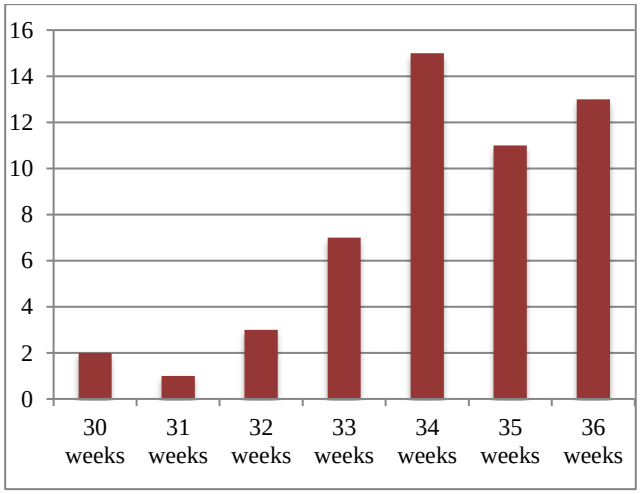

Figure 1: Distribution of participants according to the gestational age (in completed weeks).

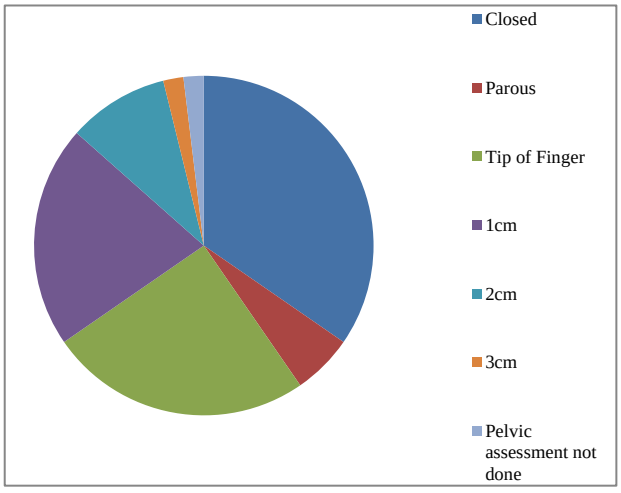

Figure 2: Distribution of participants according to status of cervical OS and cervical dilatation on admission.

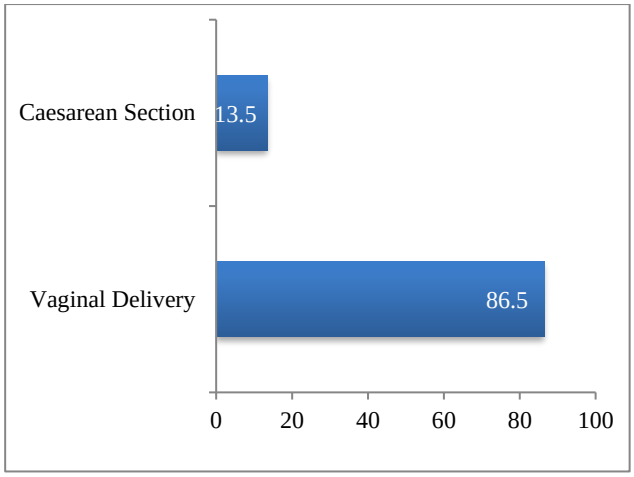

Figure 3: Mode of delivery.

DISCUSSION

The current study pictured that antenatal dexamethasone administration increases the fHRV after the first dose when compared to that prior to dexamethasone administration. This finding is consistent with that of the study conducted by Dawes and colleagues.[5]

Senat and group also showed that antenatal administration of dexamethasone is associated with increase in fHRV without significant decrease in the baseline fetal heart rate evident on the NST tracing.[10] This study further showed that antenatal dexamethasone administration was not associated with any effect on uterine contractions. It was also concluded from this current study that antenatal dexamethasone administration was not associated with foetal heart rate decelerations which corroborate to the current study.

This current study depicts that the effect of antenatal dexamethasone on foetal heart rate variability was similar in participants with different gestational age between 30 weeks to 36 weeks 6 days. Period of gestation did not significantly affect fHRV post dexamethasone injection. This observation is in line with a similar study conducted by Mulder and associates in 2004 who concluded that relative reduction in fHRV during days 2 and 3 after antenatal dexamethasone administration was similar in older and younger foetuses.[11]

Most of the participants (63.8%) had a baby who cried spontaneously at birth without resuscitation, had no respiratory distress, had good APGAR and required no intensive care. This finding is in contrast to the study in 2009 by Khashu et al which found that late-preterm infants had a significantly higher incidence of respiratory morbidity and infection and had a significantly longer duration of hospital stay.[12] The most common cause of death in preterm babies less than 34 weeks gestation is RDS. An estimated 15 million babies are born preterm every year worldwide. As per the India New born Action Plan, prematurity contributes to 35% of all neonatal deaths in India published in 2013.[13] Though in the present study there was no neonatal death noted.

It was observed that in the current study that foetal heart rate variability increased on day 1 and day 2 after administration of subsequent doses of dexamethasone. Verdurmen and colleagues conducted a similar study in 2013 where the authors followed up participants for 4 days after administration of a single dose of intramuscular dexamethasone to look for short term variations (STV) and long-term variations (LTV) in the foetal heart rate. They found that the foetal heart rate variability (both STV and LTV) increased on day 1 and but subsequently decreased on day 2 after dexamethasone administration.[14]

This study found that the most common age at presentation was after 34 completed weeks, whereas another study conducted in Netherlands in 2014 opined that the median age at delivery was 36+2 weeks in the group with onset and delivery in primary care, 35+6 in the group with onset in primary care and delivery in secondary care and 35+3 in the group with onset and delivery in secondary care.[15] It was observed during this study that majority of the participants (55.2%) had preterm labour followed by normal vaginal delivery, while 11.4% of them had to undergo emergency CS before term due to various maternal and foetal indications. 32.4% participants could continue pregnancy until term. Out of this majority (28.6%) delivered vaginally, whereas only 3.8% underwent CS.

This current study found that primigravidas (55.8%) and nulliparas (55.8%) constituted the majority of those at risk of preterm labour. On the contrary Temu and associates conducted a study in 2016 and concluded that primigravida was not significantly associated with increased risk of preterm delivery.[16]

It was observed that in majority of the participants (86.5%) labour progressed and preterm vaginal delivery took place. This finding stands in contrast to the opinion of American college of obstetricians and gynaecologists' committee published in 2016 where the authors opined that less than 10% of women with a clinical diagnosis of preterm labour will deliver within 7 days of initial presentation.[4]

In September 2016, an all-India institute of medical sciences, New Delhi based study titled "cardiotocography and diabetic pregnancy" was published in which the authors stated that maternal awareness of foetal movements should be routinely recommended and encouraged in all pregnancies after 28 weeks of gestation. In high-risk pregnancies, particularly in diabetic pregnancies, there is high risk of sudden intrauterine foetal demise, thereby prompting the use of additional modalities for antenatal foetal surveillance like NST, cardiotocography, and ultrasound biophysical profile testing weekly or twice weekly in these patients. In low resource settings, this can be accomplished by frequent antenatal visits and non-stress tests. In the intrapartum

period, there should be electronic foetal monitoring in 10 both 1st and 2nd stages for early diagnosis of foetal hypoxia and timely intervention.[17]

CONCLUSION

Role of corticosteroid to prevent RDS in preterm birth is well-known. Preterm birth being a high risk condition, monitoring of fetal and maternal wellbeing is very important in planning proper methods and timings of termination of pregnancy. Intermittent non-invasive NST is a valuable mode in monitoring fetal wellbeing in low resource countries. Thus, changes in NST tracing with administration of corticosteroid has clinical importance.

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