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High Dose Oxytocin Versus Low Dose Oxytocin for Augmentation of Labor: A Prospective, Comparative, Randomized Study

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ABSTRACT

Background: *Most common cause for delay in labor is due to inefficient uterine contractions. Various pharmacological interventions are available in shortening the duration of labor by augmentation making childbirth safe. One such drug is oxytocin being used for decades for shortening labor thus reducing maternal and neonatal morbidity.* ***Objective:*** *To compare and estimate the efficacy and safety of high dose oxytocin with that of low dose oxytocin for augmentation of labor in terms of maternal and neonatal morbidity.* ***Methods:*** *400 women with singleton pregnancy, cephalic presentation, in spontaneous onset of labor at term in District hospital were randomized into 2 groups either low-dose (starting at 1 mU/min with incremental dose at 1-2 mU/min) or high dose augmentation groups (starting at 4 mU/min with incremental dose at 4 mU/min) until adequate contractions obtained. Labor duration, cesarean rates, maternal and neonatal complications, were calculated.* ***Results:*** *Labor augmentation was significantly shorter by more than 2 hours in high dose oxytocin group than low dose group in nulliparas (2.83 ± 0.97 vs. 5.02 ± 1.43 hours, p<0.0001) and 1.6 hours in multiparas (2.05 ± 0.98 vs. 3.64 ± 1.08 hours, p<0.0001). No significant difference in the duration of second stage labor. The cesarean rates were not significantly different between the groups (4% vs. 5%, p=0.94). No difference in maternal and neonatal outcomes.* ***Conclusion:*** *High dose oxytocin effectively reduces Oxytocin augmentation to delivery interval when compared to low dose group regardless of parity but more significantly in nulliparous than in multiparous with fewer complications.*

Keywords: Labor dystocia, Oxytocin, Augmentation

INTRODUCTION

Length of labor differs among women, with primigravida laboring on average of eight hours and multigravida laboring on an average of five hours. Progress of labor takes into account not only cervical dilatation but also descent and rotation of the fetal head and strength, duration and frequency of uterine contractions. While the definition of delay varies, cervical dilatation of 2 cm in 4 hours is widely accepted as normal [1]. Rise in caesarean section is reported due to functional dystocia caused by inadequate uterine activity which further has an adverse impact on maternal, fetal morbidity and mortality [2].

The intrapartum use of oxytocin in active management of labor is advocated by O'Driscoll in 1960s who aimed at reducing the length of labor in pregnant women [3]. Despite the frequency with which oxytocin is being used in modern obstetric clinical practice, there is tremendous variability in the dose and dosing interval [4]. Though the use of high-dose oxytocin regimens has been associated with lower cesarean section rates, still there are concerns of its safety [5]. Low-dose oxytocin regimens seem to be safer but are not necessarily as efficient [6]. Our objective was to compare, in a randomized study, the efficacy and safety of high-dose versus low-dose oxytocin regimens in the augmentation of labor.

PATIENTS AND METHODS

All the patients with singleton pregnancy in spontaneous onset of active labor at 37 or more weeks of gestation with

inadequate labor progress or contractions, admitted for labor and delivery in Rajiv Gandhi Government Women and Children Hospital, Pondicherry during January 2015 - June 2016 were considered eligible for this study. Procedure of the study has been explained to the patients before enrolling into the study.

Some patients were excluded prior to randomization if case of any associated condition like previous uterine surgery, malpresentations, multiple gestations, meconium stained liquor, cephalo-pelvic disproportion, placenta previa, abnormal fetal heart rate pattern, and fetal growth restriction.

After approval of Institutional Ethical Committee review board, 400 eligible patients were enrolled into the study. Informed consent was obtained after diagnosis of dystocia was made. Patients were assigned into two groups by randomization using random number tables. Before the initiation of oxytocin all patients at our institution had a documentation of hypocontractility and adequate clinical pelvimetry. Active phase was defined by cervical dilatation of >4 cm with effective uterine contractions. Effective uterine contractions were defined as 3-5 uterine contractions each lasting at least for 40-60 seconds in 10-minute duration.

Oxytocin augmentation was commenced if progress was delayed, defined as <1 cm/hour in the first stage of labor and the absence of descent of the baby's head after 30 minutes of pushing or contractions less than one in five minutes and delivery not imminent in the second stage of labor.

Study Procedure

Oxytocin infusate was prepared with 4U oxytocin diluted in 500 ml Ringer lactate. Low dose regimen was started at an initial dose of 1 mU/min with incremental increases of 1 mU/min every 30 minutes till 8 mU/min, then 2 mU/min incremental increases up to a maximum of 32 mU/min. High-dose regimen started at an initial dose of 4 mU/min with incremental increases of 4 mU/min every 30 minutes up to 32 mU/min or until adequate uterine contractions.

Maternal pulse, blood pressure, uterine contractions were monitored every 30 minutes and infusion was stopped in any event of abnormal fetal heart rate pattern or uterine hyper-stimulation. Progress of labor was followed up and noted on partograph with per vaginal examinations every 4 hourly after admission. Fetal monitoring done by a combination of intermittent auscultation and CTG during oxytocin administration. Hyper-stimulation is defined as five or more uterine contractions in 10 minutes, each lasting for more than 90 seconds. In such case, oxytocin is stopped or started later at half dose after confirming reassuring fetal status.

Outcomes Measured

Maternal demographics, labor-delivery characteristics, and neonatal outcome were examined. Age, race, parity, gestational age, cervical dilatation, contraction pattern was analyzed. Also mean oxytocin dose, oxytocin infusion to delivery interval, and uterine contractility after augmentation were examined. Maternal outcome parameters included operative deliveries, chorioamnionitis, postpartum hemorrhage, and uterine hyperstimulation. Neonatal outcome parameters were birth weight, five-minute Apgar score, neonatal intensive care unit admission, neonatal complications, and neonatal deaths.

Statistical Analysis

Statistical analysis was performed using SSPS (statistical package for social sciences) software version 22 with descriptive statistics expressed in frequencies, percentages, and appropriate measures of central tendency and dispersion like mean, standard deviation. As per the level of measurement of data, appropriate statistical test was applied like Student's t-test for continuous data and chi-square (χ^2) test for categoric data. $p<0.05$ was considered statistically significant.

RESULTS

From January 2015 to June 2016, we recruited a total of 400 patients eligible for the study, who agreed to participate and assigned them randomly into low-dose (200) and high-dose groups (200). There were no statistical differences in maternal age, race, parity, gestational age, indication for labor stimulation as shown in Table 1.

Table 1 Maternal characteristics

Maternal Characteristics	Low dose	High dose	Significance (p-value)
Total no.	200	200	Not Significant
Nulliparas	98	98	-
Multiparas	196	196	-
Age (in years)	24.45 ± 3.29	24.12 ± 3.55	Not Significant
Gestation age (in weeks)	39.04 ± 0.86	38.9 ± 0.88	0.74

Cervical dilatation in both high and low dose groups was identical at the time of recruitment. Mean maximum oxytocin dose reached higher maximum dose in high-dose group than in low-dose group (18.57 ± 6.58 vs. 11.90 ± 4.97 mU/min, $p<0.001$ in nulliparas while 13.73 ± 5.67 vs. 7.53 ± 3.13 mU/min, $p<0.001$, in multiparas). There was no difference in duration of second stage labor between the groups. Labor augmentation has significantly shortened labor duration by more than 2 hours (2.83 ± 0.97 vs. 5.02 ± 1.43 hours) in high dose oxytocin group than low dose group in nulliparas and 1.6 hours (2.05 ± 0.98 vs. 3.64 ± 1.08 hours) in multiparas. Thus, there was strongly significant decrease in oxytocin augmentation to delivery interval in high dose group than low dose group regardless of parity ($p<0.0001$). Tables 2 and 3 summarize labor characteristics of nulliparous and multiparous participants respectively.

Table 2 Labor characteristics in nulliparas (Mean ± SD)

Labor Characteristics	Low dose	High dose	Significance
Cervical dilatation (cm**)	3.79 ± 0.43	3.73 ± 0.55	0.09
Max. oxytocin dose used (mU/min)	11.90 ± 4.97	7.53 ± 3.13	<0.001
Duration of second stage (in minutes)	10.82 ± 8.42	9.13 ± 7.99	0.09
Oxytocin-delivery interval (in hours)	5.02 ± 1.43	2.83 ± 0.97	<0.0001

Table 3 Labor characteristics in multiparas (Mean+ SD)

Labor Characteristics	Low dose	High dose	Significance
Cervical dilatation (cm)	3.89 ± 0.52	3.77 ± 0.52	0.5
Max. oxytocin dose used (mU/min)	18.57 ± 6.58	13.73 ± 5.67	<0.001
Duration of second stage (minutes)	9.17 ± 7.7	8.97 ± 8.71	0.97
Oxytocin-delivery interval (in hours)	3.64 ± 1.08	2.05 ± 0.98	<0.0001

Mode of delivery in nulliparas and multiparas is tabulated in Tables 4 and 5. No difference was seen regarding mode of delivery between both the groups regardless of parity. Twelve (6%) in low-dose and 10 (5%) in high-dose group had operative intervention. Indications being fetal distress (6 vs. 2), failure to descend (4 vs. 6), maternal exhaustion (2 vs. 2). Neither indications nor total rate differed between groups significantly, although there was decrease in rate of operative delivery with high-dose group.

Table 4 Mode of delivery in nulliparas

Mode of Delivery	Low dose	High dose
Spontaneous vaginal	91 (45.5%)	92 (46%)
Vacuum-forceps	2 (1%)	2 (1%)
Cesarean	5 (2.5%)	4 (2%)
Fetal distress	3 (1.5%)	1 (0.5%)
Fail to descent	2 (1%)	3 (1.5%)

Table 5 Mode of delivery in multiparas

Mode of Delivery	Low dose	High dose
Spontaneous vaginal	95 (47.5%)	98 (49%)
Vacuum-forceps	0 (0%)	0 (0%)
Cesarean	5 (2.5%)	4 (2%)
Fetal distress	3 (1.5%)	1 (0.5%)
Fail to descent	2 (1%)	3 (1.5%)

Although the maximum dose of oxytocin was significantly higher in the high-dose group, there was no increase in

the incidence of labor complications (Table 6). Specifically, hyperstimulation (2 vs. 3) and fetal distress did not differ between the two groups. Uterine atony was noted only in multiparas (2%) in high-dose group. There were no other maternal side effects like uterine rupture, abruption, chorioamnionitis noted in either of the groups.

Table 6 Labor complications

Labor Complications	Low dose	High dose
Hyper-stimulation	2 (1%)	3 (1.5%)
Uterine-atony	0 (0%)	4 (2%)
Chorioamnionitis	0 (0%)	0 (0%)
Abruption	0 (0%)	0 (0%)
Rupture uterus	0 (0%)	0 (0%)

Table 7 Neonatal characteristics

Neonatal characteristics	Low dose	High dose
Birth weight (kg)	2.98 ± 0.34	2.95 ± 0.31
APGAR <8	8 (4%)	8 (4%)
Birth asphyxia	1 (0.5%)	4 (2%)
Meconium aspiration	7 (3.5%)	11 (5.5%)
Low birth weight	13 (6.5%)	23 (11.5%)
Neonatal jaundice	1 (0.5%)	5 (2.5%)
Neonatal death	0	0
NICU admission	21 (10.5%)	34 (17%)

Neonatal characteristics tabulated in Table 7 above shows that there were no differences noted in birth weights, Apgar scores between the groups. No significant differences between two groups in the frequency of neonatal jaundice, low birth weight, birth asphyxia, meconium aspiration and NICU admission either, although admission in NICU was found to be more in high dose group, it was statistically insignificant, and it is more due to low birth weight.

DISCUSSION

Active management of labor is high profile in obstetric practice in modern India. In modern obstetrics, oxytocin is being used most frequently for labor stimulation but there is a considerable controversy exists concerning its administration and dosage. Though its usage in augmentation of labor started as early as 1960s, regimen-based studies are few and highly needed in order to reduce maternal and neonatal morbidity and mortality. The goal in using oxytocin for the augmentation of labor clearly is to increase the likelihood of vaginal delivery while not harming either mother or fetus.

Our hypothesis was to test whether high-dose oxytocin is superior to low-dose regimen. In this randomized study, high-dose oxytocin regimen clearly showed reduction in duration of labor of more than 2 hours in nulliparas and 1.6 hours in multiparas without any significant maternal and neonatal morbidity and mortality. Other major findings were no increase in labor complications such as hyper-stimulation and fetal distress with usage of high-dose. Chorioamnionitis, placental abruption or uterine rupture did not occur in our study.

Satin, et al. [7], Xenakis, et al. [8] concluded that high dose oxytocin regimen is clearly superior to low dose and may well serve to reduce the rate of cesarean delivery for dystocia. In contrast to above studies, Frigoletto, et al. [9], Sadler, et al. [10] and Zhang, et al. [11] found no reduction in cesarean delivery rate among the high-dose group. According to our study, there was no increase in cesarean rate with the usage of oxytocin. Oxytocin being safe to use under strict monitoring, it would reduce the overall rate of cesarean section although there was no significant difference between rate of cesarean section between high and low dose regimens. No statistical or clinical differences remained after controlling the use of oxytocin for type of delivery and indication for operative delivery in this study. The unblinded nature of the study may have resulted in a drift in the management of labor in both the groups thereby contributing similar cesarean rates.

CONCLUSION

We would conclude that high dose oxytocin effectively reduces oxytocin augmentation to delivery interval when

compared to low dose group regardless of parity. Also, it reduces duration of labor more significantly in nulliparous than in multiparous women without any significant detrimental effects on the mother or the fetus. Hence it can be recommended for use in modern obstetrics to hasten the labor. The period of study is short hence many outcomes like long term neurodevelopmental outcomes and maternal side effects may not be evaluated. Hence requires larger and long termed double masked trials to further determine the effectiveness, safety of high-dose oxytocin regimens over lower doses.

DECLARATIONS

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Conflict of Interest

We declare that we have no conflict of interest.

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