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Comparative study between high dose versus low dose oxytocin for augmentation of labor in relation to maternal and fetal outcome

Vrushali. S. Chavan
Post graduate resident, Department of Obstetrics and Gynaecology, Krishna Institute of Medical Sciences (Deemed to be) University, Karad, Maharashtra – 415110

Supriya Patil
Professor, Department of Obstetrics and Gynaecology, Krishna Institute of Medical Sciences, (Deemed to be) University, Karad, Maharashtra – 415110
Corresponding author: Supriya Patil

Dr. Sanjaykumar Patil
Professor, Department of Obstetrics and Gynaecology, Krishna Institute of Medical Sciences, (Deemed to be) University, Karad, Maharashtra – 415110.

Dr. Yamini Patil
Associate Professor, Department of Obstetrics and Gynaecology, Krishna Institute of Medical Sciences, (Deemed to be) University, Karad, Maharashtra – 415110.

***Abstract*---**Background: The use of oxytocin is common for shortening labor to reduce maternal and fetal morbidity. However, the use of various dosage forms for labor induction is limited. Therefore, the present study aimed to evaluate the efficacy and safety of high vs low dose oxytocin for labor augmentation and its impact on maternal and neonatal outcome. Materials and Method: This randomized, controlled study included100 subjects who were randomly assigned to Groups I (low dose oxytocin) and II (high dose oxytocin) with 50 subjects each. Maternal parameters like mode of delivery, labor duration, tachysystole, post-partum hemorrhage, uterine atony, uterine rupture, chorioamnionitis, and maternal mortality were assessed. Fetal parameters such as Apgar score and duration of NICU admission were assessed. Data was analyzed using Chi-square test. P value of <0.05 was regarded statistically significant. Results: Significant differences were observed among two groups with respect to age and weight (p=0.027 and p=0.001). Duration of labor showed a significant difference for augmentation to full dilatation interval (AFD) and augmentation to delivery (AD) (p<0.001) between two groups. Also, significant differences were observed with regard to duration of

labor for 2nd stage (p=0.001), maximum dose of oxytocin (p=0.001), and Apgar score at 1 min (p=0.047) between the groups. No statistically significant difference observed for maternal complications and neonatal intensive care unit (NICU) admissions between the groups. Conclusion: High dose effectively reduces oxytocin augmentation to delivery interval as compared to low dose group without any apparent adverse maternal or fetal outcomes.

***Keywords*---**Apgar score, Chorioamnionitis, Dilatation, Dystocia, Induced labor, Oxytocin, Uterine rupture.

Introduction

The escalation in cases of caesarean section is a persistent matter of obstetric concerns. High rates of caesarean sections could have a severe impact on maternal and neonatal morbidity and mortality.[1] Duration of labor varies among women, with primigravida labor lasting for about eight hours and multigravida labor lasting on an average of five hours. Delayed labor is commonly seen in nulliparous women and is the main indication for emergency caesarean section.[2-5]

For majority of pregnant women, once labor has been established, it advances without any intervention required until birth of their babies. Labor progression considers rotation of fetal head and strength, duration, and frequentness of uterine contractions in addition to cervical dilatation. The definition of delay differs, but cervical dilatation of 2 cm in four hours has been widely accepted as normal.[6]

Oxytocin is one of the commonly used medication in obstetrics for labor induction.[7] It is widely used in current obstetric practice to increase uterine activity in cases where labor process have failed with an objective to achieve vaginal delivery.[8] This synthetic polypeptide is in wide use to restore uterine contractions since it was synthesized.[9] The regimen of oxytocin has been classified as high dose or low dose based on various parameters like amount of initial dose, intervals of escalation, and rate of incremental dose.[1,10] Strong evidence on standard oxytocin regimen for labor induction worldwide is unavailable.[10,11]

Studies comparing high versus low dose oxytocin for labor induction found no variation in cesarean section rates, although more uterine stimulation was proved in the high dose group.[11] Few other studies have reported that high oxytocin dose compared to low dose for delayed labor progression might decrease the possibility of cesarean section by 15% or close to 46% without any harmful effects on maternal or neonatal outcomes.[1,12] However, the childbirth and pain experienced with oxytocin dosage and also the studies to prove the use of high dose oxytocin is limited. Hence, this necessitates further investigations especially on the maternal and neonatal outcomes with respect to oxytocin dosage. There are limited comparative studies conducted to assess the effects of high and low oxytocin dosage regimens on favorable outcomes of induction in India. Therefore, the current study was carried out to evaluate the efficacy and safety of high dose

vs low dose oxytocin for labor augmentation and its impact on maternal and fetal outcomes.

Materials and Methods

Trial design

This randomized, controlled study included subjects admitted in the labor ward of tertiary care center from October 2014 till March 2016. The Institutional review board's clearance was obtained, and prior written informed consent was taken from all the participants. Subjects who were in full term labor requiring labor augmentation with inadequate uterine contractions one hour post artificial rupture of membranes (ARM) and cervical dilatation of 3-4 cms were selected. Sample size calculation was based on 76% prevalence with 10% error to obtain a final sample size of 50 subjects per group.

Inclusion criteria

Subjects with singleton pregnancy, primigravida, vertex presentation and beyond 37 weeks of gestation were included.

Exclusion criteria

Subjects who were multipara, with malpresentation, who had earlier cesarean section, contracted pelvis and cephalon pelvic disproportion, obstructed labor and unexplained vaginal bleeding and placenta previa were excluded.

Sample Randomization and Intervention

One hundred subjects were randomly assigned to Groups I (low dose oxytocin) and II (high dose oxytocin) with 50 subjects in each group. Group I subjects were started with 2 mu/min and increased by 1-2 mu/min every 30 minutes interval to a maximum of 20 mu/min. Group II subjects were started with 6 mu/min and increased by 3 mu/min every 30 minutes interval to a maximum of 24 mu/min.

Outcome Measures

Maternal parameters: Maternal parameters were assessed by spontaneous vaginal delivery, instrumental delivery, cesarean delivery, labor duration more than 12 hours, tachysystole, post-partum hemorrhage, uterine atony, uterine rupture, chorioamnionitis, and maternal mortality.

Fetal parameters: Fetal parameters were assessed through measurement of Apgar score <6 at 1 minute, APGAR score <7 at 5 minutes, and admission to NICU >48 hours.

Statistical analysis

Data was analyzed with t test and analysis of variance (ANOVA) for continuous data. Categorical variables were evaluated by Chi-square test. Averages were reported as mean ± standard deviation (SD). P value of <0.05 was regarded statistically significant.

Results

The flow of participants through the study is depicted in Figure 1.Majority of the subjects in the study were aged >20 years. With respect to weight, majority of the

subjects weighed >60 Kgs. The differences observed between the groups with regard to age and weight were significant (p=0.027 and p=0.002), respectively. The mean gestational age was 40.35±0.37 weeks and 40.375±0.37 weeks in low dose and high dose groups, respectively. The most common mode of delivery was observed to be vaginal delivery in the study population. In terms of labor duration, there was significant difference observed between the groups for augmentation to full dilatation interval (AFD) and augmentation to delivery (AD) (p<0.0001) (Table 1).

Distribution of labor duration for 2nd stage was significantly different (p<0.001) between both the groups. Similarly, maximum oxytocin dose was significantly different between both high and low groups with p<0.001. In terms of Apgar score, there was significant difference observed between high and low groups for Apgar score at 1 min (p=0.048) With regard to birth weight, Apgar score at 5 min, and cervical dilatation, the differences were statistically insignificant (Table 2).

In terms of maternal complications and neonatal intensive care unit (NICU) admissions, the differences were statistically insignificant. Tachysystole and cervical tears were the maternal complications observed. The most common complications associated with NICU admissions included birth asphyxia and hyperbilirubinemia in high and low dose groups. There were very few NICU admissions observed during the study in both high and low dose groups (Table 3).

Discussion

Short duration of labor and reduced complications of maternal and fetal outcomes are the foremost priorities of labor management in obstetric practices. Though oxytocin is being used commonly to stimulate labor, there exists a controversy concerning the efficacy and safety of dosage. The current study tested whether high dose is superior to low dose regimen with the aim of using oxytocin for labor augmentation with the probability of evaluating the maternal and fetal outcomes.

The current study observed a significant difference between high and low dose groups in terms of age and weight (p=0.02 and p=0.001). Studies conducted by Neerukonda et al and Tesemma et al reported no significant differences in terms of age and weight.[13,14] The reason for the significance in the current study could be attributed to genetic characteristics of the population in the study. With respect to duration of labor, significant difference was observed between high and low dose groups for AFD and AD with shorter duration in high dose group (p<0.001). In addition, present study also reported significant difference (p<0.001) between two different doses of oxytocin groups in terms of shortening labor in besides second stage duration. These results were similar to the studies conducted by Wei et al and Ghidini et al which reported high oxytocin dose reduced labor duration.[1,10] This could be because of frequent rise of oxytocin dose among high dose group compared to low dose group till getting sufficient uterine contraction of right cervical outcome.

In terms of maximum dose of oxytocin, the mean concentration of oxytocin used in the present study was significantly high in the high dose group as compared to low dose group. This could be because of the frequent dose escalation in the high

dose compared to low dose group. With regard to Apgar score at 1 min, there was a significant difference observed between high and low dosage regimens. Most of them had Apgar score >6 in high oxytocin group as compared to low oxytocin group. This could be attributed to the fact that high oxytocin dose impact good health in neonates.

There was no significant difference in maternal complications between high and low dosing regimens in the present study. Similarly, no significant difference was observed with respect to NICU admissions between high and low dosing regimens. In the present study, tachysystole incidence was 4% in high and low dose groups. Merril et al, in a study reported higher incidence of tachysystole in high dose (15.5%) vs low dose (22.4%) groups which could be because of electronic fetal monitoring that was more sensitive to detect tachysystole, as compared to the current study which was clinical based diagnosis.[15] It might also be because of different criteria with hyperstimulation of oxytocin in the present study to diagnose tachysystole. The prevalence of cervical tear was 2% in high oxytocin dose as compared to low oxytocin dose group. Similar research in this regard are limited and possibly this could be the first study conducted wherein incidence of cervical tear was evaluated with comparison of two varied doses of oxytocin. In terms of NICU admissions, differences observed between the two dose regimes were statistically insignificant. These results could be because of the fact that high dose oxytocin could be administered safely without any adverse maternal and fetal complications.

Inspite of the efforts of this research, it has few limitations. It is difficult to differentiate the present study with others because of the different criteria to diagnose dystocia, different dosing intervals and incriminates used in other studies. Furthermore, confounders like parity, cervical ripening agent and fetal weight were not considered to check the actual effect of oxytocin regimen on induction scores. In addition, the study has limited sample size and hence, though there were some differences observed in few outcomes, it was not significant due to limited population.

Conclusion

The high dose of oxytocin effectively reduces oxytocin augmentation to delivery interval as compared to low dose group. Also, it reduces labor duration more significantly without any detrimental effects on maternal and fetal outcomes. Hence, it can be recommended for use in present-day obstetrics to hasten labor. Further double masked trials on larger population are warranted to evaluate the efficacy and safety of high dose oxytocin regimens over lower doses.

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Table 1: Distribution of demographic characteristics

Factors	Frequency (%)		p value
	Low dose (N=50)	High dose (N=50)	
Age group (Years)			
≤20	4	13	**0.027*M**
>20	46	37	
Mean ± SD	23.98±2.92	22.66±2.46	
Weight (Kg)			
50-60	12(24)	26(52)	**0.001*M**
>60	38(76)	24(48)	
Mean ± SD	66.62±7.23	61.98±7.46	
Height (Cm)			
≤150	24(48)	22(44)	0.2311T
>150	26(52)	28(56)	
Mean ± SD	150.74±3.08	151.58±3.84	
Gestational Age (Weeks)			1M
Mean ± SD	40.35±0.37	40.375±0.37	
Duration of labor (hours)			
AFD (Mean ± SD)	319.60±38.84	255.83±40.32	**<0.001*T**
AD (Mean ± SD)	367.98±38.30	296.89±43.06	**<0.001*M**
Mode of delivery			
Vaginal	43	47	0.3173C
LSCS	7	3	

AD: Augmentation to delivery; AFD: Augmentation to full dilatation interval; C: Chi square test of independence; LSCS: Lower segment cesarean section; M: Mann Whitney U test; T: Two sample test
**p<0.05 considered statistically significant*

Table 2: Association between various factors with low and high dose groups

Factors	Frequency (%)		p value
	Low dose (N=50)	High dose (N=50)	
Distribution of labor in relation to stage of labor characteristics			
2nd Stage (Mean ± SD)	48.44±7.43	40.85±9.54	**<0.001*M**
3rd Stage (Mean ± SD)	4.58±1.11	4.64±1.09	0.66M
Maximum dose of Oxytocin (IU/ml)			**<0.001*M**
Mean ± SD	14.7±3.66	18.72±3.91	
Birth Weight (Kg)			
<2.5 kg	7(14)	9(18)	0.191T
>2.5 kg	43(86)	41(82)	
Mean ± SD	2.92±0.38	2.82±0.35	
APGAR score at 1 Min			
<6	24(48)	16(32)	**0.048*M**
>6	26(52)	34(68)	
Mean ± SD	6.28±0.93	6.64±0.6	

APGAR score at 5 Min			
≤8	16(32)	15(30)	0.597M
>8	34(68)	35(70)	
Mean ± SD	8.5±0.89	8.7±0.46	
Cervical Dilatation (cms)			
≤4	48(96)	49(98)	0.905M
>4	2(4)	1(2)	
Mean ± SD	3.6±0.49	3.60±0.5	

M: Mann Whitney U test; T: Two sample test
**p<0.05 considered statistically significant*

Table 3: Maternal complications and NICU admission among low and high dose groups

Factors	Frequency (%)		p value
	Low dose (N=50)	High dose (N=50)	
Maternal complication			0.712C
Present	5 (10)	3 (6)	
Absent	45 (90)	47 (94)	
NICU admission			
Present	8 (16)	2 (4)	0.095C
Absent	42 (82)	48 (96)	

C: Chi square test of independence; NICU: Neonatal intensive care unit

Figure: 1