Gynecology & Obstetrics
ISSN: 2161-0932
OPEN ACCESS Freely available online
Review Article

Maternal outcomes of high dose *vs* low dose oxytocin regimen used for labor induction in Ethiopia: a multicenter comparative study

Melese Gezahegn Tesemma[1*], Demisew Amenu Sori[2], Desta Hiko Gemeda[3]

[1]Department of Obstetrics and Gynecology, Arsi University teaching referral hospital, Asella, Ethiopia;[2]Department of Obstetrics and Gynecology, Jimma University medical center, Jimma, Ethiopia ;[3]Department of epidemiology, Jimma university Institute of health, Jimma, Ethiopia

ABSTRACT

Background: Very few studies are conducted to compare the relative efficacy and safety of high-dose and low-dose oxytocin regimens on maternal outcomes. This study was aimed at comparing maternal outcomes of high-dose vs low-dose oxytocin regimen among pregnant mothers undergoing labor induction.

Method and material: Comparative cross-sectional study was conducted in four selected hospitals of Ethiopian. All pregnant women fulfilling inclusion criteria were included. Collected data was entered into epidata version 3.1 and then exported to SPSS version 20 for cleaning and analysis. chi-square test, bivariate and multivariate logistic regression was done to look for association of independent variables with Adverse Maternal Outcomes (AMO). The result was presented using 95% Confidence Interval (CI) of Odds Ratios (OR). p-value<0.05 was used to declare statistical significance.

Result: Mean average length of hospital stay was 2 days and 2.7 days among mothers receiving high dose oxytocin and low dose oxytocin regimen respectively. Of all maternal outcome variables only, puerperal sepsis was significantly related with oxytocin regimens with prevalence of 5.6% and 0% (X2=0.015, P=0.029) among low dose group and high dose group respectively. Misoprostol use for ripening [AOR 4.7, 95% CI 1.6, 13.4] and Neonatal birth weight of >4 kg [AOR 3.4, 95% CI 1.1, 10.3] were found to be associated with adverse maternal outcome.

Conclusion: Oxytocin regimen has no significant association with adverse maternal outcome. However, low dose oxytocin use was associated with increased risk of puerperal sepsis and slightly longer duration of hospital stay.

KEYWORDS: Lung Cancer; Lung Nodule; Lung Tumor; Malignancy; Metastasis

INTRODUCTION

Induction Of Labor (IOL) refers to the deliberate stimulation of uterine contractions before the onset of spontaneous labor with the aim of achieving vaginal delivery. Oxytocin has been in use for IOL for the past 70 years [1-3]. IOL is associated with poorer maternal outcome when compared with spontaneous labor. There is a greater risk of Cesarean Section (C/S), maternal complications including uterine hyper stimulation, hypotension, fever, water intoxication, perineal lacerations, increased use of uterotonic agents and anesthetic/ analgesic agents, hysterectomy, Intensive Care Unit (ICU) admission, and hospital stay more than seven days [2].

Oxytocin protocols are classified as high-dose and low-dose protocols based on starting dose, rate and interval of escalation [4]. Intervals to increase oxytocin doses vary from 15 to 60 minutes [5-10]. The high-dose regimens varied across the trials; starting doses ranged from 4-10 mili-unit/minute (mU/min), with increases in dose ranging from 4-7 mU/min and maximum rates ranging from 4-90 mU/min. Low-dose regimen will be commenced infusion at 1-4 mU/min, with rate increases ranging from 1-2 mU/min and maximum rates ranging between 1-31.7 mU/min [4]. Low-dose protocols mimic endogenous maternal physiology and are associated with lower rates of uterine tachysystole [1]. Oxytocin during labor appears to be an independent risk factor for severe PPH, with a dose-related association [11].

Worldwide, although there are different guidelines and publications to compare low and high dose oxytocin regimens, there is no

Correspondence to: Melese Gezahegn Tesemma, Department of Obstetrics and Gynecology, Arsi University teaching referral hospital, Asella, Ethiopia; Phone: +251913347330; E-mail: get.melese@gmail.com

Received: February 02, 2021, **Accepted:** February 16, 2021, **Published:** February 23, 2021

Citation: Tesemma MG, Sori DA, Semeda DH (2021) Maternal outcomes of high dose vs low dose oxytocin regimen used for labor induction in Ethiopia: a multicenter comparative study. Gynecol Obstet (Sunnyvale). 11: 553.

agreement on a standardized oxytocin regimen nor is convincing evidence to show one oxytocin regimen is superior to another. As a result, there is no hard evidence to recommend a particular dosage of oxytocin for induction of labor infusion regimens [12-14]. However, one meta-analysis done in 1998 supports use of a low dose oxytocin infusion for IOL [3].

In Ethiopia both low dose and high dose oxytocin regimen protocols are being used in different centers. The national guideline recommends low dose oxytocin regimen where induction will be commenced with 2 mu/min and escalated every 30 minutes and the maximum dose being 40 mu/min [15]. However, Jimma University Medical Center (JUMC) is using high dose oxytocin regimen where induction starts at 6 mu/min and escalating every 20 minutes till a maximum of 92.7 mu/min [16]. However, as to the knowledge of authors there is no study done to compare the effect of high dose and low dose oxytocin regimen on maternal outcomes in Ethiopia. This study was, therefore aimed at determining and comparing the adverse maternal outcomes of the high dose and low dose oxytocin regimen.

MATERIALS AND METHODS

Study area, study period, study design

The study was conducted in four hospitals namely JUMC, Shanan Gibe General Hospital (SGGH), Arbaminch General Hospital (AGH) and Kuyu General Hospital (KGH) from October 1, 2017 to May 30, 2018 using a multicenter prospective comparative study design. JUMC is tertiary hospital that uses high dose regimen while the three general hospitals use low dose oxytocin regimen for IOL [17].

Study population

All pregnant women with singleton gestation who undergo induction of labor at gestational age (GA) of >37 weeks were recruited during the study period while those pregnant mothers with Intra Uterine Fetal Death (IUFD), pregnant mothers with lethal fetal congenital anomaly, pregnancies complicated by cord prolapse, induced pregnancy for whom C/S was done for non-obstetric indication were excluded from the study [17].

Sample size and sampling technique

The required sample size was determined by using double population proportion considering the following parameters: Proportion of C/S among laboring mothers who received high dose of oxytocin (10.4%) and proportion of C/S among laboring mothers who received low dose of oxytocin (25.7%) [8], 5% level of significance, power of 80% and 1:1 ratio of exposed to un-exposed. Considering 10% for non-response, 108 laboring mothers were recruited for each group. Thus, 108 pregnant women were recruited from JUMC while the rest 108 (36 from each) pregnant women were recruited from three general hospitals. All pregnant women who had undergone induction of labor during study period were recruited consecutively using inclusion criteria [17].

RESULTS

Socio-demographic, reproductive and obstetric Variables of study participants

A total of 216 laboring mothers have participated in the study, 108 participants at high dose center and low dose centers each. Overall mean age of study participants was 26 years and was similar among the two study groups. Majorities of study participants 157 (73%) were aged between 20-29 years followed by those whose age were 30 years and above 50(33.1%). Over a quarter of laboring mothers, 57(26.4%), have attended college and university while 40(18.5%) were illiterate. Occupation wise, 123(57%) were house wife while a quarter, 55 (25.5%), were government employee. Overall mean income of laboring mothers for High Dose Group (HDG) and Low Dose Group (LDG) were 5068 ETB and 4222 ETB respectively.

Maternal outcomes and factors associated with adverse maternal outcome

AOverall maternal outcome on discharge was favorable and no mother was discharged with severe complication or permanent sequel except one mother whose uterus ruptured and repaired after receiving high dose oxytocin regimen. Overall composite adverse maternal outcomes associated with oxytocin use were observed in 22(10.2%) of study subjects of which 13(6%) were from LDG. Uterine hyper stimulation and uterine rupture has occurred only among HDG. Similarly, chorio-amnionitis diagnosed after initiation of oxytocin and puerperal sepsis, were adverse maternal outcomes solely occurred among LDG.

On cross tabulation, of all maternal outcome variables like uterine hyper-stimulation, uterine atony, postpartum hemorrhage, uterine rupture, pulmonary edema, puerperal sepsis and chorio-amnionitis, only puerperal sepsis was significantly related with use of different oxytocin regimens with prevalence of 5.6% and 0% (X2=0.015, P=0.029 among LDG and HDG respectively.

On bivariate logistic regression age, residence, previous parity, oxytocin regimen, bishop score and indication of induction did not show any kind of association with adverse maternal outcome. However, misoprostol use [COR 4.8, 95% CI 1.7, 13.7], Caesarean delivery [COR 3.3, 95% CI 1.2, 8.9] and neonatal birth weight>4000 gm [COR 3.7, 95% CI 1.3, 10.5] had shown statistically significant association with adverse maternal outcome at P-value<0.05. On multivariate logistic regression analysis, the only two variables remained in the model to show association with adverse maternal outcome at P-value<0.05 were misoprostol use [AOR 4.7, 95%CI 1.6, 13.4] and neonatal birth weight>4000 gm [AOR 3.4, 95% CI 1.1, 10.3].

DISCUSSION

The study generally showed lower adverse maternal outcomes (8.3% vs 12%) and shorter duration of hospital stay (mean difference of 0.7 hours) with HDG compared to LDG. Puerperal sepsis and chorio-amnionitis after IOL were seen among women receiving low dose regimen only. On other hand, uterine tachysystole and one uterine rupture were observed only in women receiving high dose regimen. However, no difference was observed on development of PPH and pulmonary edema in both groups as it holds true in one systematic review published on American journal of obstetrics and gynecology in 2010 [4]. But two studies showed increased risk of PPH with increased oxytocin dose [3,11].

The higher uterine tachysystole with HDG was consistent with other studies [4-5,14,18]. In study conducted by Satin AJ and associates, they found higher rate of uterine hyper-stimulation (55 vs 42%) with high dose oxytocin regimen compared with low dose [18]. This is because low-dose protocols mimic endogenous maternal physiology and are associated with lower rates of uterine

tachysystole [1,3,14]. On the other hand, although the plasma half-life of oxytocin is short (3 to 6 minutes), steady-state concentrations are reached within 30 to 40 minutes of initiation or dose change [1]. Thus, frequent dosing interval may lead to uterine hyper-stimulation. It was found that even with same dosing regimen (high dose), the incidence of uterine hyper-stimulation was greater (40% vs 31%) with the 20-minute than the 40-minute dosing interval for induction [5]. In this study, high-dose protocol was having more frequent dosing interval (every 20 minutes) than low dose (every 30 minutes) that leads to frequent oxytocin provision before steady state is reached thus increasing risk of uterine hyper stimulation.

Composite adverse maternal outcome had no significant association with different oxytocin regimen. This was similar with many literatures that didn't show any significant association with different oxytocin regimen [4,5,8,10,14]. With extensive search we authors didn't get a single research that showed significant association between composite adverse maternal outcomes and different oxytocin regimen.

However, puerperal sepsis has got statistically significant relation with low dose oxytocin regimen. This is consistent with one study which showed relatively higher puerperal infection among low dose group (22% vs 15%) [8]. Although low-dose oxytocin brings safe contractions, its longer induction to delivery interval might have increased the chance of fetal infection and chorio-amnionitis that may later risk the mother to develop puerperal sepsis. The other explanation can be, as the time between rupture of membranes and the onset of labor increases, risk of maternal and fetal infection also increases. In this study, pregnant women with PROM in low dose setting were expectantly managed for spontaneous onset of labor for 18 hours before getting induced while only 8 hours is waited in high dose setting. This prolonged waiting time for induction among low dose setting might have increased risk of puerperal infection in this study. Delivery to macrosomic baby and misoprostol use for cervical ripening was significantly associated with adverse maternal outcome. Accordingly, delivery to macrosomic baby and use of misoprostol for cervical ripening increased odds of adverse maternal outcomes by 3.4 and 4.7 times as compared to delivery to non-macrocosmic baby and not using misoprostol respectively. We didn't get study with similar outcome variables to compare with our study. Thus, researchers can use this finding as baseline for further study.

Macrosomic fetus is associated with uterine atony, labor dystocia and cephalo-pelvic disproportion that may require cesarean delivery which in turn is associated with adverse maternal outcome like PPH, uterine atony, endomyometritis, anesthesia complications. Vaginal delivery of macrosomic delivery is also associated with birth trauma which might have contributed to adverse maternal outcome. Association of misoprostol use to adverse maternal outcome seen in this study might be justified by the fact that misoprostol use is associated with some complications like uterine tachysystole, PPH and uterine rupture [1]. But it needs further study to see if there is true association.

CONCLUSION

Misoprostol use and delivery to macrosomic neonate were associated with increased odds of adverse maternal outcome. Use of low dose oxytocin was associated with increased risk of puerperal sepsis and slightly longer duration of hospital stay. However, Oxytocin regimen didn't show statically significant association with adverse maternal outcome. Thus, there is no significant difference on adverse maternal outcome when using either of the regimens.

ACKNOWLEDGEMENT

We would like to thank the study participants for providing as the necessary personal information and Jimma University medical center for allowing us retrieve patients chart.

AVAILABILITY OF DATA AND MATERIALS

The data used to generate and or analyze the current study are available from the corresponding author upon the request.

AUTHOR'S CONTRIBUTIONS

All authors participated in the design and analysis of the study. MGT searched the databases, and wrote the first and second draft of the article. DAS and DHG reviewed proposal development activities and each drafts of the result article. All authors revised the manuscript and approved the final version.

FUNDING

There is no funding source for this research.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

An official letter was obtained from the Institutional Review Board of Jimma University to conduct this research and we got permission letter from the Hospital directors to collect data. Written informed consent was obtained from each study participant.

CONSENT FOR PUBLICATION

Not applicable for this publication

COMPETING INTEREST

We declare that we don't have competing interests with publication of this article.

REFERENCES

1. Deborah AW, Lili S. Abnormal Labor and Induction of Labor. Obstetrics: Normal and Problem Pregnancies, 7th edition. China: Philadelphia, PA: Elsevier 2017;276-283
2. American College of Obstetricians and Gynecologists. Induction of labor. ACOG practice bulletin #107. Obst Gynecol. 2009;114:386-397.
3. Joan MGC, David CY. Meta-Analysis of Low Dose vs High Dose Oxytocin for Labor Induction. J Soc Obstet Gynaecol Can. 1998;20(13):1215-1223.
4. Shu QW, Zhong CL, Hui PQ, Hairong X, William DF. High dose vs low-dose oxytocin for labor augmentation: a systematic review. Ame J obs gynecol. 2010;203(4):296-304.
5. Satin AJ, Leveno KJ, Sherman ML, McIntire D. High-dose oxytocin: 20 vs 40-minute dosage interval. Obstet Gynecol. 1994;(2):234-238.
6. Merrill DC, Zlatnik FJ. Randomized, doublemasked comparison of oxytocin dosage in induction and augmentation of labor. Obstet Gynecol. 1999;94(3):455-63.
7. Frigoletto FD, Lieberman E, Lang JM, Cohen A, Barss V, et al. A clinical trial of active management of labor. N Engl J Med. 1995;333(12):745-750.

8. Xenakis EM, Langer O, Piper JM, Conway D, Berkus MD. Low-dose vs high-dose oxytocin augmentation of labor-a randomized trial. Am J Obstet Gynecol. 1995;173:1874-1878.

9. Zeno JAL, Peaceman AM, Adashek JA, Socol ML. A controlled trial of a program for the active management of labor. N Engl J Med. 1992;326:450-454

10. Satin AJ, Hankins GDV, Yeomans ER. A prospective study of two dosing regimens of oxytocin for the induction of labor in patients with unfavorable cervices. Am J Obstet Gynecol. 1991;165(4):980-984.

11. Belghiti J, Kayem G, Dupont C. Oxytocin during labour and risk of severe postpartum haemorrhage: a population-based cohort-nested case-control study. BMJ Open. 2011;1:e000514.

12. Mori R, Tokumasu H, Pledge D, Kenyon S. High dose versus low dose oxytocin for augmentation of delayed labour. Cochr Dbase Sys Rev. 2011;10:7201.

13. Alessandro G, Diann W, Victoria K, John CP, Sarah HP. Effects of two different protocols of oxytocin infusion for labor induction on obstetric outcomes: A cohort study. OJOG. 2012;2:106-111.

14. Budden A, Chen LJY, Henry A. High-dose versus low-dose oxytocin infusion regimens for induction of labour at term. Cochr Dbase Sys Rev, 2014;10:9701.

15. Management Protocol on Selected Obstetric Topics: Federal Democratic Republic of Ethiopia, Ministry of Health. Unpublished National guideline. 2010.

16. Segni H, Niguse D. Obstetrics management guideline of Jimma University specialized hospital. Unpublished hospital guideline. 2010;1.

17. Tesemma MG, Sori DA, Gemeda DH. High dose and low dose oxytocin regimens as determinants of successful labor induction: a multicenter comparative study. BMC Preg Childbirth. 2020;20(1):232.

18. Satin AJ, Leveno KJ, Sherman ML, Brewster DS, Cunningham FG. High vs low-dose oxytocin for labor stimulation. Obstet Gynecol. 1992;80:111.