Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://dx.doi.org/10.21608/zumj.2020.48464.1997 Volume 29, Issue 1, - January 2023, Page (307-312) Supplement Issue

Manuscript ID ZUMJ-2011-1997 (R1)
DOI **10.21608/zumj.2020.48464.1997**

ORIGINAL ARTICLE

Induction of Labor with Titrated Oral Misoprostol Solution versus Oxytocin in Term Pregnancy.

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Submit Date 2020-11-06
Revise Date 2020-12-03
Accept Date 2020-12-15

ABSTRACT

Background: The goal of labor induction is to stimulate uterine contractions before the spontaneous onset of labor, resulting in good pregnancy outcomes. Both uterine contractions and cervical ripening are two important factors in successful induction and vaginal delivery. **T**his study aimed to evaluate the effectiveness and the safety of orally administered misoprostol solution in comparison to that of intravenously infused of oxytocin for labor induction in term pregnant women.

Methods: This randomized clinical study was carried out in the emergency unit of Obstetrics and Gynecology Department of Zagazig University Maternity Hospitals during the period from February 2018 to January 2019**,** and this study included 110 patients were randomly assigned into two groups misoprostol group or oxytocin group. The misoprostol group received 25 µg every2hours. The oxytocin group received an infusion of 5IU which was gradually increased the maximum time for drug administration was 24 hours. The time from induction to delivery and induction to active Phases were recorded.

Results: showed that both values of mean time from induction to active phase and induction to delivery were significantly shorter in misoprostol group than in oxytocin group (10.4 and 13.2 versus 12.9and15.8) hours respectively.

Conclusions: Induction time to vaginal delivery was shorter in misoprostol group when compared with oxytocin group. So, titrated oral misoprostol solution can be used as an alternative to intravenous oxytocin infusion for induction of labor.

Keywords: Induction; Misoprostol; Oxytocin.

INTRODUCTION

Labor induction is defined as stimulation of uterine contractions to produce delivery before the onset of spontaneous labor. Prolonged gestational age still the most common cause for induction of labor in the obstetric practice worldwide [1]. Preparing the cervix for induction can be done by many methods. Pharmacological methods as Prostaglandins, Intravenous oxytocin, Misoprostol, Mifepristone, Relaxin hormones or non-pharmacological methods as Membrane sweeping, Castor oil, Hot baths and enemas or surgical methods as Amniotomy, Balloon catheters or laminaria [2].

For successful induction some characteristics should be found:

Bishop Score and recently Modified Bishop Score: Pre-induction cervical scoring system should be evaluated at first. Total score=13, Favorable score= 6-13, Unfavorable score= 0-5. Score of 5 or less suggests that normal labor is unlikely to occur without induction. A score of 9 or more indicates that labor will mostly occur spontaneously [3].

Sonographic assessment of cervical length can be used as a prediction to outcome of labor induction has been evaluated in numerous studies. Some studies found that Sonographic measurement of cervical length was more predictive for induction outcome than the Bishop score. Detection of fetal fibronectin in cervico-vaginal secretions; has also recently been used. Fetal fibronectin is a glycoprotein found in amniotic fluid and at the chorionic decidual interface .Multiparty and infant birthweight less than 3.5 kg all of these factors give a good prediction of successful induction of labor process [4].

The use of oxytocin in induction of labor is considered one of the popular methods for induction of labor all over the world. Its route of administerion is by intravenous infusion of a diluted solution, preferably by means of a variable-speed infusion pump [5].

It is one of the safest therapeutic agents. The therapeutic effect of oxytocin is by making the cervix to dilate during the first stage of labor and the head of the fetus to descend during the second stage of labor [6].

If uterine hyperstimulation occurs during induction, characterized by too frequent contractions or the development of uterine tetany, the oxytocin solution should be stopped immediately. The half-life of intravenous oxytocin is short less than (3minutes); after stopping of the infusion several minutes the hyper-stimulatory effects of oxytocin should be resolve spontaneously. Many procedures can be done as putting the patient in left lateral positioning, oxygen inhalation by face mask; hydration and intravenous magnesium sulfate (4 g over 30 minutes) could be given [7].

In 1988, the US Food and Drug Administration approved the using of misoprostol under the brand name Cytotec, for prevention of gastric ulcers among long-term users of non-steroidal anti-inflammatory drugs. But it was found that it affects the uterus and cervix as well as the gastrointestinal tract. So warning has been informed to the use by pregnant patient [8].

This side effect has been used as therapeutic agent in gynecological procedure as (Cervical ripening prior to dilatation and curettage and hysteroscopy) and obstetric practice as (Cervical ripening for labor induction, Management of spontaneous abortion, missed abortion, Medical abortion, Management of uterine atony leading to postpartum haemorrhage) [9].

Other routes of misoprostol administration include vaginal, sublingual, and rectal. These routes have been used mainly in obstetric and gynecological practice. Small doses of misoprostol can be used for induction of labor that can be adequate for starting uterine contraction [10].

According to some clinical recommendation, based on limited or inconsistent evidence misoprostol at a dose of 50 µg every 6 hours, may be suitable for induction of labor. Higher doses of misoprostol associated with great risk for uterine hyper stimulation with fetal distress and other complications [11].

The aim of this study was to evaluate the effectiveness and the safety of orally administered misoprostol solution in comparison to that of intravenous infusion of oxytocin for labor induction in term pregnant women.

METHODS

This randomized clinical study was carried out in the emergency unit of Obstetrics and Gynecology Department of Zagazig University Maternity Hospitals, Zagazig, Sharkia, Egypt, during the period from February 2018 to January 2019. Misoprostol group "Group I" (55 patient) and Oxytocin group "Group II" (55 patient).

Group(1): One 200-mcg tablet of misoprostol was completely dissolved in 200 mL of tap water with stirring bar in a medicine bottle by the duty nurse. The misoprostol solution was stored in a medicine bottle and completely used within 24 hours after preparation or discarded. Women were given 1 basal unit of 25 mL of misoprostol solution orally. Misoprostol was administered at a dose of 25mcg/2hour, until adequate uterine contractions were achieved [12].

Group(2): Women received oxytocin by IV drip infusion at a rate of 2mIU/min using syringe pump. This was prepared by adding 5 IU of oxytocin in 500 ml of 5% Glucose. The dose was increased every 15 min by 2mIU/min until regular contractions at a rate of 3-5 per 10 min were reached.

Written informal consent was obtained from all patients and the study was carried according to the research ethical committee of Faculty of Medicine, Zagazig University number of IRB approval 4342/7-2-2018. This study was carried according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans [13].

***Inclusion criteria*:** Women aged from (18-30) years with gestational age (37-41) weeks, singleton pregnancy, cephalic presentation, rupture of membrane at full term and medically indicated for labor induction (hypertension and diabetes).

Exclusion criteria: Contraindication of induction of labor e.g. uterine scar, multiple gestations, intra-uterine growth restriction, antepartum hemorrhage, active herpes infection and allergy to oxytocin or misoprostol.

The following procedures were done to every patient on admission:

Counseling patients about the nature of drug, route of administration, health benefits and side effects were clearly explained to each Patient. Careful and detailed history was taken from the patient who which included. personal history (name, age, special habits, occupation and address). Menstrual history included, first day of last menstrual period. Obstetric history included gravidity, parity, and mode of previous deliveries or abortions. Past history of diabetes mellitus and hypertension were

included. Surgical history included, any previous uterine Scar. Abdominal examination to detect presence of scars of previous operations. Obstetric abdominal examination to detect fundal level, fundal grip, umbilical grip and Pelvic grip. Ultrasound evaluation to detect fetal viability, expected gestational age, presentation of the fetus, expected fetal body weight, amniotic fluid index, placental site and biophysical proalfile. Routine laboratory investigations (CBC, coagulation profile, liver and kidney function tests) were done. Maternal assessment: success of VD or emergency CS, duration (hours) to active phase and duration (hours) from induction of labor to delivery. Neonatal assessment immediately after delivery: APGAR score in the 1st minute, APGAR score in the 5th minute, fetal birth weight, head circumference and NICU admission. Maternal complications as cervical or vaginal tear, post-partum hemorrhage, and blood transfusion.

Statistical analysis:

Data were collected, tabulated and analyzed by SPSS 20, software for PC. P <0.05 was considered as the significance level.

RESULTS

Table (1), showed that there was no significant statistical difference between both groups regarding to maternal age, gestational age, Bishop score, BMI. Table (2), showed that there was no significant statistical difference in the parity of participating women in both groups. Table (3), showed that there was no significant statistical difference between both groups with respect to indications for induction of labor. The most common indications for induction of labor were post term pregnancy about (45.45% and 47.27%) in misoprostol group and oxytocin group respectively, also term pre-labor rupture of membranes (36.36% and 38.18%) in misoprostol group and oxytocin group respectively, also gestational hypertension (14.54% and 10.9%) in misoprostol group and oxytocin group respectively and gestational diabetes (3.63%) in both misoprostol group and oxytocin group. Table (4), showed that both values of mean time from induction to active phase and induction to delivery were significantly shorter in misoprostol group than in oxytocin group (10.4 and 13.2 versus 12.9 and15.8) hours respectively, both p-values were <0.05 which is statically significant. Table (5), showed that in misoprostol group successful vaginal delivery was at a higher rate than oxytocin group and cesarean section was lower than oxytocin group but this difference was not statically significant. Table (6), showed that no significant statistical difference was found between the 2 groups in terms of maternal side effect. The common maternal side effect was shivering its incidence in both group (16.36%) also nausea (14.54%) in misoprostol group and oxytocin group (10.9%) respectively. Postpartum hemorrhage was more than in oxytocin group but without significant difference. Table (7), showed that on analyzing the neonatal outcomes in this study, misoprostol group was associated with lower incidence of Apgar score less than 7 at 5 minute but without significant differences. NICU admission found less in misoprostol group comparable to oxytocin group but without significant differences

Table (1): Demographic characteristics of the studied groups.

Variables	Misoprostol group	Oxytocin group	P
Age **(year)** **Mean ±SD**	24.17± 4.2	24.31± 4.9	0.87
Gestational age **(weeks)** **Mean ±SD**	40±1.2	40±1.3	0.30
Bishop score **Mean ±SD**	3.62±1.7	3.56±1.5	0.84
BMI **(kg/m2)** **Mean ±SD**	21.55 ±1.6	21.41±1.65	0.3

Table (2): Parity of women.

Variables	Misoprostol group	Oxytocin group	P
Nullipara **N (%)**	34(61.8%)	35 (63.63%)	0.84
Multipara **N (%)**	21 (38.18%)	20 (36.3%)	0.84

Table (3): Indication for induction of labor.

Variables	Misoprostol group	Oxytocin group	P
Post term **N (%)**	25(45.45%)	26(47.27%)	0.9
ROM **N (%)**	20(36.36%)	21(38.18%)	0.8
Gestational hypertension **N (%)**	8(14.54%)	6(10.9%)	0.6
Gestational diabetes **N (%)**	2(3.63%)	2(3.63%)	0.6

Table (4): Induction time.

Variables	Misoprostol group	Oxytocin group	P
Induction to onset of active phase(hours) **Mean ±SD**	10.4±6.1	12.9±5.4	0.025
Induction to vaginal delivery (hours) **Mean ±SD**	13.2±6.5	15.8±5.9	0.03

Table (5): Mode of delivery.

Variables	Misoprostol group	Oxytocin group	P
Vaginal delivery **N (%)**	49(89.09%)	46(83.63%)	0.82
Cesarean section **N (%)**	6(10.90%)	9(16.36%)	0.82

Table (6): Maternal side effects.

Variables	Misoprostol group	Oxytocin group	P
Shivering **N (%)**	9(16.36%)	9(16.36%)	0.066
Nausea **N (%)**	8(14.54%)	6(10.9%)	0.567
Vomiting **N (%)**	7(12.72%)	2(3.63%)	0.081
Post-partum hemorrhage **N (%)**	3(5.45%)	8(14.54%)	0.112
Blood transfusion **N (%)**	2(3.63%)	4(7.27%)	0.401

Table (7): Neonatal outcome.

Variables	Misoprostol group	Oxytocin group	P
Apgar score 1st/min<7 **N (%)**	4(7.27%)	3(5.45%)	0.71
Apgar score 5th/min<7 N (%)	2(3.6%3)	4(7.27%)	0.42
NICU **N (%)**	1(1.81%)	5(9.09%)	0.11
Birth weight **Mean ±SD**	3120±220	3100±350	0.72

DISCUSSION

The present study was designed as "randomized clinical trial "was conducted at Zagazig University Maternity Hospital, to estimate the efficacy and safety profile of titrated oral misoprostol solution versus intravenous oxytocin for labor induction. The results of this work showed no statistical differences between two studied groups regarding to maternal age, gestational age and parity. In these study the most common indication for induction of labor was post term pregnancy about 45.45% in misoprostol group and 47.27% in oxytocin group also, Term pre-labor rupture of membranes was 36.36% in misoprostol group and 38.18% in oxytocin group, gestational hypertension was 8% in misoprostol group and 6% in oxytocin group and gestational diabetes was 3.63% in both misoprostol and oxytocin group. There were no statistically significant differences between both the groups with respect to indications for induction of labor.

Our study showed that, duration from induction to onset of active phase of labor (hours) was found10.4±6.1in misoprostol group was shorter than oxytocin group 12.9±5.4, also induction to delivery time was shorter in misoprostol group than oxytocin group13.2±6.5 and 15.8±5.9 respectively which is was statically significant.

These results were in agreement.

with study of Antil et al. [14] who designed prospective randomized study for induction of labor.54 women received titrated oral misoprostol and 52 women received intravenous oxytocin. Induction to delivery was shorter in misoprostol group than in oxytocin group but in induction to active phase was the same in both groups however; the difference was not statistically significant.

In addition, Asokan et al. [15] a comparative study of titrated oral misoprostol solution and oxytocin to induce labor in 280 women all were term pregnancies. Induction to delivery time and induction to active labor was shorter in misoprostol group 10.1±6.1 and 13.2±7.7 respectively and 12.9±5.4 and 15.6±5.1 in oxytocin group.

Also Umbreen Idrees et al. [16] a randomized control trial of 760 term pregnant women, mean time from induction to delivery were shorter in misoprostol group than oxytocin group. And Yenuberi et al. [17] a randomized clinical trial. 83 pregnant women with pre-labor rupture of membranes. The mean time from induction to vaginal delivery in the misoprostol group was 8.4 hours as compared to 9.45 hours in the oxytocin group. The induction to active labor interval was similar in the two study groups.

On the other hand Aalami-Harandi et al. [18] a randomized clinical trial of 285 term pregnant women. The mean time intervals from induction to active phase and to labor were both significantly shorter in oxytocin group than the misoprostol group (10.1 and 13.2 versus 12.9 and 15.6 hours) respectively. In J.W. Kiley et al. [19] a retrospective study for different ways for induction. Induction methods included misoprostol, oxytocin, amniotomy and trans cervical Foley catheter. Overall, 88% of patient's delivered within 24 hours; the median time to fetal delivery was 11 hours 20 minutes. The shortest median interval was found in the oxytocin and amniotomy group.

In our study, it was found that misoprostol use was associated with an insignificantly higher incidence of vomiting, nausea side effects as compared to oxytocin. Also higher rate of post-partum hemorrhage 14.54% in oxytocin group comparable to 5.45 % in misoprostol group and blood transfusion 7.27% in oxytocin group and 3.63% in misoprostol group but without significant difference.

These result matched with Asokan et al. [15] which found that decreased rate of post-partum hemorrhage in misoprostol group compared to oxytocin group (7.1% and 12.1%) respectively a higher rate of GIT symptoms in misoprostol group than oxytocin group (9.3% and 3.6%) respectively. Incidence of Apgar score at 5th/min <7 equal in both groups 1%.

Also in Antil et al. [14] Tachysystole in misoprostol group 1.85% and in oxytocin group 3.85 % and GIT symptoms more in misoprostol group but without significance differences. Aalami-Harandi et al. [18] gastrointestinal symptoms were observed more frequently in the misoprostol than in the oxytocin group (10.9% versus 3.9%) and post-partum hemorrhage where (8.5% and 11.7%). 1-minute and 5-minute Apgar scores and birth weight were similar between the two groups.

CONCLUSIONS

Induction time to vaginal delivery is shorter in misoprostol when compared with oxytocin. So, uses of titrated oral misoprostol solution may be an alternative to intravenous oxytocin infusion for induction of labor, with efficacy and safety profile.

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How to cite
Mustafa, M., harira, M., abdo, A., Yousef, M. Induction of Labor with Titrated Oral Misoprostol Solution versus Oxytocin in Term Pregnancy. Zagazig University Medical Journal, 2023; (307-312): -. doi: 10.21608/zumj.2020.48464.1997