Titrated Oral Misoprostol Solution Compared with Intravenous Oxytocin Infusion for Labour Augmentation

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ABSTRACT

BACKGROUND

The ability to induce and augment labour has been of keen interest to many societies from the time immemorial till date. For majority of the women, the process of labour starts spontaneously at or near term and would result in vaginal "delivery."¹ Augmentation refers to the stimulation of spontaneous contractions that are considered inadequate because of failed cervical dilatation and foetal descent⁵. The purpose should be to relieve the parturient from the prolonged painful and exhausting delivery process into a short time frame. We wanted to compare the efficacy of titrated oral misoprostol solution with that of IV oxytocin infusion for augmentation of labour and determine the indications for failure of the augmentation process.

METHODS

The present study is a randomized control trial. 200 patients requiring labour augmentation were divided randomly into two groups by the method of colour code cards that were picked by the patients themselves from November 2011 to October 2013. Titrated oral misoprostol (TOM) solution 20 ml (1 µg / ml, 20 µg total) given for one group every hourly until the contractions were adequate. If adequate contractions were not achieved even after 4 doses, then, the dose was increased to 40 µg till adequate contractions were achieved. Another group received Oxytocin IV infusion with the maximum dosing rate of 20 mill units / min.

RESULTS

200 women were enrolled in the study, of whom 100 were given titrated oral misoprostol solution, and 100 were given intravenous oxytocin for labour augmentation. The main outcome of augmentation to delivery interval time was 4 hours in TOM and 4.2 hours in oxytocin group. 88 % and 85 % achieved vaginal delivery within 12 hours in TOM and IV oxytocin group respectively. 8 % and 4 % in the TOM and IV oxytocin group underwent lower segment caesarean section (LSCS) in view of failure to progress, whereas 2 % and 8 % in TOM and oxytocin group had LSCS in view of foetal distress. APGAR score was normal in both the groups.

CONCLUSIONS

Titrated oral misoprostol solution is as efficacious as IV Oxytocin infusion for labour augmentation. It is safe, inexpensive and easy to use. Augmentation-to-delivery interval is very much reduced with the use of titrated oral misoprostol solution and the incidence of Caesarean section is comparable to that of IV oxytocin group.

KEY WORDS

Tom, Oxytocin, Augmentation, Labour

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BACKGROUND

The ability to induce and augment labour has been of interest to many societies from time immemorial till date. For majority of the women labour starts spontaneously at or near term and result in vaginal "delivery."¹ Nothing has fascinated man more than the process of reproduction and birth, and in the last 300 years, progress has made man gain some knowledge about the intricate processes of labour. And it was then that he thought of ways and means to modify them for the betterment of the maternal and foetal outcome. Most of the times though the parturient sets into labour spontaneously, the contractions which she would be having may be inadequate for further progress of labour. Hence in majority of these cases the external aid of labour augmentation would be required in order to hasten the delivery process. Augmentation refers to stimulation of spontaneous contractions that are considered inadequate because of failed cervical dilatation and foetal "descent."² The aim of augmentation of labour is to shorten the process of delivery and resulting in a healthy mother and a healthy baby. Among the pharmacological agents used for augmenting labour, Oxytocin IV infusion is the most established one. In 1943, Page suggested that pituitary extract oxytocin be given in the form of IV infusion. Synthetic oxytocin has been in use since 1955.

Since in the early 1970's prostaglandins were used for cervical ripening and also for the labour induction successfully. The mode of administration that have studied include intravenous, intramuscular, oral, vaginal and "intracervical."³ As an upcoming modality of augmentation of labour Misoprostol has been tried in a titrated oral solution form in some countries. The advantages recorded are low cost, easy availability, stability at room temperature, patient remains ambulatory till she enters second stage of labour, shortened duration of labour and many more.⁴ There are few clinical studies on the use of titrated oral misoprostol solution in augmentation of "labour."⁵ Misoprostol is a synthetic PGE₁, which was initially used for peptic ulcer disease caused by NSAIDs.⁶ As oxytocin only affects the uterine contractions, prostaglandins are considered to be the first choice for labour induction as they help in cervical ripening by acting locally.^{7,8} In view of the above this comparative study is undertaken to evaluate the efficacy of the titrated oral misoprostol solution and oxytocin for acceleration of the labour process.

Objectives

- To compare efficacy of titrated oral misoprostol solution versus IV oxytocin infusion for augmentation of labour.
- To determine the indications for failure of the augmentation process and resulting in LSCS, Neonatal intensive care unit (NICU) admissions, neonatal and maternal morbidity and mortality.

METHODS

The present study was a randomized control trial which was undertaken from November 2011 to November 2013 at, Chigateri General Hospital, Women and Child Hospital and Bapuji hospital in Davangere. 100 cases of Titrated oral misoprostol solution and 100 cases of Intravenous Oxytocin

infusion were compared for labour augmentation. The study population were randomly divided into two groups.

After institutional ethical committee approval and with the consent of the patient, 200 pregnant ladies between 18 -35 years of age getting admitted in labour units with the onset of spontaneous labour pains in active labour were selected. A detailed history, complete general physical examination, per abdominal examination, per vaginal examinations and routine investigations were done.

The study population were randomly divided into two groups with 100 patients in each group.

- Study group A (titrated oral misoprostol solution)
- Study group B (intravenous oxytocin infusion)

Inclusion Criteria

All pregnancies between 36 - 40 weeks of gestation, in a cephalic presentation with a live singleton foetus, Spontaneous onset of active labour with inadequate contractions, per vaginal changes: multi - 50 % effaced, 3 cms dilated and primigravida - 80 % effaced, 3 cms dilated, No history of uterine surgeries, foetal heart rate must be reassuring.

Exclusion Criteria

Non-reassuring foetal heart rate pattern, parity greater than 5, Any contraindication to vaginal delivery or labour or both, Epidural analgesia, any significant cardiac, renal or hepatic disease associated with mother, hypersensitivity to misoprostol or prostaglandin analogues.

On admission to labour units the patients who fulfilled the above-mentioned criteria were subjected to a per vaginal examination and their respective Bishops' score was calculated. Then the randomization of patients to the two study groups was done.

The randomization was done by asking the patient to pick closed envelopes which had the two treatment protocols in them. Hence the bias for selection of the preferred method by the personnel was removed.

Intravenous oxytocin infusion was started at 8 drops per minute in the titrated oxytocin group and oxytocin was titrated till required contractions were achieved. Misoprostol is available as a water-soluble oral tablet. Oral titrated Misoprostol solution was prepared by dissolving 200 microgram of tablet Misoprostol in 200 mL of drinking water with a stirrer in a 250 mL graduated beaker. One basal unit of 20 ml of misoprostol solution was given to the women, which was prepared as explained above (1 microgram / mL, 20 micrograms total).

The 1-hour interval between oral misoprostol administrations was determined based on the mathematical model of the time to peak serum concentration (T max 34 minutes) and half-life (t ½, 20 - 40 minutes) of oral misoprostol after absorption, which virtually maintained a steady serum level of misoprostol acid without large fluctuations and can increase by 1.33 times the peak serum concentration (C max) of 20 micrograms of absorptive misoprostol after 4 hours.

Statistical Analysis

Statistical analysis for social services (version 20) and independent t-test and Mann Whitney U test to compare variables.

RESULTS

The study conducted evaluates the efficacy of titrated oral misoprostol solution versus intravenous oxytocin infusion for the purpose of augmentation of labour. Cases were chosen based on patients picking up a closed envelope which had the planned protocol. Out of a total of 2500 deliveries conducted during the one year, 200 cases were included in the study.

	TOM		Oxytocin	
Age group	Primi 62	Gravida 2	Primi 60	Gravida 2
a) 21 - 30 years	3	31	4	30
b) > 30 years		4		6
Gestational age				
A) primi	39.5 weeks		39 weeks	
B) multi's	39 weeks		38.5 weeks	
Height weight	161 cms (AVG)		160 cms (AVG)	
	58 kg (AVG)		60 kg (AVG)	
Bishop score	7		7	

Table 1. Gravidity

This table shows that there were no significant changes pertaining to the age group and the number of primigravidas and multigravidas were equal in number in each group. 64 % of the pregnant ladies were primigravidas in the age group of 21 - 30 years. The table also depicts that 35 % of the pregnant ladies included in the study group of IV Oxytocin were Gravida 2.

In the author's study conducted at China Medical University Hospital, Beigang, Taiwan, 231 women who were approximately 30 years of age, who gave consent for the study, were randomized into two study groups; 118 (51.1 %) to titrated oral misoprostol solution group and 113 (48.9 %) to titrated intravenous oxytocin. Hence, it also shows the distribution pattern of the gestational age included in the study.

Among the primigravidas majority that is 92 % were belonging to 39.4 - 39.6 weeks of gestation and 10 % were in the 38.6 - 39.1 weeks of gestation in the titrated oral misoprostol solution group. 94 % of the primigravidas were belonging to 38.6 - 39.1 weeks of gestation and 8 % were in the 38.4-38.6 weeks of gestation in the oxytocin group. The gestational age included were similar in both the groups. In this study the height and weight of the patients included in both the groups were identical. 88 % of the pregnant ladies included were in the range of 158 - 164 cms and 12 % were in the range of 164 - 166 cms. The average height included in the titrated oral misoprostol group and oxytocin group were 161 cms and 160 cms respectively. The average weight of the pregnant ladies included in the TOM and oxytocin group were 58 kg and 60 kg respectively which were similar and statistically insignificant.

In the author's study the average height of the pregnant ladies included in the study was 160 cms in both the groups and the average weight was 67 kg in the TOM group and 68 kg in the oxytocin group. The present study and the author's study both concluded with a Bishop's score of 7 in both the groups of pregnant ladies included.

API and ADI	TOM	Oxytocin
Active phase interval in hours	2.15 hours	2.15 hours
ADI	4 hours	4.2 hours

Table 2. Active Phase Interval and Augmentation Delivery Interval

The median interval from the beginning of augmentation to vaginal delivery in the titrated oral misoprostol group was 4 hours (3 - 5 hours) and 4 hours 20 minutes (3 hrs. - 5 hrs. 40 min) in the titrated intravenous oxytocin group.

According to the author's study, the augmentation to delivery interval in the titrated oral misoprostol group was 5.22 hours and 5.20 hours in the titrated intravenous oxytocin group.

In a study conducted by Jun Zhang et al. concluded that the high-dose regime of oxytocin of 4 milliunits reduced the acceptable daily intake (ADI) from 1.1 hours to 0.7 hours in a multigravida group and from 1.3 hours to 0.8 hours in a primigravida group.

Vaginal Deliveries	TOM	Oxytocin
Within 12 hours	88 %	85 %
Within 24 hours	90 %	88 %

Table 3. Vaginal Deliveries

Graph 1. Uterine Contractions

In the author's study, 7 women (5.9 %) in the titrated oral misoprostol group and 17 women (15 %) in the titrated intravenous oxytocin group had tachysystole. Out of these 24 women, one woman (0.8 %) in the titrated oral misoprostol group and two women (1.8 %) in the titrated intravenous oxytocin group had uterine hyperstimulation. All the 24 women delivered vaginally. One woman in the titrated oral misoprostol group had uterine hyperstimulation and she underwent Emergency LSCS for non-reassuring foetal heart rate (FHR).

Graph 2. Mode of Delivery

In the author's study, 106 (89.8 %) women out of 118 women in the titrated oral misoprostol solution delivered vaginally and 12 (10.2 %) underwent caesarean delivery. 10 women (8.5 %) underwent emergency LSCS for failure to progress. Among the 113 women in the titrated intravenous oxytocin group, 100 (88.5 %) women delivered vaginally, and 13 women (11.5 %) underwent caesarean section. 12 women (10.6 %) underwent LSCS in view of failure to progress and 1 for non-reassuring foetal heart rate.

Nausea, vomiting, diarrhoea, pyrexia, and shivering are the common side effects of misoprostol. In the conducted study, four women in the titrated oral misoprostol solution group had nausea, vomiting, shivering and pyrexia; these adverse effects were not recorded amongst the women in the intravenous oxytocin group. Similar observations were done in the author's study.

There were no differences in neonatal outcomes, in the conducted study except for one new-born with an Apgar score less than 7 at 1 minute after birth in the titrated oral misoprostol solution group. 92 % of the patients delivered babies in the range of 2.8 - 3.4 (3.1) kg and 8 % in the range of 2.4 - 2.8 kg (2.6 kg) in the titrated oral misoprostol group. In the titrated intravenous oxytocin group, 93 % of the delivered babies were in the range of 2.8 - 3.4 kg and 7 % in the range of 2.4 - 2.8 kg. No babies were admitted to neonatal intensive care unit (NICU).

DISCUSSION

More than 15 % of all the gravid women require aid for cervical ripening hence there is need for an effective and safe method for assistance.⁹ Titrated oral misoprostol solution is a new approach for cervical ripening and to decrease hyper stimulation.¹⁰ In comparison with misoprostol, TOM has lesser chances for foetal distress. An associated negative birth experience and foetal distress due to prolonged labour can result in emergency caesarean delivery, which is more common in nulliparous women.^{8,11}

Misoprostol given orally is effective in achieving vaginal delivery,¹² and lesser rate of foetal distress. Although oxytocin is used frequently for augmentation of uterine contractions to prevent slow or prolonged labour, it is not very effective in cervical ripening.^{7,13} Prostaglandins on the other hand cause cervical effacement and dilatation and stimulate myometrial contractions, hence these are another choice for labour induction and augmentation.^{14,15}

Disadvantage is that prostaglandins taken orally have side effects like vomiting and nausea which are not usually seen with oxytocin.¹⁶ However, oxytocin is a mainstay of treatment for both induction and augmentation of labour.^{17,18} The rates of foetal distress is higher in oxytocin when not titrated and monitored timely.¹⁹ In the percentage of women who delivered their new-borns vaginally within 12 or 24 hours of augmentation and in the rate of failure to progress there were no significant differences recorded between both the groups.

In conclusion, titrated oral misoprostol solution given for augmentation of labour process was found to be equally efficacious as titrated intravenous oxytocin and can be used as an alternative to the routine oxytocin. Misoprostol is stable at room temperature, has longer shelf life, easy to administrate

and patient can remain ambulant,^{4,15,20} these are the added advantages of the misoprostol in comparison to oxytocin.

CONCLUSIONS

This study was conducted to compare the efficacy of intravenous oxytocin infusion versus titrated oral misoprostol solution for augmentation of labour when there are inadequate uterine contractions. Two groups that delivered vaginally within 12 or 24 hours had no significant differences. The neonatal outcomes and the adverse effects associated also did not show much difference between the two groups.

Misoprostol has been proven to be an effective agent for cervical ripening and labour induction through multiple studies. A study on oral titrated misoprostol solution also been conducted. An intravenous infusion of oxytocin must be controlled by using an intravenous pump machine, but it may be difficult or inconvenient in few settings.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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