Augmentation of Labour - A Comparison of Oral Misoprostol and Intravenous Titrated Oxytocin Infusion

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Abstract

Background: To compare oral misoprostol with intravenous oxytocin for labour augmentation in nulliparous women.

Methods: Women (n=500) with regular contractions and an effaced cervix dilated between 3 and 9 cm, and who had inadequate uterine contractions (two or fewer contractions every 10 minutes) during the first stage of labour, were augmented with 75 μg oral misoprostol (single dose) or intravenous oxytocin. The primary parameters used to evaluate efficacy of misoprostol were the interval from the beginning of augmentation to vaginal delivery and the percentage of women who delivered their newborns vaginally within 6 to 12 hours of this interval. The primary parameters used to evaluate adverse events were incidence of tachysystole, hypertonus and uterine hyperstimulation. The secondary parameters used to evaluate efficacy or adverse events were rates of cesarean births, failure to progress and fetal distress. The neonatal outcomes included low Apgar score (less than 7 at 5 minutes after birth) and admission to the neonatal intensive care unit (NICU). Statistical significance was given to p< 0.05.

Results: Of the 500 women, 250 were augmented with 75 μg oral misoprostol and 250 with titrated intravenous oxytocin. The mean interval from the beginning of augmentation to vaginal delivery was 6.53 hours in the misoprostol group, and 6.01 hours in the intravenous oxytocin group. Complete vaginal delivery occurred within 6 hours in 102 women (48.11%) in the misoprostol group and in 93 women (46.03%) in the oxytocin group (p value 0.647). There was no significant difference between the two groups who delivered vaginally within 12 hours. Side effects and neonatal outcomes also did not differ significantly between the two groups.

Conclusion: Oral misoprostol may be an acceptable alternative to the traditional oxytocin for augmentation of labour.

Key Words: Neonatal Outcome, Caesarean Section

Introduction

Prolonged labor is a common problem, especially among nulliparous women. Caesarean birth rates are greater than 20% in many developed countries. The main diagnosis contributing to the high rate in nulliparous women is dystocia or prolonged labor. It can result in a negative birth experience for the mother and can be associated with fetal distress resulting in emergency caesarean delivery.

The traditional standard way of augmentation of labour is intravenous oxytocin infusion which has to be titrated according to the severity and intensity of uterine contractions. Oxytocin is given by intravenous infusion and drip rate is calculated as number of drops per minute to adjust the dose in mIU / ml. It has to be regulated by I/V regulator and continuous monitoring is required. Inadvertent high dosage can result in uterine hyperstimulation, hypertonus, tachysystole and fetal distress while under dosage can result in prolonged labour and delayed delivery.

In view of increased patient's influx and lack of one to one care, regulation of intravenous infusion may be difficult. It can fluctuate due to movement of patient's hands or change of posture. Intravenous infusion may be associated with allergic reactions. I/V cannulation is also a painful procedure specially in women having thin veins. Oral misoprostol is a good alternative for labour augmentation especially in developing or low resource countries where infusion pumps are not available. It does not require continuous monitoring and I/V regulation.

Misoprostol, is a synthetic prostaglandin E1 analogue. It was initially used to treat peptic ulcers caused by prostaglandin synthetase inhibitors. In April 2002, the U.S. Food and Drug Administration revised the original labeling of misoprostol and approved it for use in pregnancy. Misoprostol is used off-label for a variety of indications in the practice of obstetrics and gynecology, including medication abortion, medical management of miscarriage, induction of labor, cervical ripening before surgical procedures, and the
treatment of postpartum hemorrhage. Misoprostol’s effects are dose dependent and include cervical softening and dilation, uterine contractions, nausea, vomiting, diarrhea, fever, and chills. Misoprostol’s advantages over other synthetic prostaglandin analogues are its low cost, long shelf life, lack of need for refrigeration, and worldwide availability. Being a potent uterotropic and uterotonic agent, Misoprostol is a good alternative for labor augmentation. Based on misoprostol pharmacokinetics and clinical trial findings, including lower incidence of uterine hyperstimulation and a shorter active phase interval, oral misoprostol for labor induction can be given with consideration for individual differences and responses to its administration.

Patients and Methods
This study was carried out from January 2012 – December 2012, in DHQ Teaching Hospital, Rawalpindi. Inclusion criteria were primigravidae, pregnancy between 37 and 42 weeks of gestation (n=500), a live singleton fetus in cephalic presentation, no history of uterine surgery, spontaneous onset of active labor with regular contractions, an effaced cervix dilated between 3 cm and 9 cm after rupture of membranes, clear liquor and a reassuring fetal heart rate (FHR) pattern. Exclusion criteria were non-reassuring FHR pattern, multiparity, any contraindication to labor or vaginal delivery or both, significant maternal cardiac, renal, pulmonary or hepatic disease and hypersensitivity to misoprostol or prostaglandin analogues.

They were then divided into two groups .Group A (n=250) was augmented with single dose of 75 micro gram oral misoprostol, while Group B (n=250) was given titrated intravenous oxytocin infusion for augmentation of labour after artificial rupture of membranes. In the titrated oxytocin group, oxytocin was given via intravenous route by infusion initially set to deliver 5 milliunit / min for 30 minutes, and then the dose increased by 5 milliunit / min every 30 minutes by adjusting the number of drops in drip chamber until adequate uterine contractions were attained.

Adequate uterine contractions were defined as three moderate contractions (30 - 45 seconds ) in 10 minutes. Tachysystole was defined as the presence of at least six contractions in 10 minutes for at least two 10- minute windows. Hypertonus was defined as a single contraction lasting more than 2 minutes. Hyperstimulation was defined as tachysystole or hypertonus with non-reassuring FHR changes. FHR changes considered to be non-reassuring were late deceleration, severe variable deceleration, prolonged deceleration, tachycardia, or reduced FHR variability requiring intervention with either tocolytics or delivery.

The time of beginning of augmentation was noted down on partogram and the augmentation - delivery interval was calculated after delivery. The severity of uterine contractions was assessed by noting the duration of contractions by palpating maternal abdomen. The indications of cesarean section was also noted down. When tachysystole occurred, oxytocin was halted, and oxygen & hydration with lactated ringer's solution were given in both groups. Women who did not develop adequate uterine contractions with single dose of oral misoprostol were augmented with intravenous oxytocin and were considered as failure of misoprostol. After delivery the APGAR score of the neonate was noted at 5 minutes in both groups. The number of neonates requiring NICU admission was noted in both groups.

The primary parameters used to evaluate efficacy of misoprostol were the interval from the beginning of augmentation to vaginal delivery and the percentage of women who delivered their newborns vaginally within 6 to 12 hours of this interval. The primary parameters used to evaluate adverse events were incidence of tachysystole, hypertonus and uterine hyperstimulation. The secondary parameters used to evaluate efficacy or adverse events were rates of cesarean births, failure to progress and fetal distress. The neonatal outcomes included lower Apgar score (less than 7 at 5 minutes after birth) and admission to the neonatal intensive care unit (NICU).

Results
The mean interval from the beginning of augmentation to vaginal delivery was 6.53 hours in Group ‘A’, and 6.01 hours, in Group ‘B’. The failure rate of oral misoprostol was 11.0% (Table 1) i.e. 30 patients who were given oral misoprostol did not develop adequate uterine contractions and required augmentation with IV oxytocin (Table 1). Of the women who completed vaginal delivery within 6 hours, 48.11% were in Group ‘A’ and 46.03% were in Group ‘B’ (p-value 0.647). There was also no significant difference between two groups who delivered vaginally within 12 hours (p-value 0.418). There was no significant difference in development of tachysystole, hypertonus or hyperstimulation between the two groups (Table 2). The fetal heart beat pattern
returned to normal within 5 minutes in six of these women so they had vaginal deliveries while four women who developed hyperstimulation underwent emergency caesarean delivery for non-reassuring FHR. Two Hundred and Twelve patients (84.80%) in Group ‘A’ had vaginal deliveries compared with 202 patients (80.80%) in Group ‘B’ (p-value 0.097). While 38 patients (15.20%) underwent caesarean section in Group ‘A’ as compared to 48 patients (19.20%) in Group ‘B’ (p-value 0.097). The indications for caesarean delivery were failure of labor to progress and fetal distress (Table: 3).

There was no significant difference in neonatal outcomes between two groups. Seven newborns (2.80%) in Group ‘A’ had APGAR score <7 at 5 minutes after delivery as compared to 10 neonates (2.80%) in Group ‘A’ had vaginal deliveries compared with 202 patients (80.80%) in Group ‘B’ (p-value 0.460). In oral misoprostol group, 25 babies (10.0%) were admitted in NICU as compared to 32 babies (12.80%) in intravenous oxytocin group (p-value 0.326) (Table 4).

The common side effects of misoprostol included vomiting, diarrohea, pyrexia, and shivering. (Table 5) Six women in both groups went into postpartum haemorrhage but it was managed with medical measures except for one patient in Group ‘A’ who required uterine and internal iliac arteries ligation.

### Table 4: Neonatal Outcome

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Group A No(%)</th>
<th>Group B No(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 minutes APGAR Score &lt;7</td>
<td>7(2.80)</td>
<td>10(4.00)</td>
<td>0.460</td>
</tr>
<tr>
<td>Neonatal ICU admission</td>
<td>25(10.00)</td>
<td>32(12.60)</td>
<td>0.328</td>
</tr>
</tbody>
</table>

p-value < 0.05 Significant; p-value > 0.05 Not Significant

### Table 5: Maternal outcome (n=250 in each group)

<table>
<thead>
<tr>
<th></th>
<th>Group A No(%)</th>
<th>Group B No(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>3(1.20)</td>
<td>(-)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Shivering</td>
<td>5(2.00)</td>
<td>2(0.80)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>3(1.20)</td>
<td>(-)</td>
</tr>
<tr>
<td>Postpartum haemorrhage</td>
<td>6(2.40)</td>
<td>6(2.40)</td>
</tr>
</tbody>
</table>

### Discussion

Caesarean birth rates are greater than 20% in many developed countries.¹ A policy of early amniotomy with oxytocin administration for the prevention of delay in labor progress is associated with a modest reduction in the rate of cesarean births.⁸ There is no significant difference in cesarean delivery rate, neonatal outcome, and maternal outcome between the low and high doses of oxytocin on labor augmentation except for labor augmentation interval.¹¹ Oxytocin administration through the intravenous route needs to be under the control of an intravenous pump machine and may be inconvenient for patients. But oral misoprostol is easier to administer than titrated intravenous oxytocin. Misoprostol offers several advantages over oxytocin such as longer shelf life, stability at room temperature, and easy administration. It avoids intravenous infusion and continuous monitoring. It also relieves patient’s anxiety and allows easily mobility. It is an acceptable alternative to traditional oxytocin for labour augmentation.

According to the pharmacokinetics, the onset time and administration route of oxytocin is better than that of misoprostol. In this study, it was expected that the titrated intravenous oxytocin would be more effective than oral misoprostol in terms of the interval of augmentation to vaginal delivery. However, the difference of these intervals is not significant in actual
clinical practice. Vaginal delivery within 6 to 12 hours is the more important clinical factor. Present study found no significant difference between the two groups in the percentages of women who delivered their newborns vaginally within 6 to 12 hours of augmentation. Therefore, labor augmentation with oral misoprostol is an effective alternative method. An oral dose of 75 μg of misoprostol given at a 4-hour interval for a maximum of 2 doses is the highest tolerated dose.12

Women in the misoprostol group are more likely to experience uterine tachysystole and hypertonus compared with those in the oxytocin group. This increase is secondary to uterine hypertonus as the incidence of tachysystole did not differ between two groups. Women in the misoprostol arm were no more likely to experience a non reassuring fetal heart rate or require a caesarean delivery for this indication. There were no significant differences in maternal or neonatal outcomes.13 Orally administered misoprostol compared with titrated intravenous oxytocin for labor induction in women with favorable cervical condition (Bishop score of 6 or more) showed higher likelihood of uterine hyperstimulation with oral misoprostol.14 In our study, the rates of hyperstimulation and tachysystole were lower with oral misoprostol probably because we used single dose of 75 microgram oral misoprostol and our study was limited to nulliparous women. There was also no significant difference between the two groups regarding neonatal outcomes and NICU admission in our study.

**Conclusion**

1. Oral misoprostol is observed to be similar to intravenous oxytocin infusion in labor augmentation and may be an alternative to the traditional oxytocin.

2. Longer shelf life, stability at room temperature, and easy administration of misoprostol offers added advantages over oxytocin.

**References**