ORIGINAL ARTICLE

Comparison of Two Dosage Regimens of Vaginal Misoprostol for Induction of Labour at Term

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ABSTACT

Objective: To compare the efficacy and safety of low and high dosage regimens of vaginal misoprostol for induction of labour at term.
Design: A non-blinded randomized controlled trial.
Setting: Labour room of Gynae unit I, Services Hospital/SIMS, Lahore.
Participants: Two hundred pregnant women at term requiring induction of labour.
Method: The women were randomized to receive 50µg (group A) and 100 µg (group B) of misoprostol vaginally every four hours to a maximum of five doses.
Main outcome measures: Induction to delivery interval, need for oxytocin augmentation, mode of delivery, uterine hyperstimulation, failed induction and neonatal outcome.
Results: The mean induction to delivery interval was significantly shorter in the 100µg group-high dosage (group B) with a mean difference of 7 hours and a p value <0.05. There was a significantly reduced need for oxytocin augmentation in the high dosage group B (4% vs 20%) and the incidence of failed induction was less in the high dosage group but this was not statistically significant. There was a 7% less incidence of caesarean section in the high dosage group with no significant difference in the incidence of uterine hyperstimulation and neonatal outcome between the two groups.
Conclusion: 100 µg of vaginal misoprostol is more effective than 50 µg dose for induction of labour at term because of shorter induction delivery interval and reduced need for oxytocin augmentation withno difference in the caesarean section rate and other safety parameters.
Key words: Misoprostol, vaginal misoprostol, induction of labour, cervical ripening.

INTRODUCTION

Misoprostol, a methylester of PGE1, additionally methylated at C-16 is marketed for prevention and treatment of peptic ulcer disease. However, it is widely used in Obstetrics and Gynecology because of its effectiveness, low cost, stability in light and hot climate conditions and ease of administration as compared to its licensed counterparts—dinoprostone and gemeprost. A large number of studies have shown that misoprostol is effective in first and second trimester abortions, late pregnancy labour induction and third stage of labour management[1-6].

The use of misoprostol was first reported in 1987 for labour induction in case of intrauterine fetal death in the third trimester[7]. Despite multiple misoprostol regimens, the optimal dose and route of administration remains to be determined. The pharmacokinetics of misoprostol suggest that it is more bioavailable when administered vaginally as compared with oral misoprostol. Most studies suggest that vaginal misoprostol results in shorter induction to delivery interval and a decreased need for oxytocin augmentation as compared to oralmisoprostol[6,8,9,10,11,12]. However, there is more frequent occurrence of uterine hyperstimulation and higher intervention rate for fetal distress in the vaginal group[10,11,12,14,15].

A Cochrane review compared the effects of different doses of vaginal misoprostol[16]. Lower doses compared to higher doses were associated with more need for oxytocin augmentation (dose <50 microg), less uterine hyperstimulation, with and without fetal heart rate changes, and a non-significant trend to fewer admissions to neonatal intensive care unit. The lower dosage regimens did not show more failures to achieve delivery within 24 hours. Based on the analysis, the Cochrane reviewers recommend a starting dose of 25 mcg every four hours. A comparison between 25 mcg and 50 mcg intravaginal misoprostol for cervical ripening and labour induction showed the higher dose was associated with a shorter interval to vaginal delivery, greater proportion of deliveries within 24 hours, and less frequent need for oxytocin augmentation, but it is unclear whether it is as safe as the 25 mcg dose[17]. Another similar study showed the same results in relation to time to delivery and need for oxytocin augmentation. In contrast, more women achieved vaginal delivery with 25 microg misoprostol (79.3 vs. 60.7%; $P < 0.05$). The proportions of patients with tachysystoles and

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hypersystoles showed not significant differences between the two groups. The rate of caesarean sections due to non-reassuring foetal status was higher with the higher dose (28.6 vs. 10.3%; P < 0.05). The number of neonates with a low 1-min Apgar score (<7) was significantly higher in the 50mcg misoprostol group (26.8 vs. 8.6%; *P* < 0.05), but 5-min Apgar scores and umbilical artery blood gas values at the time of delivery were not significantly different between groups. One patient in the 25 mcg group suffered uterine rupture[18]. A more recent RCT compared two schedules of intravaginal misoprostol: 100 microg, every 6 hours or 50 microg every 4 hours. In the two groups the number of doses of misoprostol used was similar. There was no difference between the two groups in the time to delivery and cesarean rate. Likewise, there was no significant difference in the rates of 5 min Apgar score and meconium passage[19]. Another RCT compared the effectiveness of 25 microg vs. 50 microg of intravaginal misoprostol for cervical ripening and labor induction beyond 41 weeks' gestation. The dose was repeated every 4 hours (maximum number of doses limited to six) until the patient exhibited three contractions in 10 min. There was no significant difference between the two groups with regard to the induction–vaginal delivery interval (685±201 min in the 25 microg group vs. 627±177 min in the 50 microg group, *P*=0.09). The proportion of women delivering vaginally with one dose of vaginal misoprostol was significantly greater in the 50 microg group (0/49 vs. 41/47, *P*<0.001). There were no differences in the rates of cesarean and operative vaginal delivery rates, or in the incidences of tachysystole and hyperstimulation syndrome in the two treatment groups. Neonatal outcomes were also similar[20].

Our aim in this study was to compare the efficacy and safety of low and high dosage regimens of vaginal misoprostol for induction of labour at term.

METHOD

From January 2008 to June 2008, two hundred pregnant women at term with indications for labour induction in Labour room of Gynae Unit I, Services Hospital/ SIMS, Lahore were evaluated for study participation which was a non- blinded randomized controlled trial.

After taking informed consent for study participation, women were randomly allocated to receive 50µg (group A) and 100µg (group B) of misoprostol vaginally every 4 hours to a maximum of 5 doses. Inclusion criteria were singleton pregnancy, cephalic presentation, G/A ≥37 weeks, reactive fetal heart rate pattern, bishop score of <5 and cervical dilatation <3 cm. Exclusion criteria included parity≥6, EFW >4.5 Kg, IUGR or EFW<2 Kg, previous uterine scar, polyhydramnios and any contra-indication to vaginal delivery.

A NST was performed and uterine activity assessed before administration of each dose. Subsequent dose was withheld in the presence of active labour i.e. regular contractions with cervical dilatation ≥3 cm or bishop score ≥8. In these conditions ARM was done and oxytocin augmentation started if required. Those women who did not go into labour or cervix remained unfavourable for ARM at the end of 5 doses were categorized as failed induction which were then delivered by re-induction with oral misoprostol after a rest period of 24 hours or by caesarean section.

The primary outcome measure was mean induction to delivery interval. A number of secondary outcome measures i.e. need for oxytocin augmentation, mode of delivery, incidence of uterine hyperstimulation and failed induction and neonatal outcome were also compared between the two groups.

The baseline maternal characteristics at the start of induction were also compared. Statistical analysis was done on SPSS version 11. Student t test was applied on quantitative and chi square/ Fisher exact test on qualitative variables. Descriptive statistics were calculated.

RESULTS

Two hundred pregnant women were selected for this trial of which 100 received 50µg of vaginal misoprostol (group A)and 100 received 100µg of vaginal misoprostol (group B). There were no differences in maternal demographic characteristics between the two groups.

Table 1: Maternal Demographic Characteristics.

Characteristics	Group A (n=100)	Group B (n=100)
Age	24 (16-38)	25 (17-40)
Parity	0 (0-5)	0 (0-5)
Gestational age	39 (37-42)	40 (37-42)
Initial Bishop score	3 (0-4)	3 (0-4)

Similarly, there was no difference in the indications for labour induction with postdates being the largest indication in both the groups and second major indication being prelabour rupture of membranes.

Table 2: Indications for Labour Induction.

Indications	Group A	Group B
Postdates	34%	32%
P/V leaking	21%	22%
PIH	19%	28%
Scanty liquor	8%	5%
Others	18%	13%

The mean induction delivery interval was significantly shorter in the 100µg group with a mean difference of almost 7 hours and a p value <0.05.

Table 3: Values are given as mean [SD] or n (%)

	Group A (50µg)	**Group B (100µg)**
Mean induction delivery interval (hrs)	14.4 ± 8.62	7.75 ± 5.17
Needing oxytocin augmentation	20%	4%

The need for oxytocin augmentation was significantly lower in the high dosage group. There was a 7% less incidence of caesarean section in the high dosage group.

Table 4: Mode of delivery

Mode of delivery	**Group A (n=100)**	**Group B (n=100)**
Vaginal delivery	80%	73%
Caesarian section	20%	27%

There was no significant difference in the incidence of uterine hyperstimulation, meconium staining and neonatal outcome between the two groups.

Table 5: Expressed as %

	Group A (n=100)	**Group B (n=100)**
Failed induction	8	4
Uterine hyperstimulation	1	2
Meconium staining	15	17

Table 6: Neonatal outcome expressed as Mean±SD or %

Neonatal outcome	**Group A (n=100)**	**Group B (n=100)**
Birth weight (Kg)	2.98±0.392	3.11±0.433
A/S <7 At 1 min At 5 min	 92% 8%	 98% 11%
Neonatal resuscitation	29%	33%
Shifted to NNU	10%	14%

DISCUSSION

This study showed that high dose (100µg) of oral misoprostol resulted in a significantly shorter induction delivery interval with reduced need for oxytocin augmentation. There was a reduced incidence of failed induction in the high dosage group although it was not significant. These results are consistent with the study conducted by Ramos et al[17], Has et al[18] and Diro et al[21] but the doses of vaginal misoprostol used in these studies were 25 and 50µg. These was no significant difference in the induction delivery interval according to two RCTs[19,20s]

There were less chances of caesarean section and decreased incidence of failed induction in the high dosage group although these results were not statistically significant. Ramos et al [17]and two other RCTs'[19,20] showed similar results with decreased incidence of caesarean section in the high dosage group but Has et al [18]showed higher rate of caesarean section in the high dosage group.

There was no difference in the incidence of uterine hyperstimulation, meconium staining and neonatal outcome between the two groups. These results are also consistent with many RCTs[s]There was a higher incidence of uterine hyperstimulation according to Diro et al[21] not seen in our study. There were more neonates with less apgar score at one minute according to Has et al[18].

Comparison of vaginal misoprostol dosage regarding induction of labour at term has not been extensively evaluated and more studies are required to determine the optimum vaginal misoprostol dose for induction of labour at term.

CONCLUSION

Thus our study concludes that 100µg of vaginal misoprostol may be more promising because of shorter induction delivery interval and less need for oxytocin augmentation and no difference in the safety parameters i.e. caesarean section rate, uterine hyperstimulation, meconium staining and neonatal outcome between the two groups.

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