

Efficacy of Intra Vaginal Misoprostol as Various Doses versus Intra cervical Dinoprostone in Cervical Ripening and Induction of Labor

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Abstract:

Objective: To compare the efficacy of intra vaginal misoprostol as various doses versus intra cervical dinoprostone in cervical ripening and induction of labor. **Study Design:** A Prospective Randomized Controlled Trial. **Place and Duration of Study:** Obstetrics and Gynecology Department of Nishtar Medical University and Hospital, Multan from May 2016 to July 2018. **Methodology:** We divided 168 patients into three groups; Group M1 and M2 were given 25 μ g and 50 μ g misoprostol, respectively; Group D was given 0.5mg dinoprostone. Complete history was followed by complete examination. Outcome variables, age, parity, gestational age, indications for the induction of labor and initial Bishop Score were compared. Data was put in SPSS 23 and analyzed by applying one way ANOVA and Chi-square tests, as appropriate considering $p < 0.05$ statistically significant. **Results:** Induction to vaginal delivery interval was 15.51 \pm 6.18min in Group-M1, 12.14 \pm 4.65min in Group-M2 and 13.43 \pm 6.96min in Group-D ($p=0.008$). The women who need oxytocin supplementation were 30.6%, 17.7% and 41.9% from Group M1, M2 and D, respectively ($p=0.013$). Bishop Score after 6 hours of delivery was 3.45 \pm 1.2, 4.41 \pm 1.5 and 4.21 \pm 1.3 in group M1, M2 and D, respectively, and the difference was highly statistically significant ($p < 0.001$). All other variables were comparable among the groups ($p > 0.05$). **Conclusion:** Higher dose of misoprostol i.e. 50 μ g misoprostol is higher in efficacy than 0.5mg dinoprostone which is in turn better than 25 μ g misoprostol. But 50 μ g misoprostol can cause hyper-stimulation and dinoprostone needs oxytocin augmentation. Misoprostol is a good and cheap agent for the induction of vaginal delivery.

Keywords: misoprostol, dinoprostone, cervical ripening, induction of labor.

Introduction:

Labor induction has very long history dated back to the time of Hippocrates. A pregnancy lasting for more than 41 weeks is considered prolonged pregnancy. The incidence of prolonged and post term pregnancies is thought to be 15-20% and 1% in pregnant women, respectively. Emergency cesarean section rate increases 1.5 time in cases of prolonged pregnancies. Perinatal mortality increases from 0.7% to 5.8% between 37 to 43 weeks of gestation. Meconium aspiration syndrome incidence increases from 0.24% to 1.42% between 38 to 42 weeks of gestation. It is a life threatening condition, especially for the fetus. There is a progressive increase in the risk of neonatal acidosis, admission to neonatal care units and < 7 Apgar score at 5 minutes from 38 to 42 gestational weeks¹. WHO conducted a global survey consisting of 0.3 million deliveries in 373 health care units in 24 different countries and found that there is need for inducing labor in almost 9.6% of the pregnant women².

There are various methods being used for the induction of labor. The use of prostaglandins in the induction of labor was first introduced in 1968. After that, the use of prostaglandins in various form has become common for labor induction. Misoprostol tablets and dinoprostone gel are most commonly used agents for inducing labor. Many studies have been conducted for the comparison of misoprostol and dinoprostone for cervical ripening and labor induction. But it is difficult to interpret the efficacy of any of these agents from the previously conducted studies because both complicated as well as uncomplicated cases have been included in the past studies³. Doses of various drugs can be altered for decreasing the incidence of adverse effects. Alexander JM et al.⁴ showed that increase in the risk of cesarean section was more due to maternal risk factor such as undilated cervix than it was due to the induction of labor.

Dinoprostone is an expensive agent which needs to be stored in refrigerator. Dinoprostone needs to be inserted into the cervix which is rather difficult procedure. Oxytocin injection is required in majority of the cases using dinoprostone for the induction of labor. On the contrary, misoprostol is a cheaper agent and there is no need for refrigeration. Misoprostol is available in tablet forma and can be given via oral, sublingual and vaginal routes. Various doses of misoprostol such as 25 μ g or 50 μ g can be given at various intervals i.e. 6 hourly or 12 hourly. Various studies have been conducted on a wide range of patients for the comparison of various doses of misoprostol and dinoprostone in the past⁴⁻⁸.

Previously many studies have been conducted for comparing the efficiency of 25 μ g and 50 μ g of misoprostol and 0.5 mg of dinoprostone but those studies included wide range of patients and patients with other complications were not excludes. In this study, we are comparing efficacy and outcomes of labor induction with 25 μ g of misoprostol, 50 μ g of misoprostol and 0.5 mg dinoprostone in three equal and comparable groups of

patients with no other significant comorbidity.

Material and methodology:

We performed a prospective randomized controlled trial in the Obstetrics and Gynecology Department of Nishtar Medical University and Hospital, Multan. The time of our study was from May 2016 to July 2018. A proper written approval was taken from the hospital review committee. Study performed by Saxena P et al.¹⁵ was taken as reference study and sample size was calculated by nonprobability consecutive sampling technique. Total 186 women were include in the study who had Bishop Score less than 6. Women who had singleton pregnancy with cephalic presentation and intact membranes, unfavorable cervix, and amniotic fluid index more than 5 were included in our study. The women who had ruptured membranes, severe intrauterine growth restriction (IUGR), multiple pregnancies, cephalo pelvic disproportion, non cephalic presentation, history of uterine perforation, previous uterine scars, prostaglandin allergy, Bishop score more than 6, severe oligoamnios, mild pregnancy induced hypertension and diet controlled gestational diabetes mellitus were excluded from this study.

All the included patients were fully aware about the scope, nature and possible hazards of the procedure and they provided consent for the intervention. One hundred and sixty eight patients were randomly distributed into the groups which consisted of equal number of the patients i.e. 62. Group M1 was to be given 25 µg of misoprostol and Group M2 was to receive 50 µg of misoprostol, intravaginally. On the other hand Group D was to receive 0.5 mg of dinoprostone, intra cervically. The drugs were to be administered after every six hours. Complete gynecological as well as obstetrical history was noted followed by complete general, systemic as well as obstetrical examination. Bishop score of all the patients was recorded. Ultrasonography was the modality of choice for the verification of gestational age and amniotic fluid index (AFI). We also performed non stress tests before the administration of the drug under test. After the insertion of the drug, fetal heart tracings were recorded continuously for about 30 minutes. We monitored uterine contractions along with the descent of fetal head which were the indicators of progress of labor. In high risk patients, we noted fetal heart patterns with external electronic monitor while in others, it was done by intermittent auscultation. Vaginal examination was repeated after every 6 hours and Bishop Score was noted. Drug insertion was repeated in case of Bishop Score ≤6. Maximum three doses were inserted of the test drug. In the patients with more than 3 cm cervical dilatation, membranes were ruptured artificially. If the active labor did not start after 3 doses of the test drug, intravenous oxytocin was injected. Administration of oxytocin was done 6 hours after the last dose of test drug, when needed. We assessed fetal heart rate for tachycardia i.e. fetal heart sound >150 /min, bradycardia i.e. <110, variable deceleration or late deceleration pattern. Uterine activity was also minored for occurrence of hyper stimulation, hyper tonicity and tachysystole. Occurrence of one contraction continued for more than 2 minutes was called hyper tonicity. Minimum of 6 uterine contractions in ten minutes occurring for at least 20 minutes was defined as tachysystole. The association of abnormal fetal heart rate patterns with above findings was diagnosed as hyper stimulation. In case of hyper stimulation, oxytocin was discontinued if it was still being administered, patient was placed in left lateral position, oxygen inhalation along with intravenous Ringer lactate infusion was started and all the residuals of the drugs were removed. Routine intra partum management was done of all the patients when they entered the active phase of labor.

Patients were assessed after every six hours for the development of potential adverse effects. Outcome parameters included induction to vaginal delivery interval, Bishop Score after six hours following delivery, vaginal delivery within 24 hours, vaginal delivery after single dose, oxytocin augmentation, need for cesarean section and hyper stimulation following induction of labor. Outcome variables along with age of the patients, parity, gestational age, indications for the induction of labor and initial Bishop Score were compared among the groups. All the data was collected by the researches on a proper form. The data was put in SPSS 23 and analyzed. Test applied included one way ANOVA and Chi square tests, where appropriate considering $p \leq 0.05$ as statistically significant.

Results

Mean age of the patients was not statistically different in all groups ($p = 0.432$). The ratio of parity was also comparable in the three groups ($p = 0.413$). Gestational age was 38.98 ± 1.88 weeks in group M1, 39.31 ± 1.84 weeks in group M2 and 38.85 ± 2.06 weeks in group D, and the difference was not statistically significant. Indications for induction of labor included gestational age more than 40 weeks, primary Intrapartum hemorrhage, gestational diabetes mellitus, intrauterine growth restriction, Oligoamnios, cholestasis and decreased fetal movements and were comparable in all groups ($p = 0.996$). Initial Bishop score was 2.44 ± 1.2 on group M1, 2.46 ± 1.1 in group M2 and 2.79 ± 1.3 in group D ($p = 0.207$). Table-I

Outcome parameters included induction to vaginal delivery interval, Bishop Score after six hours following delivery, vaginal delivery within 24 hours, vaginal delivery after single dose, oxytocin augmentation, need for cesarean section and hyper stimulation following induction of labor. Induction to vaginal delivery interval was

15.51 ± 6.18 minutes in Group M1, 12.14 ± 4.65 minutes in Group M2 and 13.43 ± 6.96 minutes in Group D (p =0.008). After induction of labor, 83.9% women of Group M1, 91.9% women of group M2 and 87.1% women of Group D delivered within 24 hours (p =0.390). The women who delivered after single dose of drug included 25.8% of group M1, 38.7% of group M2 and 32.3% of group D (p =0.307). The incidence of cesarean section was 27.4% in group M1, 33.9% in group M2 and 41.9% in group D (p =0.234). The women who need oxytocin supplementation were 30.6%, 17.7% and 41.9% from Group M1, M2 and D, respectively (p =0.013). Incidence of hyper stimulation was not significantly different among the groups (p =0.620). Bishop Score after 6 hours of delivery was 3.45 ± 1.2, 4.41 ± 1.5 and 4.21 ± 1.3 in group M1, M2 and D, respectively, and the difference was highly statistically significant (p <0.001). Table-II

Table-I
Baseline Data

Variable	Group M1 (n=62)	Group M2 (n=62)	Group D (n=62)	P value
Age, years	29.58 ± 4.35	28.66 ± 4.05	29.52 ± 4.76	0.432
Parity (1 / 2 / >2)	26 / 23 / 13	27 / 26 / 9	27 / 18 / 17	0.413
Gestational Age, weeks	38.98 ± 1.88	39.31 ± 1.84	38.85 ± 2.06	0.408
Indication for induction of labor, N (%)				
>40 weeks	19 (30.6)	17 (27.4)	18 (29.0)	0.996
PIH	10 (16.1)	9 (14.5)	8 (12.9)	
Gestational DM	8 (12.9)	6 (9.7)	8 (12.9)	
Cholestasis	6 (9.7)	7 (11.3)	8 (12.9)	
IUGR	6 (9.7)	7 (11.3)	9 (14.5)	
Oligoamnios	5 (8.1)	8 (12.9)	5 (8.1)	
Decreased fetal movements	8 (12.9)	8 (12.9)	6 (9.7)	
Initial Bishop Score	2.44 ± 1.2	2.46 ± 1.1	2.79 ± 1.3	0.207

Data is put as mean ± S.D unless stated otherwise.

Table-II
Outcome parameters

Variable	Group M1 (n=62)	Group M2 (n=62)	Group D (n=62)	P value
Induction to vaginal delivery interval, hours	15.51 ± 6.18	12.14 ± 4.65	13.43 ± 6.96	0.008
Vaginal delivery within 24 hours, n (%)	52 (83.9)	57 (91.9)	54 (87.1)	0.390
Delivery after one dose, n (%)	16 (25.8)	24 (38.7)	20 (32.3)	0.307
Cesarean section, n (%)	17 (27.4)	21 (33.9)	26 (41.9)	0.234
Oxytocin augmentation, n (%)	19 (30.6)	11 (17.7)	26 (41.9)	0.013
Hyper stimulation, n (%)	4 (6.5)	7 (11.3)	5 (8.1)	0.620
Bishop score after 6 hours of delivery	3.45 ± 1.2	4.41 ± 1.5	4.21 ± 1.3	<0.001

Data is put as mean ± S.D unless stated otherwise.

Discussion

Although number of women delivering within 24 hours and after single dose of drug was higher in Group M2 as compared to group M1 and D, the difference didn't achieve statistical significance. Women receiving 50 µg of misoprostol had shortest induction of labor to delivery interval and highest postpartum Bishop Score. The women who were given 0.5 mg dinoprostone needed oxytocin supplementation in higher number while this requirement was lowest in patients receiving 25 µg misoprostol. Misoprostol at the dose of 50 µg was associated with more hyper stimulation. Overall best results were seen in the group receiving 50 µg of misoprostol and then came 0.5 mg of dinoprostone. Poorest results were seen in the group which received 25 µg misoprostol. The results observed were in accordance with the results of other studies⁵⁻¹¹. Austin SC et al.¹² found no significant difference in incidence of cesarean section, neonatal outcomes and the incidence of uterine hyper stimulation when delivery was induced with misoprostol or dinoprostone.

Saxena P et al.¹³ found out that the induction to vaginal delivery interval was shortest and improvement in Bishop Score was highest in patients receiving 50 µg misoprostol as compared to the patients receiving 25 µg misoprostol or 0.5 mg of dinoprostone. However, no significant difference in hyper stimulation, cesarean section or fetal outcomes was observed among the groups. The results of this study were in accordance with ours. On the other hand, Chitrakar NS¹⁴ found 25 µg misoprostol superior to 0.5 mg of dinoprostone in terms of shorter induction to delivery interval and lesser need for oxytocin augmentation. Mandal A. et al.¹⁵ have concluded in their study that misoprostol tablets are safer when inserted intra vaginally as compared to dinoprostone gel which

is inserted intra cervically, in the pregnancies which have prolonged to 41 weeks or more. According to Ayaz A et al. ¹⁶, 6 hourly dosing of 50 µg misoprostol is more effective in inducing the labor and ripening of cervix as compared to dinoprostone, but it can be associated with some adverse effects including hyper stimulation for which the patients need to be monitored continuously.

In the study conducted by Kulshreshtha S et al. ¹⁷, the results showed shorter induction to delivery interval and lesser incidence of cesarean section in the group which was treated with misoprostol as compared to the group treated with dinoprostone. APGAR score, perinatal outcomes and fetal outcomes were significantly better in the misoprostol treated group. Gupta HP et al. ¹⁸ compared various doses of misoprostol for the induction of labor and observed that 50 µg misoprostol is more effective than 25 µg misoprostol but higher dose is associated with more intrauterine meconium passage, hyper stimulation and tachysystole; and therefore, it can be harmful to both baby and the mother. Wang L et al. ¹⁹ conducted a meta-analysis on various trials conducted for the comparison of efficacy of misoprostol and dinoprostone. Although majority of the outcomes were similar for both the drugs but the need for oxytocin supplementation was significantly lower in the misoprostol group. Nigam A. et al. ²⁰ found no significant difference in the efficacy of 25 µg misoprostol and 50 µg misoprostol, when inserted intravaginally, but the lower dose was associated with more need for oxytocin augmentation.

Conclusion

Current study concludes that higher dose of misoprostol i.e. 50 µg misoprostol is higher in efficacy than 0.5 mg dinoprostone which is better than 25 µg misoprostol. But 50 µg misoprostol can cause hyper stimulation and dinoprostone needs oxytocin augmentation. Misoprostol is a good and cheap agent for the induction of vaginal delivery.

Conflict of interest: No

Funding Source: No

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