

Misoprostol Vaginal Pessary Versus Dinoprostone Vaginal Gel in Induction of Labour

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ABSTRACT

Aim: To compare misoprostol vaginal pessary with dinoprostone vaginal gel to know which of these two agents is more safe and effective for induction of labour

Method: A Interventional quasi experimental study was carried out in Sir Ganga Ram hospital, Lahore over a period of six months from 13th Feb, 2007 to 13th Aug, 2007. A total of 100 women at 37-42 months of gestation were assigned into two groups. Fifty women in group A received dinoprostone vaginal gel and 50 women in group B received misoprostol vaginal pessary.

Results: 68% in group A and 87% in group B deliver within 24 hours of induction. 60% patients in group A and 56% in group B had spontaneous vaginal delivery, 64% patients in group A and 66% patients in group B required oxytocin for augmentation. Nausea and vomiting was observed in 8% patients in group-B with no case reported in group A. Fetal and maternal complications were also comparable in both groups. Overall babies delivered with good APGAR score at 1 & 5 minute interval.

Conclusion: Both dinoprostone vaginal gel and misoprostol vaginal pessary appears to be equally safe and effective for induction of labour.

Keywords: Dinoprostone vaginal gel, misoprostol vaginal pessary, induction of labour.

INTRODUCTION

Induction of labour involves artificial initiation of uterine contractions prior to their spontaneous onset leading to progressive dilatation and effacement of cervix and delivery of baby. This term is only applicable to pregnancies at or beyond legal definition of fetal viability¹. It is an important and common procedure performed for medical, obstetrical and social indications. During past 15 years, rate of induction of labour has almost doubled in prevalence². The proportion of pregnancies undergoing induction varies between countries, but it is estimated that approximately 20% labours in United States of America (USA) and United Kingdom (UK) are induced^{3,4}. It is indicated when the benefits of delivery to the mother or fetus outweigh the potential risk of continuing pregnancy⁵. The common indications of induction of labour in Pakistan are post dated pregnancy, pregnancy induced hypertension, diabetes mellitus, RH isoimmunization and pre-labour rupture of membranes⁶. Favourability of cervix plays a substantial role in a determining success of induction, it is assessed by Bishop scoring system. A score of 6 or more predicts the likelihood of successful induction of labour. A score of 5 or less is regarded as being unfavourable for induction of labour⁷. Induction in case of an un-favourable cervix

results in prolonged induction to delivery interval, prolonged hospitalization, failed induction and increase rate of caesarean section⁸.

Various methods used for induction of labour are mechanical (foleys catheter, laminaria tents, membrane stripping) and pharmacological dinoprostone (PGE₂), misoprostol (PGE₁), PGF₂α cytokines, nitric oxide and relaxin⁵. Method of induction are used according to Bishop score. When cervix is unfavourable the principal method of induction of labour is with the help of prostaglandins. In case of favourable cervix, induction can be achieved with oxytocin and amniotomy⁷. Prostaglandins for induction of labour are used in 23% of all these confinements⁹. Dinoprostone, A prostaglandin E₂ analogue is only pharmacological agent approved by FDA for cervical ripening and labour induction⁵. It helps in cervical ripening and gives good results especially in patients with poor Bishop score¹⁰. It is available in the form of vaginal tablet, pessary gel (intra-vaginal, intracervical) and a slow release vaginal insert. PGE₂ when applied locally induced collagen break down dispersion and fluid absorption by stromal tissue and effective cervical ripening for induction of labour.¹¹ When given in gel form it has greater bioavailability with a quicker release and absorption profile as compared to tablet form¹². Gel produces favourable Bishop score more rapidly and also decreases number of patients requiring oxytocin augmentation as compared to tablet form¹³. Its use in case of unfavourable cervix is superior to use of amniotomy and oxytocin and was

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found to be safe and effective with minimum of patients interference¹⁴. Its use is associated with uterine hyperstimulation and fetal heart rate abnormalities¹⁵. Furthermore, dinoprostone is costly and must be refrigerated during its transportation and storage because of its thermal instability¹⁶.

Misoprostol, a synthetic prostaglandin E₁ analogue developed initially for the prevention and treatment of non-steroid anti-inflammatory drug use related gastric disease is now being increasingly used for labour induction¹⁷. For induction of labour it can be given by oral sublingual vaginal and intracervical routes. Its advantage over dinoprostone is its low cost and stability at room temperature due to which its use has been increased in developing countries but it is found to be associated with more chances of uterine contraction abnormalities and meconium staining of amniotic fluid leading to increased rate of abdominal deliveries. Misoprostol is also not approved by FDA for labour induction^{18,19,20}. The purpose of this study is to compare misoprostol vaginal pessary and dinoprostone vaginal gel to know which of these two agents is more safe and effective for labour induction so that it can be used for benefit of patients.

MATERIAL AND METHODS

The Interventional; Quasi experimental study was conducted over six months from 13th February, 2007 to 13th August, 2007 in Obstetrics & Gynaecology Department, Sir Ganga Ram Hospital, Lahore. A total of 100 women were recruited into the trial. They were divided into two groups. Fifty women were allocated dinoprostone vaginal gel and fifty women to misoprostol vaginal pessary by non-probability convenience sampling technique. Patient at term (37-42 weeks of gestation) confirmed on ultrasound, unfavourable cervix with bishop score less than 7, singleton pregnancy, cephalic presentation and reassuring fetal heart rate pattern were included. Grand multipara, pelvic structural deformities, previous uterine scar and placenta previa were excluded. A detailed history, general and obstetrical examination and investigations were carried out. In patients where LMP was not known gestational age was estimated by an early or late ultrasound. Hundred women at 37-42 weeks of gestation having an indication for induction of labour fulfilling the study criteria were included in this study. They were divided into two equal groups. The groups were comparable with respect to age, parity, gestational age and Bishop score. The study was approved by the hospital ethical committee and informed consent was taken from all participants.

The patients in group A were induced with 2mg dinoprostone gel in nulliparous women and 1mg in multiparous women 1mg dose was repeated at 6 hour interval (maximum two doses) in all patients. Patients in group B were induced with 50µg misoprostol vaginal pessary repeated at 4 hourly intervals with maximum of 3 doses. In both groups cervical ripening was assessed by change in Bishop score after initial application of four hours in misoprostol group and six hour in dinoprostone group. If there was no change in Bishop score, a second dose was given. Throughout procedure maternal uterine contractions and FHR were monitored through palpation and intermittent auscultation with Doppler or CTG respectively every 15 minutes. In the patient who had palpable uterine contractions and where there was a change in Bishop score, artificial rupture of membranes was performed. Subsequent management of labour was same in both groups. Oxytocin infusion was started if the rate of cervical dilatation was less than 1 cm/hour.

All data were entered in SPSS version 11 for data analysis. Descriptive statistics were calculated like age of the patient, gestational age, induction to delivery interval, duration of use of syntocinon presented as Mean± SD. Parity, need for syntocinon, mode of delivery, indications for instrumental / caesarean delivery and APGAR score were calculated as percentages. Induction to delivery interval between two groups was compared by using independent sample t-test. Need for syntocinon, mode of delivery, indications for instrumental/caesarean delivery and APGAR score were compared through Chi-square. A p value <0.05 or equal was considered as significant.

RESULTS

The demographic characteristics of both groups were similar. The age of the women ranged from 18–35 years. The mean age of the women was 24.64±3.84 years in group A and 25.26±4.32years in group B ($p=>0.05$). In group A and group B mean gestational age was 40.02±0.93 and 39.94±1.13 respectively ($P=>0.05$). Twenty three (46%) in group A and 24(48%) patients in group B were primigravida. Twenty seven (54%) in group A and 26 (52%) in group B ranges between 2nd to 4th gravida. Thus both groups were also comparable with regard to parity. Both groups were also comparable in terms of Bishop score. In group A 45 (90%) patients and in group B 94% patients in group B were induced at a Bishop score equal to or less than 3, while 5 (10%) patients in group A and 3(6%) patients in group B were induced with Bishop score more than 3 ($P=>0.05$). The most common indication for induction

of labour was found to be post dated pregnancy 23(46%) patients in group A and 26(52%) patients in group B. Second indication was pregnancy induced hypertension 7(14%) patients in group A and 8(16%) patients in group B. Other indications were found to be oligohydramnios incoordinate uterine contractions, sluggish fetal movements, gestational diabetes mellitus and placental abruption. Table 1 summarizes induction to vaginal delivery interval in both groups although misoprostol group had a shorter induction to delivery interval this difference was not statistically significant. In those who delivered vaginally Syntocinon was used for augmentation of labour in 32(64%) patients in group A and 33(66%) in group B, however the difference between these two groups was not statistically significant $p > 0.05$ (Table 2).

Thirty (60%) patients in group A had SVD compared to 28 (56%) patients in group B. There was one instrumental delivery in the form of vacuum extraction in dinoprostone group due to maternal failure to push and two in misoprostol group one due to maternal failure to push and other due to fetal bradycardia but this difference is again statistically not significant ($p > 0.05$). Similarly rate of lower segment caesarean section was also comparable in both groups (38%) in group A and 40% in group B (Table 3). Regarding maternal side effects, no incidence of uterine hyperstimulation was found in both groups. Nausea and vomiting was observed in 4 (8%) patients in group B while no case reported in dinoprostone group (Table 4). Cardiotocographic abnormalities were reported more frequently in 8 (16%) patients in group B as compared to 5 (10%) group A (Table 4).

Common indications for lower segment caesarean section were fetal distress noted by meconium staining of amniotic fluid and cardiotocographic abnormalities 11(58%) patients in group A and 12(60%) in group B. Failed induction was observed in 6(32%) in group A and 4(20%) in group B. This difference is statistically not significant ($p > 0.05$). Other indications for caesarean section in these groups were also comparable (Table 5). Forty seven (94%) babies in group A and 48 (96%) in group B were delivered with APGAR score of more than 6 at 1 minute interval whereas only 1(2%) baby in group A and 2(4%) babies in group B had APGAR score of equal to or less than 6 at 5 minute interval (Table 6,7).

Table 1: Frequency of Induction to vaginal delivery Interval in hours (n=61)

Delivery interval	Group A	Group B	
Within 24 hrs P value: >0.05	21(68%)	26(87%)	14.85±5.08 13.84±4.26
More than 24 hrs P value: >0.05	10(32%)	4(13%)	26.50±1.15 26.00±1.29

Table-2: Frequency of need for Syntocinon of patients (n=100)

Group	n	P value
A	32(64%)	Chi-square=0.015 P value: >0.05
B	33(66%)	

Table 3: Comparison of mode of delivery of patients in both groups (n=100)

Mode of delivery	Group A	Group B	P value
SVD	30(60%)	28(56%)	Chi-square=0.69 P= >0.05
Caesarean section	19(38%)	20(40%)	Chi-square=0.26 P= >0.05
Instrumental delivery	1(2%)	2(4%)	Chi-square=0.26 P= >0.05

Table 4: Maternal and fetal side effects of patients (n=100)

Parity	Group A	Group B
Maternal side effects		
Nausea	0	4(8%)
Vomiting	0	4(8%)
Uterine hyperstimulation	0	0
Fetal side effects		
CTG abnormalities	5(10%)	8(16%)

Table-5: Indications for caesarean section (n=39)

Indication	Group A	Group B	P value
Fetal distress	11(58%)	12(60%)	Chisquare=0.333 P= >0.05
Failed induction	6(32%)	4(20%)	Chisquare=1.333 P= >0.05
Failed progress	1(5%)	3(15%)	Chi square=0.429 P= >0.05
Placental abruption	1(5%)	1(5%)	Chi square=0.000 P= >0.05

Table-6: Frequency of APGAR Score 1 minute interval (n=100)

APGAR Score	Group A	Group B	P value
> 6	47(94%)	48(96%)	Chi-square= 0.011 P =>0.05
<6	3(6%)	2(4%)	Chi-square = 0.200 P=>0.05

Table 7: Frequency of APGAR score 5 minute interval (n=100)

APGAR Score	Group A	Group B	P value
> 6	49(98%)	48(96%)	Chi-square = 0.010 P = >0.05
<6	1(2%)	2(4%)	Chi-square = 0.333 P = >0.05

DISCUSSION

Induction of labour is widely used nowadays especially prostaglandin analog^{28,29}. Many studies have addressed this topic in order to find the most effective and economical treatment with less side effects. This study provides the comparison of safety and efficacy of dinoprostone vaginal gel and misoprostol vaginal pessary in women at term with Bishop score less than 7. In this study, most common indication for induction of labour was post dated pregnancy similar to the results of Raza et al⁶ and Ibrahim et al²⁹ where 50% of patients were induced due to post dated pregnancy. Other indications of induction like pregnancy induced hypertension and diabetes mellitus were also common⁶.

Induction to vaginal delivery interval was also comparable in both groups in this study with $p>0.05$ as shown in the study of M. Elhassan et al²¹ and Ibrahim et al²⁹ where no significant difference were found in induction to delivery (17.5±7.6 hour) with misoprostol and (19.15±6.9 hour with dinoprostone with $p>0.05$ ²¹. In this study, no significant differences in terms of patients delivering within 24 hours of induction of labour were found similar to study of Gregson et al²² where 69% patient induced with misoprostol delivery within 24 hours of induction. Ramsey et al²³ also showed insignificant difference in terms of deliveries within 24 hours between two groups.

Difference between mode of delivery between the two groups was also insignificant. Similar trends has been found in the study done by Wing et al where 14.7% misoprostol treated and 19.4% of dinoprostone treated patients had caesarean section deliveries²⁴. The results are consistent with the

previous studies done by Ramsey et al and Gregson et al^{22,23}. Oxytocin was used to augment labour after induction with one or more dose of either dinoprostone or misoprostol, which lead to improvement in Bishop score. Patients requiring oxytocin for augmentation were same in both groups as in the study of Calder et al²⁵ where 45% patients in each group required syntocinon for augmentation. The major indications for caesarean section were fetal distress followed by failed induction and the results were same as described by Carian et al²⁶.

APGAR score of 0-3 shows severe depression, of 4-6 shows mild depression. More than 94% of babies in both group delivered with good APGAR score at 1 minute and 5 minutes interval with no significant different between the two groups. There was no admission to neonatal intensive care unit or neonatal death. This is similar to findings of Lindsay²⁷. The most significant maternal side effect recorded with misoprostol was nausea and vomiting. No case of uterine hyperstimulation was found in either group. This is similar to observations in the study of Nausheen¹⁹. Fetal cardiocotographic abnormalities were observed more frequency in the misoprostol group than in the dinoprostone group although this difference is not statistically significant. This is most probably because of 50µg dose of misoprostol reducing the dose to 25µg will reduce the incidence of fetal cardiocotographic abnormalities as in the study of Gregson et al²² where 25µg misoprostol dose reduced the incidence of fetal side effects. In this I found no significant difference in terms of safety and efficacy between the groups thus confirming the results of various studies. Monitoring during labour is important during induction of labour to detect uterine hyperstimulation and fetal distress and early intervention if any such problem arises in orders to achieve a good maternal and fetal outcome.

The results of this study suggest that both dinoprostone vaginal gel and misoprostol vaginal pessary are equally safe and effective for labour induction at term. Traditional prostaglandin like dinoprostone is expensive beyond reach of more patients. Dinoprostone gell requires proper storage at cold temperature so it will be difficult to transport it to far off areas of Pakistan due to hot climate. Syntocinon is ineffective when cervix is unfavourable. Although misoprostol is not FDA approved, it is effective inexpensive and safe induction agent and its efficacy is not effected by hot weather so more studies should be carried out on a large scale to prove safety and efficacy of misoprostol so that it can be used to improve patient outcome in developing countries like Pakistan.

CONCLUSION

Both dinoprostone vaginal gel and misoprostol vaginal pessary are equally safe and effective for induction of labour at term. Both were comparable with regard to mode of delivery, induction delivery interval, oxytocin requirement and indications of caesarean section. Maternal and fetal outcome was satisfactory in both groups.

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