

## Comparison of Intravaginal Misoprostol (PGE1) with Dinoprostone (PGE2) for Termination of 2<sup>nd</sup> Trimester Pregnancy

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### ABSTRACT

**Aim:** To compare the effectiveness and side effects of intravaginal misoprostol(PGE1) with dinoprostone (PGE2) for labour induction in second trimester termination of pregnancy.

**Design:** Prospective experimental study.

**Setting:** Lady Aitchison Hospital, Lahore.

**Duration:** For a period of eight months from July 2014 to February 2015.

**Methods:** Hundred women with mid-trimester foetal loss or congenitally malformed foetus on ultrasonography were selected. These women were randomized to receive either intravaginal misoprostol or dinoprostone. Main outcome measures were efficacy and safety in terms of abortion-induction interval and side effects. Induction was considered successful where abortion was achieved within twenty four hours.

**Results:** The average induction-abortion interval in the misoprostol group was 15.05 hours and successful abortion was achieved in 80% (40/50) of cases whereas in PGE2 group 48% (24/50) aborted in the same time interval (15.05 hours). The rate of incomplete abortion requiring evacuation and curettage was 20%(10/50) in misoprostol group and 52% (26/50) in PGE2 group. In PGE1 Group frequently observed side effects were chills 12(24%),fever 7(14%)while abdominal pain occurred in 20(40%)

**Conclusion:** The less expulsion time, higher rate of complete miscarriage and minimal side effect seen in misoprostol group in our study showed that vaginal misoprostol is superior as a labour inducing agent in comparison to PGE2 dinoprostone) for termination of 2<sup>nd</sup> trimester of pregnancy.

**Keywords:** Misoprostol, Dinoprostone, 2<sup>nd</sup> trimester termination of pregnancy.

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### INTRODUCTION

Prostaglandins are eicosanoids, principally derived from arachidonic acid in cell walls. They are particularly important in female reproductive cycle. During the 8<sup>th</sup> decade of last century, mckenzie found that vaginal prostaglandin preparations were very useful for ripening of cervix. Now days, prostaglandins preparation in the form of gels and pessaries are used for cervical ripening.

Various methods for second trimester termination have been tried with reasonable success<sup>1</sup> which include surgical and medical methods. Surgical dilatation and evacuation is associated with significant rates of anaesthetic and procedure related morbidity and mortality. Medical induction with prostaglandins has been recognized as a safe and effective alternative to surgical termination of pregnancy. Pharmacological cervical ripening for induction of 2<sup>nd</sup> trimester miscarriage and intrauterine death with the prostaglandins analogue is becoming more popular after its first use in 1993 by Sanches

Ramose. PGE2 (dinoprostone) in the form of gel or pessaries have high cost and huge requirement regarding temperature control and transportation. On the other hand, prostaglandin E1 analogue (misoprostol) can be purchased on reasonable price as well as its shelf life is tremendously better<sup>2,3</sup>.

Misoprostol, synthetic prostaglandin analogue, is not an approved drug by FDA for pregnancy termination in second trimester, though has been originally approved by FDA for treatment of gastric ulcer. Misoprostol is being (off label) used for termination of pregnancy in different doses and routes in between 13-20 weeks with satisfactory results<sup>4,5,6,7</sup>. The purpose of this study is to compare the labour inducing potential of intravaginal Misoprostol and compare its effectiveness and safety over Dinoprostone (PGE2) for 2<sup>nd</sup> trimester termination of pregnancy particularly in our poor resource rsettings.

### MATERIAL AND METHODS

This interventional study was carried out in obstetrics and gynaecology department of Lady Aitcheson hospital Lahore. One hundred women admitted to Lady Aitchison Hospital from July 2014 to February

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2015 with gestational age ranging from 13 weeks to 27+6 weeks for pregnancy termination. Simple random sampling was used in the formation of groups. Two groups were made with 50 patients in each. First group patients received PGE2 (dinoprostone) for termination of pregnancy while the second group received PGE1 (misoprostol).

Inclusion criteria were missed abortion, major structural anomalies and therapeutically indicated miscarriage (medical disorder). Bishop score 0-4 remained same in all. Exclusion criteria were unexplained vaginal bleeding, bleeding disorders (diathesis), molar pregnancy, septic induced abortion, uterine anomalies. Patient with history of allergic disorders, uncontrolled hypertension, deranged liver function test and with previous more than one lower segment caesarean section were also excluded from the study.

Each group included 50 patients. Each patient was fully assessed by complete history and examination as per protocol. Baseline investigations and ultrasound report reviewed. In misoprostol group, 200µgm tablet of misoprostol was inserted intravaginally every 6 hours, a total of 4 doses. In PGE2 group, 3 mg tablet inserted intravaginally, a total of 4 doses. Symptoms of pain, excessive vaginal bleeding and vital monitoring was done. Analgesia was given if required. Vomiting and diarrhoea were treated with metocloperamide (10 mg every 8 hours) and codine phosphate 30 mg (enflor sachet) respectively. Data is presented in the form of tables for the age, parity, induction-abortion interval and side effects. Continuous variable are presented as range. Categorical variables are given in numbers (%)

## RESULTS

Randomly selected cases in our study were hundred, all in their 2<sup>nd</sup> trimester (i.e., between 14-28 weeks) of pregnancy, being fifty in each group. In both groups gross structural abnormalities of the foetuses were the commonest reason for termination of pregnancy (anencephaly, spinal cord abnormalities, dandy walker syndrome, abdominal wall malformations, maternal medical reasons e.g., nephritic syndrome, hepatic encephalopathy) Among multigravida in both groups 10 had previous C/S, while others have vaginal deliveries without any complications. Characteristics of the study groups are summarized in table 1.

Mean age of participants /patients in the misoprostol group was 28.9 and PGE2 group 30.6 years. Mean of gestational age was 22.0 weeks in misoprostol and 23.8 in PGE2 group. The variable gravida in both groups was almost same (range from

0-7) with an average of 3 children in the family, however 4 participants were gravida 10-11.

Table 1: Characteristics of study groups

Characteristics	Misoprostol	PGE2 group
Age (years) Mean±SD	28.9±7.1	30.6±4.6
Parity (Mean±SD)	2.8±1.22	2.8±1.22
Period of Gestation (Mean±SD)	224-1	23.8±3.4

Table 2: Outcome of termination of pregnancy

Outcome	Misoprostol Group	PGE2 Group
Complete expulsion of foetus	40(80%)	24 (48%)
Evacuation needed	10 (20%)	26 (52%)
Total	50 (100%)	50 (100%)

There was no significant difference in the success of both drugs (Table 3). Side effects and complications are compared in table 4. Treatment was considered successful as those in which abortion achieved within 24 hours and those in whom surgical evacuation was required for retained products of conception.

Table 3: Induction abortion interval

Duration between 1 <sup>st</sup> dose till expulsion (hours)	Misoprostol Group	PGE2 Group
<12 hours	04(8%)	03(6%)
13-18 hours	26(52%)	17(34%)
19-24 hours	15(30%)	21(42%)
>24 hours	05(10%)	09(18%)

Table 4: Side effects and complications associated with termination of pregnancy

Side Effects/ Complications	Misoprostol Group	PGE2 Group
Diarrhoea	1(02%)	13(26%)
Abdominal Pain	4(08%)	20 (40%)
Headache	2(04%)	08(16%)
Shivering/Chills	12(24%)	01(02%)
Fever	7(14%)	03(06%)
Nausea/Vomiting	1(02%)	13(26%)
Dizziness	1(02%)	05(10%)
Fatigue	0	05(10%)
Breast Tenderness	2(04%)	07(14%)
Vaginal Bleeding	03(06%)	18(36%)
Fever	07(14%)	03(06%)

## DISCUSSION

The medical induction in the management of 2<sup>nd</sup> trimester termination of pregnancy for varying reasons has replaced the conventional way of surgical evacuation of the uterus. In the present study two such uterotonic agents have been used in the same settings and design to compare their efficacy and safety. There is higher number of patients with

foetal abnormalities being referred to our tertiary care hospital. The same is explained in study done at Singapore<sup>8</sup>. Carbonell regimen used 800µgm of vaginal misoprostol every 24-48 hours up to a maximum of 3 doses and success rate of 87-94%<sup>9</sup> whereas in our study, 200 µgm misoprostol every 4 hourly/6hourly used showing limited dosage regimen for short period. Nagina FL found misoprostol safe and an effective agent for cervical ripening. Moreover found convenient way of inducing abortion in 2<sup>nd</sup> trimester of pregnancy<sup>10</sup>. It is also noted that misoprostol was successfully used in patients with previous uterine scar. Houssain –N study proved the same results<sup>11</sup>.

Complete expulsion of the foetus occurred in 80% Of misoprostol group while lower (48%) in PGE2 group. In a study by Machlouf the rate of Complete abortion was 100% and 66.67% where intravaginal misoprostol and dinoprostone for second trimester pregnancy termination were compared. The induction – abortion was also significantly shorter and the number of doses needed was less with misoprostol than with PGE2<sup>12</sup>.

Agrawal NR found in the comparative study that intravaginal misoprostol (PGE1) group patients had significant (p<0.001) shorter abortion induction interval with lesser requirement of oxytocin than the conventional dinoprostone (PGE2) group<sup>(13)</sup>. In the study by Wildschut H in which forty randomised controlled trials(RCTs) were included to compare various agents for pregnancy termination and methods of termination for their efficacy and effects. Misoprostol was found effective where used alone, though it appeared more effective in combination with mifepristone<sup>14</sup>.

The average induction to expulsion duration with misoprostol group was 15 hours and 21 hours in PGE2 group in our case, the prostaglandins being repeated every six hourly. Four RCTs showed that the induction abortion interval is shorter with 3-hourly vaginal administration of prostaglandins than 6-hourly without an increase in side effects<sup>24</sup>. The result was clinically significant with reduced hospital stay and expenditure. In a series of studies by Samina, Dinoprostone, intracervical Foley's catheter and misoprostol were equally effective in terms of cervical ripening, induction delivery interval, mode of delivery and maternal complications in labour induction<sup>15</sup>.

The incidence of minor side effects was very low in our study with both PGE1 and PGE2. Shivering, fever, nausea /vomiting observed in few patients. Major complications as excessive vaginal bleeding observed in PGE2 group (18 patients) and only 3 in misoprostol group showing misoprostol more safe and effective. Evacuation needed in 10 and 26 patients in misoprostol and PGE2 group respectively.

Reason for evacuation was being significant vaginal bleeding, suspicion of incomplete emptying of uterus and confirmed RPOC's in uterine cavity on ultrasound scan. The lower incidence of evacuation is seen in a comparative study where only 20% of cases with misoprostol had to undergo evacuation<sup>16</sup>. Only one patient in our study reported with fever, foul smelling vaginal discharge and abdominal tenderness showing medical abortion as safe and effective option for termination of early pregnancy. A review of studies of medical abortion regimens, reported infection (0.92) is lower than that reported after either surgical abortion procedure or childbirth<sup>16,17</sup>.

## CONCLUSION

Our comparative study concluded that misoprostol is superior as an inducing drug than PGE2. It is safe, effective and non invasive regimen for termination of mid trimester pregnancy. As the resources in a country like ours are limited and same with medical services, expertise and skill to carry out safe dilatation and evacuation. Misoprostol that do not incur high cost in storage and transport makes the provision of safe termination of pregnancy in 2<sup>nd</sup> trimester of pregnancy for varied indications feasible.

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