

DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20180455>

Original Research Article

Role and efficacy of vaginal dinoprostone gel (PGE₂) plus vaginal misoprostol (PGE₁) in second trimester termination of pregnancy

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Received: 31 January 2018

Accepted: 05 February 2018

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ABSTRACT

Background: The addition of dinoprostone gel (PGE₂) to standard regimen of second trimester abortion using vaginal misoprostol (PGE₁) reduces failure rate and decrease induction abortion time interval. We evaluated the role and efficacy of vaginal dinoprostone gel with vaginal misoprostol in women undergoing second trimester abortion. Objective of present study was to assess the safety and effectiveness of vaginal dinoprostone gel plus vaginal misoprostol for second trimester termination of pregnancy.

Methods: This study was a prospective cohort involving 100 women with 12-20 weeks gestation requesting termination of pregnancy. In study group 0.5mg dinoprostone gel applied vaginally followed by 400µg misoprostol every four hourly (max 3 doses) after six hours of dinoprostone gel application. The mean age of the women study was 27.2 years and mean gestational age was 18.9 weeks. The primary effectiveness of the study was the efficacy of the treatment to terminate pregnancy at 20 hrs. Secondary outcomes were induction abortion interval, failure rate, side effects. statistical analysis of study was carried out using chi square test.

Results: At 20 hours, the complete abortion rate was 100%. Within 16 hours 98% women aborted without any significant side effects. Mean induction abortion interval was 14.56 hours.

Conclusions: Combination of vaginal dinoprostone gel (PGE₂) plus misoprostol (PGE₁) is effective, safe and alternate method for second trimester pregnancy termination with. In this protocol induction to abortion interval time is less as compared to other methods of second trimester pregnancy termination.

Keywords: Dinoprostone gel, Misoprostol, PGE₁, PGE₂, Prostaglandin, Second trimester termination of pregnancy

INTRODUCTION

Second trimester termination contributes approximately 10% to 20% of all induced abortions cases and about 65% to 70% of all fatal complications are related to induced abortions. Various agents are used to ripen the cervix and stimulate uterine contractions and induce abortion after 12 weeks, but available data regarding their safety and effectiveness are limited.^{1,2} Various agents include hypertonic saline, or hyperosmolar urea, injected intra-amniotically; ethacridine lactate administered intra-

or extra-amniotically; prostaglandin analogues administered parenterally or intra- or extra-amniotically; and oxytocin injected intravenously or intramuscularly. These methods and routes of administration, however, are invasive and likely to be less safe, and the time to complete abortion is longer when compared to the use of methods such as misoprostol alone, combined dinoprostone and misoprostol combined mifepristone and misoprostol.²⁻⁵ Second trimester abortion also includes surgical procedure, but it can result in complications like uterine perforation, cervical incompetence, uterine

synechiae and even maternal mortality. The intent of this study is to study the effectiveness and safety of intravaginal dinoprostone gel plus misoprostol in second trimester pregnancy termination. Among prostaglandins, prostaglandin E1 and E2 analogues have been tried in different doses and by various routes for second trimester abortion.⁶ Misoprostol, a synthetic 15-deoxy16-hydroxy 16-methyl analogue of PGE1 being much cheaper, safe and capable of being easily stored at room temperature has been tried by both oral and vaginal routes in different dosage regimens with varying degrees of success.⁷

Oral misoprostol is associated with faster achievement of peak levels, but the effect lasts for less time and it is also associated with more side effects.⁸ However vaginal route is associated with slower peak level achievement, but the effect lasts longer with fewer side effects.⁹ Prostaglandin E2 gel was used for cervical ripening before induction of labor in patient having low bishop score. Studies and result indicate that local prostaglandin E2 is superior to placebo or no therapy in enhancing cervical effacement and dilation, reducing initial induction failures, shortening the induction-delivery interval, decreasing oxytocin use.¹⁰⁻¹² On the premise of additive effect of both PGE1 and PGE2 for cervical dilation, and on labour induction. Each having slightly different mechanism of action adding to better clinical efficacy and safety.¹³⁻¹⁶

METHODS

T Prospective non randomised open label study was carried out in military hospital over period of two year (2015-2016). 116 healthy women, between age 18 to 38 years, with 12-20 weeks of pregnancy, requesting second trimester termination of pregnancy, were included in this study. The indications for termination were as per indication of MTP Act. Gestational age was estimated as per guidelines issued by ACOG. informed consent of all pregnant women was taken before enrolment and the study was approved by the ethical committee of the institution. Exclusion criteria were women with multiple pregnancy, baseline hemoglobin less than 8gm/dl, previous cesarean section, maternal local or systemic infection and any degree of cervical dilatation. We also excluded patients who had any pulmonary, hepatic, renal or cardiovascular disease. All the women received initially 0.5mg dinoprostone gel (PGE2) vaginally followed by 400 µg misoprostol every four hourly (max 3 doses) after six hours of dinoprostone gel (PGE2) application.

Women's vital signs were monitored every two hours and the process of abortion was assessed by vaginal examination four hourly during each dose administration. If any women failed to abort after three doses of misoprostol (400 mcg four hourly), the same protocol was repeated 24 hours later of first dose of dinoprostone gel (PGE2). After the abortion was complete the products of conception were checked for its completeness and induction-abortion interval was calculated and noted. If

the abortion was incomplete, it was completed using oxytocin drip. After abortion patients were observed for 24 hours before discharge and failure of abortion was considered when a woman failed to abort within 48 hours of the start of treatment. Other method for termination of pregnancy were undertaken for failed cases. Information about side effects was taken from each woman including nausea, vomiting, diarrhoea, fever and abdominal pain. On discharge they were asked to come for follow up after a week or earlier if need arises. On follow up, a pelvic examination was performed on all the women and an inquiry made of any abnormal bleeding or delayed side effects.

Trial outcomes

The primary outcomes the study was the effectiveness of the treatment to terminate pregnancy at 20 hrs. The secondary outcome measures were induction-abortion interval (hours), number of failure cases, need for surgical evacuation in incomplete cases and side effects. The in-duction-abortion interval was defined as the interval between the time of administration of the first dose of dinoprostone gel (PGE1) and the time when the fetus was aborted.

Statistical analysis

The statistical analysis was performed by using Chi-square analysis were done to assess the significance of variables and p-value less than 0.05 was considered as statistically significant value.

RESULTS

Table 1 shows age distribution in our study. Age ranged from 18 to 40 years. Maximum number (52/100, 52%) of women was in 26-30 year age group and mean age was 27.2 years. Seventy four women (74%) had gravidity of two or more and the mean gravidity was 2.6.

Table 1: Age distribution (n=100).

Age (years)	Number (%)
≤20	4 (4%)
21-25	27 (27%)
26-30	52 (52%)
31-35	15 (15%)
>35	2 (2%)
Mean age 27.2 years	

Table 2: Period of gestation (n=100).

Weeks	Number (%)
12-14	10 (10%)
14-16	18 (18%)
16-18	34 (34%)
18-20	38 (38%)
Mean gestational age was 18.9 weeks	

The two common indications were congenital anomaly and intrauterine fetal death.

Table 3 shows the relationship of induction abortion interval to the gestational age. Most of the women (72%) aborted between 12 and 14 hours, while 98% aborted within 16 hours and 96.6%. The mean induction abortion

interval was 12.58 ± 1.02 (SD) hours. There is no relationship between gestational age and induction abortion interval ($P > 0.5$). Except minor side effects like nausea, vomiting and diarrhoea, no major drug related side effects were observed in the study population. The average total dose of misoprostol in our study was 800 microgram.

Table 3: Induction abortion interval.

Weeks	4-6 hrs	6-8 hrs	8-10 hrs	10-12 hrs	12-14 hrs	14-16 hrs	>16hrs	Total
12-16	-	-	2	12	12	2	-	28
16-20	-	-	4	4	60	2	2	72
P>0.5, Chi square= 0.044, Mean induction abortion interval 12.58 ± 1.01 (SD) hours								

There was no case of failure in this regime as per method of this study. Also, there was no need for any surgical evacuation as there was no case of retained product of conception. Side effect like nausea, vomiting, pain abdomen was less as compared to other methods of termination however statistically insignificant.

DISCUSSION

Abortions during second trimester represent only 10%-15% of all induced abortions but it leads to 65% to 70% of all maternal morbidity, 50% of maternal mortality is accounted for this practice.^{1,2} Hence it is imperative to develop effective and safe method for second trimester abortions to decrease maternal morbidity and mortality. In the past misoprostol, in combination with other agents such as mifepristone, oxytocin, PGF2A, PGE2 has been investigated for second trimester medical abortion.³⁻⁵ Different studies have shown that pre-treatment with dinoprostone gel (PGE2) resulted in a shorter induction abortion interval compared with regimens without dinoprostone gel.⁶ Abortifacient properties of misoprostol for termination in the second trimester have been reported in the medical literature since 1993.⁷ Several numbers of studies have demonstrated that it is safe and efficient drug for achieving fetal expulsion. Moreover, it is inexpensive and can be stored in room temperature.⁸ Due to lack of evidences from well controlled randomized studies, consensus is yet to be reached regarding optimal dose, route and time interval of misoprostol administration for induction of medical abortion. Oral route is easy to administer, but there is increased incidence of gastrointestinal side effects along with increased induction-abortion interval. Vaginal route had been found to be more promising than oral route probably due to an accumulating plasma level with fewer gastrointestinal side effects.⁹⁻¹¹ In such a context, we found this regime of vaginal administration of 0.5mg of dinoprostone gel (PGE1) followed by 400µg misoprostol 4 hourly very effective for second trimester pregnancy termination. Mean induction abortion interval in our

study was 12.58 ± 1.02 hours which is comparable to 12-16 hours in other studies and with better induction to interval time.¹²⁻¹⁵

Thus, vaginal dinoprostone gel with misoprostol is found to be an efficient and time saving drug for second trimester pregnancy termination. These drugs are easily available in any obstetric unit. Drug related side effects and procedure related complications were very low, which is comparable to different studies.^{9,13,15} In present prospective study 98% women aborted within 16 hours, which is comparable to about ninety percent as reported by other studies.¹³⁻¹⁵

CONCLUSION

Vaginal dinoprostone (PGE2) gel plus misoprostol (PGE1) is a safe and effective protocol with less induction to abortion interval method for second trimester pregnancy termination. Further studies to compare its safety and efficacy with other methods of termination of mid trimester pregnancy can be carried out.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kumar A, Agarwal R. Role and efficacy of vaginal dinoprostone gel (PGE2) plus vaginal misoprostol (PGE1) in second trimester termination of pregnancy. *Int J Reprod Contracept Obstet Gynecol* 2018;7:888-91.