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Vaginal misoprostol alone for first trimester termination of pregnancy

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Abstract
Objective: To assess the efficacy and safety of vaginal administration of a single dose of misoprostol 800 mcg alone for first trimester termination of pregnancy and to compare the efficacy and safety of the same at gestational age less than 8 weeks and 8-12 weeks.
Material and Methods: This post-hoc analysis included 35 pregnant women with intrauterine pregnancies up to 12 weeks gestational age. All the patients were administered 800 mcg misoprostol by the vaginal route. Success was defined as complete abortion within 24 hours. Failures were classified into incomplete abortion and complete failure.
Results: The overall success rate was 62.86% after 24 hours of administration of single dose of 800 mcg of misoprostol. Success rate at less than 8 weeks gestation was 69.23% while it was 59.09% between 8-12 weeks.
Conclusion: Vaginal misoprostol alone had a success rate of 62.86% for first trimester termination of pregnancy and there was no statistically significant difference in the success rate with respect to gestational age.

Keywords: Misoprostol, vaginal, termination of pregnancy

Introduction

An estimated 56 million pregnancies are terminated every year throughout the world [1] and out of these, around 25 million per year are unsafe abortions, mostly happening in developing countries [2]. In developed regions, it is estimated that 30 women die for every 100,000 unsafe abortions. That number rises to 220 deaths per 100,000 unsafe abortions in developing regions [1]. According to a WHO systematic analysis published in 2014, unsafe abortions contributed to 7.9% of all maternal deaths all over the world [3].

India legalized medical termination of pregnancy (MTP) through the MTP Act of 1971 in order to enable women to opt out of an unwanted pregnancy in certain specific situations. However, despite legalization of abortion, the incidence of illegal and unsafe abortion has increased tremendously in our country while quality and coverage of MTP services remains poor. Large number of abortions are primarily achieved by suction-curettage. But in recent years, medical abortion has emerged as a method of choice and a safe, effective and feasible alternative to the surgical procedure of suction-curettage for women seeking abortion in first trimester of pregnancy. The main advantage of medical abortion is that it allows a woman to avoid the risks of surgery and anesthesia.

There are various regimens for medical abortions in first trimester including mifepristone with misoprostol, methotrexate with misoprostol or misoprostol alone. Though the combined use of mifepristone with misoprostol is already considered as gold standard for medical abortion, regimens using misoprostol alone may be useful in situations where mifepristone is either not available or not affordable. Misoprostol's efficacy varies depending on the gestational age, dose and administration route [4]. Many studies have shown misoprostol alone to be reasonably effective for the first trimester termination of pregnancy (See Table 4). A Cochrane review published in 2004 concluded that misoprostol in a single dose of 800 mcg was more effective than any other prostaglandin.[5] Misoprostol is affordable, easily stored at room temperature and possesses a shelf life of several years.

The current study was needed to assess whether medical MTP could be effectively done with misoprostol alone, so as to reduce the cost of procedure, especially for poor patients. This study was done in a resource-constrained setting amongst patients with low socio-economic status

who could not afford mifepristone tablet.

The specific objectives of this study were

1. To assess the efficacy and safety of vaginal administration of a single dose of misoprostol 800 mcg alone in first trimester termination of pregnancy.
2. A secondary objective was to compare the aforementioned when administered at gestational age less than 8 weeks versus gestational age 8-12 weeks.

Materials and Methods

The present study included all women (n=137) admitted to a tertiary care teaching hospital in South India over a period of 14 months for the purpose of first trimester MTP. All women were given the option for medical method of MTP. The risks, benefits and failure rates of the medical method of MTP with misoprostol alone were explained to them.

Inclusion criteria were women more than 18 years of age, in good general health, and with undesired pregnancies (as per MTP laws of India). Exclusion criteria were suspected or confirmed gestational trophoblastic disease, patients who had anemia (Hb <10gm%), bleeding disorders, bronchial asthma, cerebrovascular disorders, diastolic BP>100 mm Hg, glaucoma, sickle cell anemia, acute inflammatory bowel disease, uterine infection, uterine fibromas, any known allergy to prostaglandins, previous uterine scars, and threatened or spontaneous abortions. Also, women refusing surgical procedure, i.e. suction curettage, in case medical methods fail, were excluded.

Out of all the women who gave consent (n=59) for vaginal administration of 800 mcg of misoprostol alone for the purpose of MTP, 35 were found to be eligible to participate in this study after considering the inclusion and exclusion criteria.

Gestational age was confirmed for all participants by transvaginal sonography. These 35 women were divided into 2 groups: Group 1 comprised of 13 women with gestational age less than 8 weeks and Group 2 comprised of 22 women with gestational ages between 8 to 12 weeks.

All women were explained the procedure and the risks involved and were given the option of surgical termination of pregnancy. Written, informed consent was obtained. In this study, all the participants were admitted in the hospital for the desired intervention. Detailed history of the participants was taken and physical examination including a pelvic examination was done. Hemoglobin and blood grouping including Rh typing was done. A 50 mcg dose of Anti D intramuscularly was given to patients with negative Rh type before administering misoprostol. All 35 participants received 800 mcg misoprostol by vaginal route after moistening the misoprostol tablets with 3 drops of distilled water per tablet and were observed for spontaneous expulsion of the products of conception. In case of failure of medical methods after 24 hours, as confirmed clinically and with transvaginal sonography, suction curettage of products of conception was done.

The outcome of treatment was classified as

1. Success was defined as termination of pregnancy with complete expulsion of the products of conception as confirmed clinically and by transvaginal sonography after 24 hours of insertion of misoprostol without the need for surgical procedure.
2. Failure was defined as the need for surgical procedure. Failures were further classified into incomplete abortion and complete failure. Incomplete abortion was defined as clinical or sonographic signs of incomplete abortion. Complete failure was defined as continuation of pregnancy after 24 hours of misoprostol administration as observed on sonography.

Data was collected using a data collection form and stored digitally as a spreadsheet. Data analysis was done using SPSS package (Statistical package of social sciences). The data obtained were analyzed by the "unpaired 't' test", "chi square test", "chi square for trend" wherever applicable. A 'p' value of less than 0.05 was considered significant and 'p' value of greater than 0.05 was considered not significant.

Results

No statistical difference in the clinical characteristics was noted between Group 1 and 2 in terms of maternal age and gestational age (Table 1).

Table 1: Baseline Characteristics of patients

	Group 1 (<8weeks) [n=13]	**Group 2 (8-12 weeks) [n=22]**	
	Mean +/-S.D.	**Mean +/- S.D.**	**'P' value**
Age(years)	26.1 (+/- 3.3)	26.95 (+/- 4.7)	0.56
Gestational age (days)	6.8 (+/- 0.4)	10.55 (+/-1.4)	<0.0001

Out of total 35 women, only 6 were primigravidas, 15 were second gravidas, and 14 were pregnant for the third or more time. There wasn't any statistically significant difference between the two groups in terms of their gravidity as depicted in table 2.

Table 2: Comparison of gravidity between two groups.

Gravidity	**Group 1**	**Group 2**
G1	1	5
G2	6	9
>/=G3	6	8

$\chi 2=1.326$, p= 0.52, not significant

Table 3: Comparison of parity between the two groups.

Parity	**Group 1**	**Group 2**
P0	2	6
P1	6	8
>/=P2	5	8

$\chi 2=0.711$, p= 0.70, not significant

Both the groups were comparable in terms of parity as depicted in table 3.

Table 4: Comparison of two groups in terms of history of prior abortion.

Prior Abortion	**Group 1**	**Group 2**
Yes	2	1
No	11	21

$\chi 2=0.232$, p= 0.63, not significant

Majority of the patients (32 patients) in this analysis didn't have any prior history of abortion. Also, the two groups were comparable in terms of prior history of abortion as depicted in table 4.

The outcomes after usage of single dose of misoprostol for first trimester termination of pregnancy are shown in *Figure 1*. Overall a single dose of 800 mcg of vaginal misoprostol was successful in achieving complete abortion in 22 women (62.86%) 24 hours after insertion. Out of the remaining 13 women, 10 (28.57%) had incomplete abortion and 3 (8.57%) had complete failure. In the 10 women with incomplete abortion, the cervix had ripened and the internal os was partially dilated so

as to permit the insertion of at least 6 mm suction cannula.

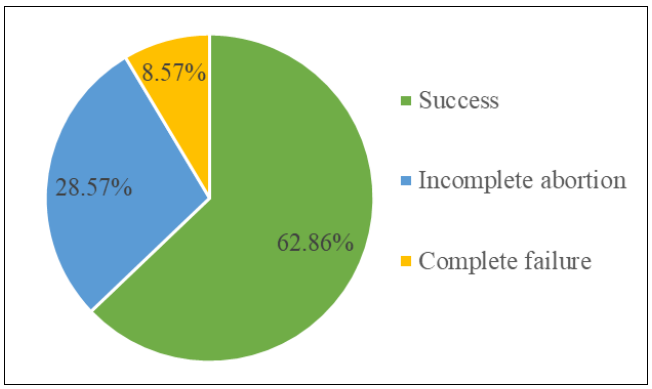

Fig 1: Outcome measures

As depicted in Figure 2, there wasn't any statistically significant difference in the outcomes between the two groups. The success rate was 69% at less than 8 weeks while the success rate was 59% between 8-12 weeks. Out of 4 patients in group 1 who required suction curettage, 3 had incomplete abortion while 1 had ongoing pregnancy after 24 hours of misoprostol insertion. In group 2, out of 9 patients who required suction curettage, 7 had incomplete abortions and 2 had ongoing pregnancy after 24 hours.

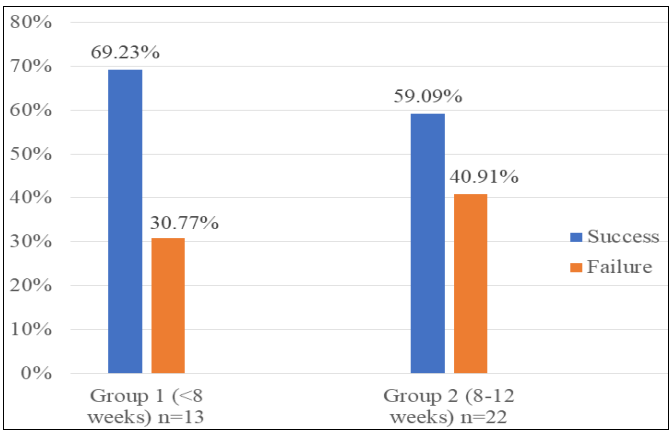

Fig 2: Comparison of outcome measures between the two groups.

$\chi 2$=0.566, p= 0.81, not significant

Table 5: Comparison of induction abortion interval among the women with successful abortion between the two groups

*Induction abortion interval (in hours)	Group 1 (n=13)	Group 2 (n=22)
< 6	3	4
6 to <12	3	5
12 to <18	1	2
18-24	2	2

*From time of administration of misoprostol to expulsion of the products of conception

$\chi 2$ (for trend) = 0.0216, p= 0.88, not significant

As seen in *Table 5*, there wasn't any significant difference between the two groups in terms of induction abortion interval. This induction abortion interval has been calculated only for those women who aborted successfully. There were 4 patients in group 1 and 9 patients in group 2 who didn't abort successfully with vaginal misoprostol alone, and hence were excluded from this analysis.

The mean insertion to bleeding onset interval was 4.9 hours in group1 and 3.0 hours in group 2, but this difference was not significant statistically. One patient in group 1, and 2 patients in group 2 didn't have any bleeding. So, they were removed from the calculation of mean.

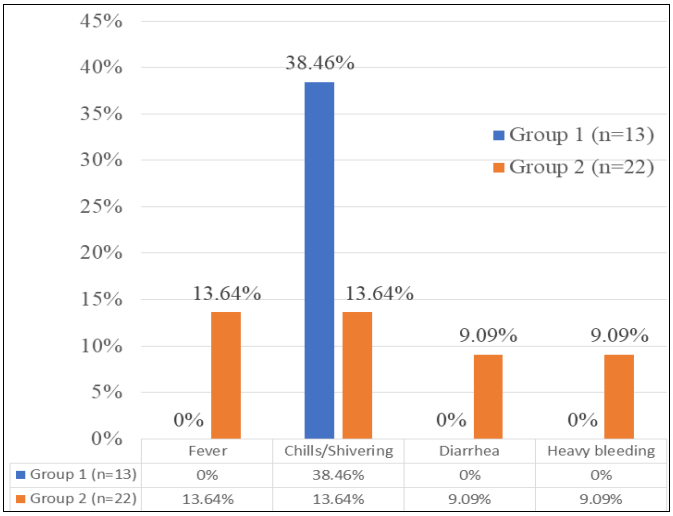

Fig 3: Incidence of side effects

The incidence of side effects and comparison of side effects between the two groups has been depicted in figure 3. Overall chills/shivering was the most frequent side effect in either group. Only 2 patients in group 2 required emergency curettage for heavy bleeding. None of the patients in either group required blood transfusion for hemorrhage. There wasn't any case of post-abortion infection. None of the patients had temperature greater than 101degree Fahrenheit. Most of the patients did not require analgesia for pain. There was one patient in group 2 who had fever, chills as well as heavy bleeding and hence has been included in all the three. Five patients in group 1 and 8 patients in group 2 had side effects. After applying appropriate statistical test (Standard error of proportion), the p value was found to be 0.8 which means that there wasn't any significant difference in the incidence of side effects between the two groups.

Discussion

We observed that a single dose of 800 mcg vaginal misoprostol decreased the need for surgical procedure of suction curettage in approximately 63% of patients. Efficacy of vaginal misoprostol was not altered at higher gestational ages for first trimester termination of pregnancy. Overall, there weren't any serious side effects in either of the 2 study groups.

Creinin *et al.* compared the efficacy of 400µg oral misoprostol with 800µg vaginal misoprostol for uterine evacuation of early pregnancy failure and found 800µg vaginal misoprostol to be more effective [4]. Jain *et al.* compared the abortifacient effect of intravaginally administered moistened misoprostol tablets with that of combined regimen of mifepristone and oral misoprostol in pregnancies less than or equal to 8 weeks gestational age and found similar abortion rates [6].

Sudha *et al.* reported complete abortion rates of 94.2% after a single dose of 800mcg vaginal misoprostol among women undergoing MTP up to 49 days gestational age, which is much higher than the rates observed in our study but in their study, outcomes were assessed after one week of misoprostol insertion [7].

In another study done by Mahaseth BK *et al.*, 65% success rates

were observed after a single dose of 800 mcg vaginal misoprostol for medical termination of pregnancy in first trimester, like the results in our study. In the same study, moistened misoprostol was observed to yield better success rates than dry misoprostol tablets [8].

Table 6: Comparison of outcomes with 800mcg vaginal misoprostol among various studies: [6, 7, 8, 9, 10]

Outcome	Jain *et al.* (≤8weeks) [n=100]	T,okman-kilic *et al.* (<12 weeks) [n=30]	Sudha *et al.* (≤7weeks) [n=70]	Mahaseth BK *et al.* (≤11 weeks) [n=100]	Pant *et al.* (≤12 weeks) [n=69]	Present study (Gandhi G *et al.*) (≤12 weeks) [n=35]
Success	73%	70%	94.2%	65%	78.2%	62.86%
Failure	27%	30%	5.8%	35%	21.8%	37.14%

In a study reported from India for first trimester medical abortion, 67 % success rates were reported at gestational ages less than 8 weeks following the use of 800mcg misoprostol vaginally while the success rates were found to be 83% after similar treatment in women with gestational age between 8-12 weeks [11]. Success rate in our study in group 1 is comparable to the similar group in their study. But contrary to our study and many similar studies done so far, the success rate was higher in their study at higher gestational ages within first trimester.

Table 7: Comparison of incidence of side effects in our study with previous study

Side effect	Jain, Meckstroth & Mishell, 1999 [n=100]	Present study [n=35]
Fever or chills/shivering	68%	31.4%
Diarrhoea	44%	5.7%
Heavy bleeding	5%	5.7%

As seen in table 7, the incidence of side effects was much less in our study compared to the study of Jain *et al.* In previous studies the major disadvantage with the regimen of intravaginal misoprostol alone was significantly higher rates of prostaglandins related side effects, but in our study, it was not so. Also, most of the studies done so far selected patients with pregnancies less than 8 weeks duration for attempting medical methods of abortions as less success rate was found at higher gestational ages. But in our study, in the vaginal group there was no significant difference in the clinical efficacy in relation to gestational age. This difference may be due to smaller sample size in our study.

The strength of our study was that all the participants were hospitalized and closely observed objectively by a single observer (GG) for various outcomes and side effects and hence accurate data for the same could be gathered. The major limitation of this study was the lack of appropriate controls. Also, the researcher was not blinded to the gestational age of the participants, which may have resulted in a bias.

Conclusion

After analyzing the outcomes of both the groups, our analysis shows that the use of 800 mcg vaginal misoprostol for first trimester termination of pregnancy resulted in complete expulsion of the products of conception in 63% of the patients, thus reducing the need for surgical treatment. There wasn't any statistically significant difference in the success rates at higher gestational age in the present study. Also, administration of 800mcg misoprostol alone for first trimester termination of pregnancy is not associated with any significant side effects or complications. Further research on whether additional doses of misoprostol or longer periods of observation after misoprostol administration are helpful to increase the success rate of misoprostol alone, is recommended especially in low resource setups where patient may not be able to afford mifepristone for medical abortion. Also, randomized controlled trials for the use of vaginal misoprostol alone for first trimester termination of pregnancy are warranted.

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