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ORIGINAL ARTICLE

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Intravaginal misoprostol for termination of second trimester pregnancy

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OBJECTIVE(S) : To find out the efficacy and safety of intravaginal misoprostol insertion for second trimester termination of pregnancy

METHOD(S) : One hundred and forty cases of second trimester termination of pregnancy done from September 2001 to August 2004 using intravaginal misoprostol 600 µg followed by 400 µg every 4 hourly till abortion or a maximum of 2600 µg over 24 hours were analyzed.

RESULTS : A majority of the women was married, the mean gestational age was 26.42 years, and the mean gravidity 2.96 ± 1.56. The success rate was 99.26%. The mean induction abortion interval was 12.27± 5.71 hours. However, it was more in primigravidas as compared to that in multigravidas. The mean dose of misoprostol required was 1638.57 ± 322.67 µg. The side effects observed were nausea, vomiting, diarrhea and fever.

CONCLUSION(S) : Intravaginal misoprostol is a safe, effective, cheap and acceptable method for second trimester termination of pregnancy.

Key words : second trimester termination of pregnancy, intravaginal misoprostol

Introduction

Abortion is defined as termination of pregnancy before the period of viability which occurs at 20 weeks of gestation and the fetus weighing 500g. About 40-60 million abortions occur per year globally. Out of these 33 million are illegal. In India there is an unacceptably high incidence of septic abortions, most of which occur following illegally induced abortion (90.5%) but a substantial number does occur following legally induced surgical abortion as well (2.5%).

Second trimester termination of pregnancy is more risky in terms of maternal morbidity and carries a mortality of 322/ 100000 compared to 25 /100000 in first trimester abortion.

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Various medical and surgical methods are used for second trimester termination of pregnancy eg. dilatation and evacuation, aspirotomy, abdominal hysterotomy and vaginal hysterotomy. All these methods require hospitalization and have disadvantage of surgical trauma and anesthetic complications. Intraamniotic and extraamniotic instillation of ethacridine lactate, urea, saline and prostaglandin are associated with variable success rate of 70-90% and induction abortion intervals (IAI) 11.5 - 40.61 hours. Use of prostaglandin PG $F_2\alpha$ by various routes has resulted in high success rate and reduced IAI but at the same time it is associated with high incidence of side effects. PGE_1 analogue misoprostol originally used for the treatment of peptic ulcer has been found to have uterotonic effect as well and is used for the termination of pregnancy with great success. Its use in conjunction with mifeprostone in the termination of first trimester pregnancy is well established. Using misoprostol alone for second trimester termination of pregnancy has been tried by various authors with varying success. It is cheap, stable at room temperature, doesn't need refrigeration and is associated with few side effects. The present study had been undertaken to assess the efficacy and safety of vaginal

misoprostol for induction of second trimester termination of pregnancy.

Methods

The study analyzes 140 cases admitted for termination of second trimester (14-24 weeks) pregnancy from September 2001 to August 2004.

At the time of admission detailed history was taken and general, systemic and obstetric examinations were done. Medical and surgical disorder if any was detected. Careful obstetric examination including pelvic examination was done. Duration of pregnancy was assessed and pelvic pathology ruled out. The gestational age was determined by menstrual history and pelvic examination and confirmed by ultrasound when necessary. Routine investigations done included blood grouping, hemogram, blood sugar, urine examination, platelet count, bleeding time and clotting time, and test for sickling. Special investigations were done as and when required. An informed consent was obtained after counseling regarding the procedure, its advantages and disadvantages, and possible side effects. Women were excluded from the study if they had adrenal insufficiency, coagulopathy, contraceptive device in situ, corticosteroid therapy, ectopic pregnancy, hemophilia, thrombocytopenic purpera, porphyria, adnexal mass, diabetes and jaundice.

All inductions were carried out on inpatient basis by inserting into the posterior fornix 600 µg of misoprostol tablets keeping the patient strictly in bed for half an hour. Thereafter 400 µg tablets were inserted intravaginally every 3 hourly until abortion or to a maximum of 2600 µg over 24 hours. Vital signs, time of onset of contraction, bleeding, and expulsion of the products of conception including placenta and membrane were recorded. If abortion was found to be incomplete or it failed, surgical intervention was done. Patients were kept under observation for 24 hours and discharged with the advice to come for follow up after 14 days or earlier if necessary.

Results

Majority of our patients were married, of 20-30 years of age, and belonged to low socioeconomic status (Table 1). The success rate of the procedure was 100%. 97.15% aborted within 24 hours after the insertion of the first misoprostol tablet. (Table 2).

The complete abortion rate was (82.85%). In majority of the patients the placenta was expelled within 15 minutes of expulsion of the fetus. The placenta was retained in 17.14% (24/120); whole placenta in 5% (17/120) and part of it in 12.14% (17/24). Surgical evacuation was done when placenta was retained wholly or partly. The mean blood loss was 70.85 ± 29.77 mL. None of the case required blood transfusion.

Table 1. Patient characteristics (n=140).

Characteristics	
Mean age	26.42 years
Married	85.8%
Unmarried	14.2%
Primigravidas	20.71%
Mean gravidity	2.96±1.56
Mean gestational age	18.27 ± 3.79 weeks

Table 2. Induction abortion interval (n=140).

Induction abortion interval (IAI) (hours)	Number	Percent	Cumulative abortion rate
<6	04	02.85	02.85
6-12	88	62.85	65.70
13-18	35	25.00	90.70
19-24	09	6.42	97.15
>24	04	2.85	100
Total	140	100%	100%

Shortest IAI 3.30 hours Longest IAI 33 hours
Mean IAI 12.27 ± 5.71 hours

The mean dose of misoprostol required was 1638.57 ± 322.67µg and it was not statistically different in different gestational ages (Table 3).

Table 3. Gestational age, mean induction abortion interval (IAI) and mean dose of misoprostol required (n=140)

Gestational age (weeks)	IAI (mean±SD) (hours)	Dose of misoprostol (mean ± SD) µg
14 (n=38)	11.49 ± 4.71	1637.84 ± 349.09
15-16 (n=16)	12.46 ± 4.79	1725.93 ± 380.88
17-18 (n=33)	13.11 ± 10.41	1541.18 ±197
19-20 (n=21)	13.27 ± 6.09	1585.71 ± 282.47
>21 (n=32)	11.66 ± 3.29	1606.52 ± 319.95
Mean ± SD	12.27 ± 5.71	1638.57 ± 322.67

The mean IAI and mean dose of the misoprostol were not significantly different in different gestational age periods.

The mean IAI decreased with the gravidity being more in primigravidas than that in multigravidas (Table 4).

Side effects observed were vomiting in 12.85%, diarrhea in 1.42% and fever in 14.28% of the cases. (Table 5).

Table 4. Gravidity, induction abortion interval (IAI) and misoprostol required (n=140).

Gravidity	IAI (hours) (Mean ± SD)	Dose of misoprostol (µg) (Mean ± SD)
1 (n=29)	13.64 ± 5.13	1703.30 ± 339.56
2 (n=19)	12.68 ± 5.17	1640.00 ± 294.15
3 (n=40)	12.00 ± 3.28	1680.95 ±333.67
4 (n=27)	09.81 ± 5.38	1540.00 ± 350.04
5 (n=15)	12.30 ± 11.02	1482.35 ± 187.87
6 (n=06)	13.04 ± 2.26	1720.00 ± 334.66
7 (n=04)	13.20 ± 3.72	1733.33 ± 416.33
Mean ± SD	12.27 ± 5.71	1638.57 ± 322.67

The mean IAI and mean dose of misoprostol were not significantly different in different gravidities.

Discussion

Second trimester termination of pregnancy is associated with a proportionately great morbidity. There is a need to find out a method that is cost effective, has shorter IAI, and is free of side effects and complications.

Misoprostol has got uterotonic activity; it can be given by oral, sublingual, vaginal and rectal routes. Its uterine activity is better when given vaginally as compared to when given orally as vaginal administration bypasses the liver. In a study conducted by Khan et al[1] Misoprostol demonstrated a route dependent pharmacokinetic profile, with best absorption following vaginal administration. Oral misoprostol reached a high peak concentration quickly before a rapid fall in its plasma levels. In the present study with intravaginal misoprostol the mean IAI was 12.27 ± 5.71 hours, the shortest being only 3.30 hours and the longest 33 hours. The IAI observed was shorter than that observed in previous studies[2-10] (Table 5). The IAI was also shorter than that observed by other authors

Table 5. Comparative analysis of different studies

Author	Year	Dose schedule	Observation time (hours)	IAI (hours)	Success rate		Complete abortion rate	Side effects
					At 24 hours	At 48 hour		
Wong et al [2]	2000	400 mg vaginal 3 hourly x5	24	15.2	-	90.5%		Fever 7%
		400 mg vaginal 6 hourly x 3	24	19.0	-	75.7%		
Herabutya et al [3]	2000	600 µg vaginal x 12 hourly		24.12 ± 21.6	68.6%	89.5%		Pyrexia 41% Diarrhea 20%, Nausea 15%
Pongsatha and Tongsong [4]	2001	800 mg vaginal x 12 hourly		21.38 ± 13.68				Diarrhea 40%
Herabutya et al [5]	2001	600 mg vaginal x 12 hourly		15.2 (10.5-20.8)	82.1%	92.5%	77.6%	Pyrexia 26.9%
		800 mg vaginal x 12 hourly		15.3 (10.2-21.8)	78.9%	92.1%	72.4%	Pyrexia 71.1%
Gilbert and Reid [6]	2001	400 mg vaginal followed by 200 mg vaginal after 2 hours and then 4 hourly	32	17.5	93%	100%		
		400 mg orally followed by 200 mg orally after 2 hours & then 200 mg vaginally x 4 hourly		33	19%	70%		
Ramin et al [7]	2002	400 mg orally x 4 hourly	24	15.2±6.7	91%			
Dickinson and Evans [8]	2003	400 mg vaginally x 3 hourly		14.5	85.7%			
		400 mg orally x 3 hourly		22.5	44.8%			
		600 mg vaginally then 200 mg orally x 3 hourly		16.4	74.1%			
Tang et al [9]	2004	400 mg vaginally x 3 hourly x 5		12.0(3.7-48.0)	85%	95%		
		400 mg sublingually x 3 hourly x 5		13.6(6.3-45.3)	64%	91%		
Pongsatha and Tonsong[10]	2004	400 µg orally x 4 hourly		13.2 ± 8.4	84.1%			Chills 33.3%
Present study		600 µg vaginally then 400 ug vaginally x 3 hourly x 4		12.27±5.71	97.14%			Vomiting 12.85%, diarrhea 1.42%, fever 14.28%.

who used misoprostol for second trimester termination of pregnancy orally [6-8,10]. In the study conducted by Gilbert and Reid[6], the IAI was 33 hours on oral administration and 17.5 hours on vaginal administration. Ramin et al[7] reported 15.2 ± 6.7 hours IAI on oral administration.

Using a high loading dose initially followed by low dose at proper intervals to maintain sustained effect brings about effective uterine contractions and shorter IAI. In our studies we used an initial high dose of 600 µg followed by 400 µg 4 hourly and achieved an IAI shorter than that observed in other studies, where only low dose schedule was used without a high loading dose [2,7,8,10]. Herbutya et al [5] used a high 12 hourly doses of 600 µg and 800 µg intravaginally and observed the IAI to be 15.2 hours (10.5-20.8 hours) and 15.3 hours (10.2-21.8 hours) respectively. Thus, not only a high initial dose but a proper interval between doses also decides IAI.

Our mean blood loss was significantly less than that observed by Wong et al [4]. The success rate of 97.14% within 24 hours in our study was significantly higher than that observed in other studies [2-4, 8-10] but was comparable to that in the study of Gilbert and Reid [6].

In 82.85% women, complete abortion was achieved and this was comparable with the previous studies [2,3,6,9,10].

Side effects observed were minor in nature and required symptomatic management only. Other authors have observed fever as the most frequent side effect [3,5,9.10].

Conclusion

Intravaginal misoprostol for second trimester pregnancy termination is very effective, safe, convenient and free from any serious side effect.

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