J Obstet Gynecol India Vol. 56, No. 6 : November/December 2006 Pg 518-521

ORIGINAL ARTICLE

The Journal of Obstetrics and Gynecology of India

A comparison of intravaginal misoprostol with extraamniotic ethacridine lactate for second trimester MTP

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OBJECTIVE(S) : To compare safety, efficacy, complications, and cost effectiveness of extraamniotic instillation of ethacridine lactate with vaginal misoprostol for voluntary termination of second trimester pregnancy.

METHOD(S) : A prospective comparative study on 120 pregnant women between 13 and 20 weeks was conducted from July 2004 to June 2005. Women were randomized in two groups. In one group extraamniotic ethacridine lactate (10mL/ week of gestation) instillation was done and in the other, 400 ? g tablet of misoprostol was inserted in the vagina every 12 hours for a maximum of 4 doses.

RESULTS : The rate of successful abortions within 48 hours was 95% (57/60 women) in each group. Among those who had aborted within 48 hours, the mean interval from induction to abortion was shorter in misoprostol group (15.5 hours vs 31.3 hours, P<0.0001). The rate of complete abortion, defined as expulsion of both fetus and placenta without operative assistance, was 66.6% for misoprostol and 70% for ethacridine lactate (P=0.344). The average cost per treatment was Rs. 57.95 for misoprostol as compared to Rs.86.10 for ethacridine lactate. Side effects were uncommon and did not differ between the two groups.

CONCLUSION(S) : Success rates of misoprostol and ethacridine lactate were comparable but the induction abortion interval was almost half in misoprostol group when compared with that in ethacridine lactate group.

Key words : voluntary termination of midtrimester pregnancy, ethacridine lactate, vaginal misoprostol

Introduction

In spite of availability of varieties of safe and effective contraceptive methods, couples fail to use them and sometimes come for second trimester voluntary termination of pregnancy (MTP). Cohen first described the use of ethacridine lactate for second trimester abortion by extraamniotic route in 1946 [1]. Since then it has been extensively used for midtrimester MTP. However this procedure has its drawbacks in the form of a longer instillation abortion interval, higher incidence of incomplete abortion, and greater chance of fetus being born alive [2]. Misoprostol, a synthetic prostaglandin structurally related to prostaglandin E_1 was developed to prevent ulcerative effects of chronic use of antiinflammatory drugs [2]. It has been shown to induce 2nd trimester abortion [2,3]. This drug has, however, not been extensively compared with extraamniotic ethacridine lactate. This study was conducted to compare the safety and efficacy of intravaginal misoprostol with extraamniotic ethacridine lactate for midtrimester pregnancy termination.

Paper received on 03/02/2006 ; accepted on 12/08/2006

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Methods

This prospective randomized study was carried out from July 2004 to June 2005. One hundred and twenty women requesting termination of pregnancy of 13-20 weeks gestation with a valid legal indication as per our MTP Act were taken up for the study. In 116 women the indication was failure of contraception used. In other women indications were

systemic scleroderma in one, HIV infection in one, and mental health affection in two unmarried ones. Women with asthma, previous uterine surgery, and those with hepatic, renal or cardiovascular disease were excluded from the study. The study was approved by the institution's ethics committee and all women had consented to participate in the study. Gestational age was determined from dates of last menstrual period (LMP) and abdominal examination findings. Ultrasonography was done in selected women where LMP and clinical findings did not agree. Inclusion criteria were normal vital parameters, hemoglobin and blood sugar levels.

Randomization was done using a table of random numbers. Group I (n=60) women received ethacridine lactate (0.1%, 10 mL/week of gestation) extraamniotically via a Foley catheter No.16 in the operation theater. Catheter bulb was inflated with 20 mL of distilled water and was left in situ for 6 hours. Vaginal examination was done very 12 hours. When cervix was 2 cm dilated or if 24 hours had passed, uterine contraction was augmented with a drip of 10 units oxytocin in 500 mL Ringers lactate solution. Those who did not expel the fetus by 48 hours were considered failures.

Group II (n=60) women received 400 ?g misoprostol tablet in posterior fornix every 12 hours till onset of contractions or a maximum of 4 doses. Failure of procedure was defined as failed expulsion of the fetus at 48 hours or the occurrence of systemic adverse signs and symptoms severe enough to preclude further use of the drug. Women who failed were given 250 ?g of PGE_2 ? ?intramuscularly unless contraindicated.

Vital signs were monitored every 4 hours. Occurrences of fever, chest pain, breathing difficulty, vomiting, diarrhea, and signs of water intoxication were recorded. After expulsion of the fetus and placenta cervical injury was looked for and check curettage done in every case. Completeness of abortion was defined as expulsion of both placenta and fetus without operative assistance. The induction abortion interval was defined as time from instillation of ethacridine lactate or administration of 1st dose of misoprostol to abortion. Hemorrhage was defined as an estimated blood loss exceeding 500 mL or a need for blood transfusion. Fever was defined as a temperature of 38°C or more occurring 24 hours or more after pregnancy termination.

The parameters studied were induction abortion interval, completeness of procedure, failure of abortion, side effects, and cost per procedure. Statistical analysis was carried out with Epi Info statistical software. Z test and $?^2$ test were used to determine test of significance. P<0.05 was considered as value of significance.

Results

The two groups had similar age, parity, and gestational age (Table 1).

Table 1. Characteristics of the study groups.

Characteristics		Ethacridine lactate n=60	Misoprostol n=60	P value
Age (years)		26.4. ± 4.4 [a]	24.8 ± 6.91[a]	P > 0.05
Parity	0	0	2 (3.33%)	$?^2$ = 2.04;DF=2
	1	24 (40%)	23 (38.33%)	P > 0.05
	2	36 (60%)	35 (58.33%)	P > 0.05
Gestational age (weeks)		16.5 ± 2.7[a]	15.45 ± 2.81[a]	P=0.981

[a] Mean ± standard deviation

Fifty-seven (95%) of the 60 women in each of the two groups had successful abortion within 48 hours. Seventy five percent (45/60) women in Group II had successful abortion within 24 hours in comparison to only 30% (18/60) in Group I. This difference was statistically significant ($?^2$=24.36, P<0.0001) (Table 2).

Table 2. Induction abortion interval.

Induction abortion interval (hours)	Extraamniotic ethacridine lactate n=60	Misoprostol	P value
< 12	0	21 (35%)	
12 – 24	18 (30%)	24 (40%)	
24-36	26 (43.33%)	8 (13.33%)	
36-48	13 (21.66%)	4 (6.66%)	
> 48	3 (5%)	3 (5%)	
Mean	31.3[a]	15.5[a]	<0.001

[a] $?^2$ = 36.15, DF = 4, P<0.001

One of the three women in Group II in whom abortion was unsuccessful, had chest pain, tachycardia and shortness of breath after administration of four doses of misoprostol. Chest x-ray and cardiogram were within normal limits, and she responded well to oxygen inhalation and deriphyllin injection. Her pregnancy was terminated by hysterotomy. The remaining two had received single dose of 250 ?g of PGF_2 ? intramuscularly after 48 hours and had successful abortion within 4 hours.

The three women who failed in Group I were given one

dose of 400 ?g of misoprostol intravaginally and had successful abortion within 6 hours. Successful abortion in respect to gestational age is shown in Table 3. No significant difference was noted between the groups. The mean induction abortion interval in women with successful result was 15.5 hours in Group II and 31.3 hours in Group I (P<0.0001) (Table 2). The rate of complete abortion, defined as expulsion of fetus and placenta without operative interference, was 70% (42/60) in Group I compared to 66.6% (40/60) in Group II (P=0.344). Subsequent check curettage in these women revealed no grossly apparent placental tissue. In the remaining women in whom the placenta was not expelled or only partially expelled a thorough curettage was performed and all placental tissue removed. The mean number of doses of misoprostol tablet was 1.9 (760 ?g; average cost Rs.57.95) and mean amount of ethacridine lactate solution used was 164 mL (average cost Rs.86.10).

Table 2. Gestational age and success rate.

Gestational age (weeks)	Extra-amniotic ethacridine lactate	Vaginal misoprostol	$?^2$ test Yates correction	P value
13-14	16/18 (88.88%)	24/24 (100%)	0.89	0.3466
15-16	12/12 (100%)	15/15 (100%)	-	-
17-18	12/12 (100%)	8/9 (88.88%)	0.02	0.88
19-20	17/18 (94.44%)	10/12(83.33%)	0.14	0.71

Eight women (13.3%) in Group II had fever as compared to 6 (10%) in Group I (P=0.287). Uterine pain necessitating analgesia with 50 mg tramadol hydrochloride occurred in 43 (71.6%) women in Group II and 36 (60%) in Group I (P=0.090). Nine (15%) women in Group II had vomiting in comparison to 4 (6.6%) in Group I (P<0.0001). The blood loss was less than 500 mL in all women. No woman required a blood transfusion.

Discussion

Ethacridine lactate for midtrimester MTP has a long history of use in our country and its safety is well documented [4]. There is no apparent contraindication for its use. However, its use has certain disadvantages like longer instillation abortion interval, a higher failure rate, and more chances of incomplete abortion. So there is a need for a newer agent to overcome these demerits. Several studies have evaluated the use of misoprostol for induction of abortion in second trimester. The optimal regimen has not been determined. Studies have used doses ranging from 200 to 800 ?g at intervals ranging from 3 to 12 hours [2,3,5,7,9]. Use of higher doses is associated with higher rate of adverse effects [2]. We had chosen 400 ?g every 12 hours hoping that success will be high and side effects minimal.

In our study success rates with misoprostol and extraamniotic ethacridine lactate were similar. Agarwal and Chaturvedi [5] administered 200 ?g of misoprostol every 12 hours and 80.5% women had abortion within 24 hours. In one prospective study of 40 women Bhattacharjee et al [6] report 95% success rate with misoprostol for midtrimester MTP. Mean induction abortion interval was 8.8 hours in 13-16 weeks gestation and 16.6 hours in 16-20 weeks gestation. Edwards and Sims [7] compared two regimens of vaginal misoprostol, one low dose (200 ?g every 12 hours) and one high dose (400 ?g every 6 hours), for second trimester pregnancy termination at 13 – 27 weeks. They found high dose regimen resulted in more abortions (98% vs 84%; P=0.014) and shorter induction abortion interval (13.25 vs 22.5 hours, P=0.001) without any greater side effects. In our study 12 hourly vaginal application of 400 ?g of misoprostol resulted in successful abortion in 95% (57/60) with a mean induction abortion interval of 15.5 hours (Table 2). It is an effective and convenient method of midtrimester MTP.

Sofat et al [1] report 92% success rate within 48 hours and 98% within 72 hours following ethacridine lactate instillation for second trimester MTP. The mean induction abortion interval was 31 hours 31 minutes which is comparable with our results. In one large series of second trimester termination of pregnancy by ethacridine lactate, Kamat and Anjaneyulu [8] report an overall success rate of 80-90% within 72 hours and 100% success after reinstillation. However, in their study some women had a pregnancy beyond 20 weeks of gestation. Maru and Bansal [9] compared intravaginal 200 ?g misoprostol with extraamniotic ethacridine lactate and found misoprostol to be safe, cost effective, and having better results (success rate 98% vs 96% and shorter induction abortion interval (12-18 hours vs 36-48 hours).

Success rate and induction abortion interval are major aspects of clinical importance in second trimester MTP. Our study confirms the superior efficacy of vaginal misoprostol regimen as measured by significant shortening of the induction abortion interval (15.5 hours vs 31.3 hours; P<0.001) and increased rate of successful abortion at 24 hours (75% vs 30%, $?^2$ = 24.36; P<0.001). With both the groups, side effects and complications were uncommon. Concerns remain regarding the potential for uterine rupture, especially when misoprostol is used in women with a previous cesarean delivery [2]. Because of this issue, we excluded women with a previous cesarean delivery from participation in our study.

Conclusion

For 2nd trimester MTP misoprostol is safe, effective and cheaper than ethacridine lactate.

Acknowledgement

We are greatful to Dr. Nirmal Kumar Mondal, Assistant Processor, Department of Community Medicine NRS Medical College, Kolkata, for working out the statistical calculations and inferences.

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