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Original Article

Obstetrics and Gynaecology Section

Role of Sublingual Misoprostol for Cervical Priming in First Trimester Medical Termination of Pregnancy

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ABSTRACT

Objective: To evaluate the efficacy and safety of sublingual misoprostol as facilitator in first trimester medical termination of pregnancy (MTP) by surgical method.

Materials and Methods: This was a prospective open label study conducted at a tertiary center. A total 150 patients at 6-12 wks gestation requesting for MTP were randomized into two groups. Patients in study group (n=75) received sublingual misoprostol three hours before surgical abortion and in control group (n=75) directly underwent surgical abortion without prior cervical priming with misoprostol. The outcomes of both groups were recorded in terms of baseline cervical dilatation, need of additional cervical dilatation, intraoperative blood loss, operative time and procedure related complications. The results were statistically analyzed using student-t test and chi-square test. p-value of <0.05 and <0.001 were considered significant and highly significant respectively.

Results: The mean baseline cervical dilatation was significantly more in study group compared to control group (8.6±1.3mm versus 5±2.3mm; p <0.001) and the operative time and intraoperative blood loss were also less (p<0.001). Higher incidence of side effects like nausea, vomiting and pyrexia were recorded in sublingual misoprostol group but were well tolerable to the patients.

Conclusion: Sublingual misoprostol is an effective and safe drug for cervical priming prior to surgical evacuation and has good patient acceptability.

Keywords: Baseline cervical dilatation, Cervical priming, Misoprostol, Surgical Abortion

INTRODUCTION

Medical methods of abortion using mifepristone in combination with misoprostol or misoprostol alone have significantly decreased the rate of surgical abortion and the complications associated with it. It is however not always the method of choice because of the long time consumed to complete the abortion, inconvenience due to prolonged bleeding per vagina (P/V) and the risk of excessive bleeding P/V makes it unsuitable for its use in rural areas because of inadequate, inaccessible round the clock emergency services. Besides these, the risk of treatment failure and incomplete abortion also increases with advancing gestation. Therefore the surgical method like vacuum aspiration, dilatation and evacuation still remains the procedure of choice for termination of pregnancy for many women. Insufficient dilated cervix may cause difficulty in evacuating the uterus, excessive hemorrhage and increases the risk of incomplete abortion. Forceful mechanical dilatation before surgical abortion, especially in hand of unskilled persons may cause cervical laceration and uterine perforation [1]. Even delayed complications of forceful mechanical dilatation like cervical stenosis or cervical incompetence can occur, and the risk is increased in nulliparous women. Prior cervical priming with pharmacological agents make the surgical abortion easier, reduce the operative time, blood loss and the overall complication rate, and henceforth recommended and mentioned in several guidelines [2,3]. A lot of cervical priming agents like laminaria tent, hypan and prostaglandins (gemeprost and misoprostol) have been studied to evaluate their efficacy to bring favorable cervical changes. Misoprostol, the PGE1 analogue which was initially used for the treatment of gastric ulcer, now shows promising features in this area with the advantage of easy availability, ease of administration, cost effective, stability at room temperature and fewer systemic side effects. Different routes, doses and time interval of misoprostol administration have been studied for its optimal efficacy.

Our study was aimed to determine the role of 400 micrograms (µg) sublingual misoprostol as facilitating adjunct in surgical termination of pregnancy in first trimester and also to evaluate its safety and efficacy.

MATERIALS AND METHODS

This study was carried out at a tertiary care center following approval from institutional ethical committee over a period of one and half year (1st December 2005 to 31st may 2007). Total 150 patients at 6-12 weeks gestation requesting for MTP were enrolled for the study after obtaining informed consent and filling the MTP form. Gestation age was confirmed by menstrual history, bimanual pelvic examination and if any doubt by ultrasonography. Exclusion criteria were contraindication to misoprostol including glaucoma, sickle cell anemia, poorly controlled seizure or known allergy to prostaglandin, history of previous uterine surgery, hemoglobin < 8mg/dl, known cardiorespiratory disease or coagulopathy.

After enrollment, patients were randomized into either group (of 75 each), study group and control group by using opaque sealed envelope. A detailed history was taken followed by complete physical and pelvic examination of patients. Pre-operative routine investigations including haemoglobin, urine analysis, blood group and Rhesus antigens were done. Study group received 400 µg sublingual (S/L) misoprostol three hours before the surgical abortion and the Control group directly underwent suction evacuation for first trimester MTP without prior cervical priming. Patients of both groups were observed preoperatively for the incidence of bleeding per vagina, pain abdomen and nausea or vomiting. Suction evacuation was performed by same surgeon using Karman's cannula of appropriate size and electric vacuum aspirator under intravenous Diazepam (10mg) and Pentazocin (30mg). Before starting suction evacuation, the baseline cervical dilatation was measured by Hegar's dilator. The largest number of Hegar's which could be passed easily through

Variables	Study group	Control group	p-value
Age (years)	25.6±3.4	26.3±3.8	0.2364
Parity	3.3±1.2	3.5±1.3	0.3292
Gestation (in weeks)	8.3±1.2	8.1±1.3	0.3292
Hb (gm %)	10.6±1.6	10.4±1.2	0.3879

[Table/Fig-1]: Demographic variables in two groups
p-value >0.05; no significance

Operative details	Study group	control group	p-value
Base line cervical dilatation (mm)	8.6±1.3	5±2.3	<0.001
No.of patients required additional cervical dilatation (%)	11(14%)	70(93%)	<0.001
Operative time (min)	5.3±1.2	9±2.6	<0.001
Intraoperative blood loss (ml)	27±11.2	38±12.5	<0.001

[Table/Fig-2]: Intraoperative findings
p-value<0.001; highly significant

Complications	Study group (n=75)	Control group (n=75)	p-value
Lower pain abdomen	11(15%)	6(8%)	0.3029
Nausea and vomiting	18(24%)	3(4%)	<0.001
Diarrhoea	nil	nil	
Pyrexia	5(6%)	nil	
Vaginal bleeding			
Pre-operative	21(28%)	Nil	
Postoperative	WNL	WNL	
Uterine perforation	nil	nil	
Incomplete abortion	nil	2(3%)	

[Table/Fig-3]: Incidence of complications
p-value >0.05; no significance and p value<0.001; highly significant, WNL; with in normal limit

internal os without resistance, was recorded as the baseline cervical dilatation and if additional mechanical dilatation of cervix required, was also noted. Intra-operative blood loss was calculated from volume of aspirate in the jar after sieving the product of conception and the operative time recorded as the time from start of cervical dilatation until the end of suction evacuation.

The primary outcome recorded was the baseline cervical dilatation. The secondary outcomes noted were need of additional mechanical cervical dilatation, intraoperative blood loss, operative time and procedure related complications.

STATISTICAL ANALYSIS

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 15.0 for Windows). Mean and standard deviation were used for symmetrical distributed continuous variables. The recorded outcomes of two groups were statistically analyzed by student-t test and chi-square test. The p-value <0.05 and <0.001 was considered significant and highly significant respectively.

RESULT

The demographic characteristics of both groups were comparable [Table/Fig-1]. In both groups, majority (86%in study group, 83% in control group) of women were younger than 30 year showing parity in the range of 1-6 and mostly (34-36%) were third gravida. 87% underwent surgical abortion before 10 weeks of gestation, and 9% had so before 12 weeks. Baseline cervical dilatation was significantly greater in the S/L misoprostol group compared to the control group (p<0.001) [Table/Fig-2]. No bleeding P/V was observed in the patients of control group, whereas 13% patients in Study group had pre-evacuation bleeding P/V, varying from spotting to mild bleeding however were well tolerable. Post suction evacuation, both groups had bleeding P/V within normal limit. Adverse effects of misoprostol like nausea, vomiting and pyrexia were observed in fewer patients in study group, but were milder [Table/Fig-3].

DISCUSSION

Studies have proven the misoprostol as an effective cervical priming agent with significant effect on initial cervical dilatation rate, reducing the need of further cervical dilatation and operating time, when compared with placebo [4,5]. The various route of misoprostol administration have been studied and compared with each other regarding their efficacy, pharmacokinetic properties and side effects profile to find the most appropriate route of its administration for cervical priming. Major studies have evaluated the misoprostol by oral and vaginal route [4-6]. Though vaginal misoprostol is found to be more effective due to its slow and more constant absorption through the vaginal mucosa, oral misoprostol has higher patient acceptability because it avoids the pain and discomfort associated with its administration through vaginal route [7]. Few studies document sublingual route as better alternative and preferable for misoprostol administration, compared to vaginal route [8]. A pharmacokinetic study has demonstrated highest peak concentration and significantly higher systemic bioavailability of S/L misoprostol compared to oral and vaginal route, indicating this as most potent route of its administration for cervical priming [9]. In contrast, another study found no difference in efficacy between S/L and vaginal route misoprostol, and limited side effects were seen with vaginal route [8].

S/L misoprostol can be self-administered even at home without any discomfort and offering more privacy to the patients. It does not need water for ingestion in contrast of oral misoprostol and hence can be given safely to the patients requiring general anaesthesia for suction evacuation. There are only few Indian studies demonstrating the role of sublingual misoprostol as facilitator before surgical abortion [10,11]. Our study observed that administration of sublingual misoprostol made the cervix favorable and operative procedure was more convenient in the study group compared to the patients of control group.

Sixty four patients (86%) had adequate cervical dilatation to undergo suction evacuation, and only 11 women (14%) out of total 75 in the study group required additional cervical dilatation by Hegar's dilator compared to 70 patients (93%) out of 75 in control group (p<0.001). The mean baseline cervical dilatation was observed as 8.6±1.3 mm in patients who received S/L misoprostol and 5±2.3 mm in the control group (p<0.001). The findings are consistent with the results obtained by Vimla N et al., who observed the baseline cervical dilatation as 7.7±1.3 mm in misoprostol group and 3.4±1.7 mm in placebo group (p<0.001) [10]. Operative time was significantly lesser in study group (5.3±1.2 min) compared to the control group (9±2.6 min). Intraoperative blood loss was also significantly lesser in study group (study group 27±11.2 ml versus 38±12.5 ml in control group; p<0.001). Similar results are described in above mentioned studies [10,11].

Lower abdominal pain was observed in more number of patients receiving S/L misoprostol (15% versus 8%) but the difference was not statistically significant. This was in contrast to the result obtained by earlier studies which reported significantly higher incidence of lower abdominal pain in misoprostol group than in placebo (p<0.001) [8].

A study by Saxena et al., found that intraoperative pain was significantly higher in placebo group and all patients required paracervical block while in misoprostol group no analgesia was required during the surgical procedure [11]. In our study, all patients were given intravenous sedation.

Incidence of nausea, vomiting and bleeding P/V varying from spotting to mild bleeding P/V was reported significantly higher in patients of study group (p<0.001), but the symptoms were well tolerable. An another study comparing vaginal and S/L misoprostol

for cervical priming before surgical evacuation of first trimester pregnancy, demonstrated rather high staff acceptability (p= .0001) for S/L misoprostol and no difference in patient satisfaction level in two groups (p=0.11), despite higher incidence of gastrointestinal side effects like nausea (p= .008), vomiting (p= .01), diarrhea (p= .01), and unpleasant mouth taste (p= .0001) in the sublingual group compared with the women in the vaginal group [8]. In our study, two cases of incomplete abortion were reported in the control group but no major complication like cervical tear or uterine perforation occurred in either group.

CONCLUSION

Sublingual misoprostol causes adequate cervical dilatation and facilitate surgical abortion by reducing blood loss, operative time and complication rate significantly. Henceforth this is an effective and safe alternative to mechanical cervical dilatation. However, larger studies are required to advocate its routine use before surgical abortion in first trimester abortions.

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