



## Effect of Intravaginal Isosorbide Mononitrate for First Trimester Preoperative Cervical Ripening

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### Abstract

*To compare the safety and efficacy of intravaginal administration of isosorbide mononitrate tablet as pre-surgical cervical ripening agent with those of intravaginal application misoprostol tablets before MVA for first trimester termination of pregnancy.*

**Methodology:** *It was randomized trial control study with conducted on 50 women, randomly divided into 2 groups- A and B. The women in group A were given Isosorbide mononitrate tablet(two 20 mg tablets) into the posterior fornix of vagina 3 hrs before MVA.*

**Results:** *In Group A 36% required further dilatation, in Group B 16% required further dilatation, In Group A 64% & Group B- 84% did not require further dilatation. And we have found statistically significant p value in Group B in respect of Group A i.e (0.02).*

**Conclusion:** *To conclude this study reveals that intravaginal Misoprostol can also be used as an effective and safe alternative to Isosorbide mononitrate for cervical ripening prior to first trimester surgical termination of pregnancy.*

### Introduction

Unsafe abortion and associated morbidity and mortality in women are preventable. In developing countries, there is poor utilization of recognized facilities and unmet need for an easily available method of early pregnancy termination which is both safe and effective.<sup>[1]</sup>

The WHO's preferred methods to safely and effectively terminate pregnancy during the first trimester of pregnancy are vacuum aspiration and medication abortion<sup>[2]</sup>.

Cervical priming prior to surgical evacuation reduces the risk of cervical injury by making the cervix softer and easier to dilate up to the desired size.

The World Health Organization provides clear guidelines on the use, benefits and risks of misoprostol for abortions.<sup>[3]</sup>

Prostaglandins (PGs) and their analogues of the E series are the most commonly used drugs for preinduction cervical ripening<sup>[4,5]</sup>. Although PGs are effective cervical-ripening agents, they are associated with several adverse effects, such as gastrointestinal symptoms, fever, pain, and high incidence of tachysystole, uterine hyperstimulation, and even uterine rupture<sup>[6,7]</sup>.

### Methodology

The study was conducted among the women attending gynaecology outpatient department of

BLDE (Deemed to be University), Shri B M Patil Medical College Hospital & Research Centre, Bijapur with a period of gestation between 6 and 12 weeks, requesting MTP.

**Study Type:** Randomized trial control study.

**Study Period:** 1 Year (January 2018 to December 2019).

**Place of Study:** Department of Obstetrics & Gynaecology of BLDE (Deemed to be University), Shri B M Patil Medical College Hospital & Research Centre, Bijapur.

All patients were receive routine history, physical examination, and blood tests. Gravida, Parity, Menstrual history, Last normal menstrual period (LNMP), Gestational age, USG findings of Fetal profile (for confirmation of gestational age and no of foetus), No of prior normal and caesarean deliveries and any previous h/o D/E or D/C, h/o any previous cervical surgery, preoperative Hb%, h/o allergy to prostaglandin group of drugs, h/o bronchial asthma, any cardiovascular disease if any, was documented. A predesigned proforma for history taking and collection of preoperative, operative data would be used. Data was collected

and recorded according to the case record form and analysed according to statistical analysis plan.

### Study Procedure

Patients Requesting termination of pregnancy with a period of gestation between 6 and 12 weeks, scheduled to have surgical termination of pregnancy by MVA, was included in this study after going through the inclusion and exclusion criteria was admitted after clinical examinations and detailed history taking. Routine baseline investigations was done. Written informed consent were obtained from each woman prior to inclusion into the study. Then the eligible Patients was divided into two groups (A and B) using a computer-generated randomization protocol having 25 women in each arm.

### Two Groups

- **Group A:** They were receive 400 mcg of tablet misoprostol (200mcg 2 tablets) into the posterior fornix 3 hours before MVA.
- **Group B** They were receive moistened intravaginal study drugs i.e. 40 mg of Isosorbide mononitrate tablet (two 20 mg tablets) into the posterior fornix of vagina 3 hrs before MVA.

## Results

**Table: 1.** Clinical Details of the women participating in the study

Characteristic	Group A (Misoprostol)		Group B (Isosorbide mononitrate)		P Value
	Mean	SD	Mean	SD	
Age	23.210	±2.421	24.120	±1.516	0.39 (NS)
Gestational age	10.06	±1.22	9.875	±1.302	0.41 (NS)

The mean age of Group A patients and Group B patients was 23.210 ±2.421 and 24.120 ±1.516 respectively. The mean gestational age of Group A and B was 10.06 ±1.22 and 9.875 ±1.302. Over

analysis for mean age and gestational age of the two groups we found no significance difference (p value =>0.05).

**Table: 2** Cervical resistance of the responders in two groups

Cervical resistance	Group A (Misoprostol)		Group B (Isosorbide mononitrate)	
	No	%	No	%
Nil	14	56	21	84
Mild	11	44	04	16
Severe	00	00	00	00
Total	25	100	25	100
Chi square – 4.666		p value 0.03		

In Group A 44% required further dilatation, in Group B 16% required further dilatation, In Group A 56% & Group B- 84% did not require further

dilatation. And we have found statistically significant p value in Group B in respect of Group A i.e (0.03).

**Table: 3** Cervical dilatation of the women participating in the study

Cervical dilatation (mm)	Group A (Misoprostol)		Group B (Isosorbide mononitrate)	
	No	%	No	%
≤ 8	10	40	04	16
10	08	32	05	18
12	07	28	16	66
Total	25	100	25	100
<b>Chi- square- 6.785 p value 0.03</b>				

Table 3 shows 16 patients in Group B and 07 patients in Group A had 12 mm dilatation, 10 women in Group A and 4 women in Group B had

≤8 mm dilatation and 08 patients of Group A and 05 patients of Group B had 10 mm dilatation with a significant p value of 0.03.

**Table 4** Postoperative Adverse effect

Specific adverse effect	Group A (Misoprostol)	Group B (Isosorbide mononitrate)	p value
Abdomen Pain	7 (28%)	14(56%)	0.04 (S)
Fever	04 (16%)	11 (44%)	0.03(S)
Headache	09 (36%)	4 (16%)	0.03 (S)
Nausea	03 (12%)	12 (48%)	0.00 (S)
Vomiting	01 (04%)	07 (28%)	0.02 (S)
Palpitation	07 (28%)	04 (16%)	0.24 (NS)

Post-operative adverse effects of both groups are mentioned in Table 4. In Group A patients headache and palpitation (36%) was the most common finding followed by abdominal pain (28%), fever (16%), nausea (12%) and vomiting (4%). In Group B the most common post operative adverse effect was abdominal pain (56%) followed by fever (44%), nausea (48%), palpitation (16%), vomiting (28%), headache and dizziness (8%). Above analysis for post operative adverse effects we found significant difference in both groups for abdomen pain, fever, headache, nausea with a p value of ≤0.05.

### Discussion

In our study we have found, The mean age of Group A patients and Group B patients was 23.210 ±2.421 and 24.120 ±1.516 respectively. The mean gestational age of Group A and B was 10.06 ±1.22 and 9.875 ±1.302. Over analysis for mean age and gestational age of the two groups

we found no significance difference (p value =>0.05).

The similar study by Vineeta mohindra, vaginal misoprostal for first trimester termination the study group was irrespective of the maternal age and according to Thomson Aj et al, (1998)<sup>[8]</sup> study, the patients were maximum in the age group of 21-30 yrs. In the gestational age was less than 12 wks.

Suk et al published in Human Reproduction in 1999, the average period of gestation was 9.5 weeks which is similar to that in our present study<sup>[9]</sup>

In our study, in Group A 44% required further dilatation, in Group B 16% required further dilatation, In Group A 56% & Group B- 84% did not require further dilatation. And we have found statistically significant p value in Group B in respect of Group A i.e (0.03).

According to Licf, chan cw (2003)<sup>[10]</sup> study of comparison of ISMN with misoprostol in cervical

ripening before suction evacuation more than 80% cervical ripening agent acceptable.

**Suk et al**,<sup>[9]</sup> the mean cervical dilatation in the group using 400µg misoprostol by vaginal route was 6.8 mm, whereas in our study, the corresponding value is 10 mm.

The mean dilatation achieved on following similar protocol using misoprostol in the study by **Fong et al**<sup>[11]</sup> was 8.2mm, whereas that in case of study by **Ngai et al**<sup>[12]</sup> published in *Contraception* in 1995 was 8.1 mm.

In a study by **Mandlekar et al** published in *Prostaglandins and medicine* in 1981, cervical dilatation was studied in 223 cases of first trimester abortion using prostodin. They found that cervical dilatation of 10 mm or more was achieved within 4 hours in 86% cases, whereas the cervical dilatation of > 10 mm in the present study was seen in 66% in group B and 28 % in group A.

In study by **Krishna et al**<sup>[13]</sup> published in *Contraception* in 1986, they concluded that misoprostol was more effective than prostodin in terms of cervical dilatation. And we have also found misoprostol group was more effective than Isosorbide mononitrate group.

We shows 16 patients in Group B and 07 patients in Group A had 12 mm dilatation, 10 women in Group A and 4 women in Group B had  $\leq 8$  mm dilatation and 08 patients of Group A and 05 patients of Group B had 10 mm dilatation with a significant p value of 0.03.

In our study, Post-operative adverse effects of both groups are In Group A patients headache and palpitation (36%) was the most common finding followed by abdominal pain (28%), fever (16%), nausea (12%) and vomiting (4%). In Group B the most common post operative adverse effect was abdominal pain (56%) followed by fever (44%), nausea (48%), palpitation (16%), vomiting (28%), headache and dizziness (8%). Above analysis for post operative adverse effects we found significant difference in both groups for abdomen pain, fever, headache, nausea with a p value of  $\leq 0.05$ .

The study by **Bygdaman** published in *International journal of obstetrics and gynecology*

in 1988 compared the side effects between prostaglandin E analogues and F analogues in pregnancy termination, among other things. They noted that with the E analog, the frequency of gastrointestinal side effects was significantly lower than with the F analog. The mean number of episodes of vomiting and diarrhea per patient was for the E analog 1.0 and 0.4, respectively. The corresponding figures for prostodin were 2.3 episodes of vomiting and 2.2 episodes of diarrhea per patient<sup>[14]</sup>.

### Conclusion

Intravaginal Isosorbide mononitrate achieves better cervical dilatation compared to. Misoprostol. Use of misoprostol gives poor patient satisfaction as compared to Isosorbide mononitrate.

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