Randomized Controlled Study Comparing Sublingual to Vaginal Misoprostol for Cervical Priming Prior to Surgical Termination of Pregnancy in First Trimester

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ABSTRACT

Background: To compares the effectiveness and acceptability of sublingual versus vaginal route of misoprostol for cervical priming prior to vacuum aspiration. Material and methods: In this prospective clinical study, a total of 70 women with period of gestation between 6 and 12 weeks selected randomly for day surgery abortion were sequentially allocated into two groups of 36 and 34. All selected women received 400 mg of misoprostol 3 hours prior to vacuum aspiration either by sublingual or by vaginal route in the hospital. Results: For all periods of gestation, sublingual misoprostol significantly improved cervical dilatation. Duration of the procedure and amount of blood loss were comparable in both the groups. Patient acceptability was higher in the sublingual group. Conclusion: Cervical priming with sublingual misoprostol is effective and convenient route with high patient acceptability rate.

Keywords: Vaginal, sublingual, misoprostol, cervical priming, first trimester, abortion

Vacuum aspiration is currently one of the standard management for the termination of pregnancy in first trimester with success rate of >95%, but it is associated with cervical injury, uterine perforation, hemorrhage and incomplete uterine evacuation. Cervical priming prior to surgical termination of pregnancy reduces the risk of various complications. Previously Laminaria tent, Dilapan have been used, but pharmacological cervical priming is preferred to mechanical dilatation. Various prostaglandins like gemeprost (prostaglandin E₁ [PGE₁] analog) have been found to be more beneficial, because they are easy to administer and very effective but they are expensive and require refrigeration storage and are associated with high gastrointestinal effects like nausea, vomiting and diarrhea. Misoprostol is a synthetic analog of PGE₁. Misoprostol has the advantage of easy availability ease of administration by various routes, lower cost and stability of room temperature with few systemic side effects. Various studies established the efficacy and safety of oral and vaginal route. Oral misoprostol has the advantage that patient can take the medicine at home prior to hospital admission, but oral misoprostol needs to be administered 12 hours prior to surgery for cervical ripening. Vaginal route has been found to be more effective than oral because of slower, but more constant absorption through the vaginal mucosa. Vaginal route is associated with less gastrointestinal side effects. It was found that 400 mg misoprostol given 3-hour before the procedure was the optimal dose for vaginal application. Vaginal route is most preferred route inspite of having inconvenience and lack of privacy. There are studies that showed the efficacy of sublingual route for cervical priming in first trimester abortion. Sublingual route has been proven to be more effective than oral. There are limited number of studies comparing the effect of sublingual misoprostol with vaginal misoprostol for cervical priming prior to first trimester abortion. Ngai et al reported oral administration of misoprostol 3-hour prior to vacuum aspiration was as effective vaginal misoprostol for cervical priming but administration of oral misoprostol 3-hour before the operation may causes if problems, if the patient undergoes the operation under general anesthesia. Misoprostol is absorbed through...
vaginal mucosa in vaginal administration. The buccal mucosa being very vascular is able to serve the same purpose. The misoprostol is very soluble in water and dissolves within 10-15 minutes when administered under the tongue. Sublingual administration of misoprostol avoids the first pass effect via the liver as in oral administration.

Sublingual misoprostol is convenient to use, avoids painful vaginal administration and avoids the ingestion of water before anesthesia with less gastrointestinal side effect. It is the aim of this randomized study to assess the efficacy and patients acceptability of sublingual misoprostol and compare it with vaginal misoprostol for preoperative cervical priming before surgical termination of pregnancy in first trimester.

MATERIAL AND METHODS

It is a prospective randomized controlled study. A total of 70 pregnant women with gestational age between 6 and 12 weeks were recruited from among women requesting legal termination of pregnancy from April 2009 to March 2010 in Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh; a medical college hospital for this prospective study. The local Ethical Committee approved the study protocol. A written informed consent was obtained after explaining the study. Women aged over 18 years with period of gestation between 6-12 weeks were included in the study. Criteria for inclusion were a normal general and gynecological history and physical examination. Gestational age was calculated by last menstrual periods (LMP) and was confirmed by clinical examination or ultrasonographic examination. Women suffering from chronic diseases like hypertension, diabetes, asthma, hemoglobin (Hb) <9 g/dL, allergic to prostaglandins, had an intrauterine contraceptive device (IUCD) and previous lower-segment cesarean section (LSCS) were excluded. Routine investigations included Hb, blood group and Rh typing.

The patients in each treatment group were sequentially allocated to receive 400 μg of misoprostol 3-hour prior to vacuum aspiration either by sublingual or by vaginal route (after wetting the tablet with water in order to increase the absorption through vaginal mucosa). Before the surgical evacuation the patients were asked about the side effects like abdominal pain graded from 0 to 3 (0 for no pain, 1 for mild pain, 2 for moderate pain that did not require treatment with analgesic, 3 for severe pain), nausea, vomiting, shivering, hyperthermia and vaginal bleeding noted. Vacuum aspiration was done by either of the two senior persons (NS or JBK) to reduce individual variation. The operation was done under sedation. All subjects were given to midazolam 2 g before the operation. Intraoperatively, cervical dilatation before performing vacuum aspiration was measured using Hegar dilators.

The dilators were passed through the cervix in descending order starting with size 12. The largest Hegar’s dilator passing through the internal os without resistance was regarded as the dilatation achieved. No further dilatation was performed, if the cervix had gestation appropriate dilatation. In patients with insufficient dilatation, paracervical block was given to reduce pain perception. Suction evacuation was done by Karman’s cannula. At the end of this procedure, the uterus was gently curetted by a curette.

Duration of surgery was measured from the start of dilatation until the end of curettage. Intraoperative blood loss was measured as the volume of the uterine aspirate after sieving away the products of conception. Intraoperative pain score was based on a numerical scale 0-10 with 0-3 mild, 4-6 as moderate and 7-10 as severe pain requiring injectable analgesics. Any cervical or uterine injury was noted. The women were observed for 3 hours before discharge from the hospital. Follow-up was done twice, first after 7 days and subsequently after 1 month. No major complaints were noted. The main study outcome measures were cervical dilatation prior to suction evacuation, amount of blood loss during surgery and time duration of surgery. Other evaluation factors were pain intensity, complications during surgery, side effects of misoprostol and acceptability of route of administration.

RESULTS

Age and obstetric profile is summarized in Table 1. Preoperatively, of the 70 patients who were given sublingual (n = 36) or vaginal (n = 34) misoprostol. Fifteen (41.66%) in the sublingual group versus 9 (26.47%) in the vaginal group had mild bleeding after 3-hour of administration of misoprostol. Mild spasmodic pain was experienced by 25 (69.44%) and 20 (58.62%) in sublingual and vaginal group, respectively. Four patients in sublingual group and one patients in vaginal group had nausea. One patient had hyperthermia in sublingual group (Table 2). There was a significant difference in average internal os diameter between two groups. Value of t-test is 0.00005627, which is significant. Three (8.33%) women in sublingual group as compared to 8 (23.52%) women in vaginal group were given paracervical block for the mechanical cervical dilatation, as these women had not
desired cervical dilatation. In 6 (17.64%) women out of 34 in vaginal group tablet was partially absorbed while in 2, it was intact after 3 hours of administration. In sublingual group, tablet was absorbed in all women within 10-50 minutes. The findings at operation are summarized in Table 3. A higher patient acceptability of sublingual (90%) route as compared to the vaginal (40%) route was noted. Reasons were that the vaginal route requires the patients to report to the hospital 3-hour prior to vacuum aspiration, while sublingual route was convenient and time saving.

**DISCUSSION**

This study suggest the feasibility of the sublingual route of misoprostol administration for cervical priming prior to first trimester surgical abortion using vacuum aspiration as the commonly used method for first trimester abortion. Cervical dilatation is the crucial step in vacuum aspiration as most of the cervical and uterine injuries are due to forceful cervical dilatation of the cervix. Cervical priming has been shown to result in shorter operation time, less blood loss and easier mechanical dilatation. The beneficial effects of pharmacological agents for cervical priming have been established. It does not require a trained medical personnel to administer and not painful for the patient. Mifepristone and PGE₁ analogs are effective cervical priming agents, but mifepristone is expensive and it has the disadvantage of requiring 36-48 hours for cervical priming. PGE₁ analog is drug of choice. Misoprostol is preferred, since it is cheap and stable at room temperature and it is associated with less gastrointestinal side effect than gemeprost. Various routes of administration of misoprostol have been used for cervical priming in the first trimester. Both oral and vaginal routes were shown to be equally effective when given 3 hours before the vacuum aspiration.

In one of the studies (Zieman et al 1997), the systemic bioavailability of vaginally administered misoprostol was three times higher than that of orally administered misoprostol and effect was prolonged, but there is wide variation in absorption of vaginal misoprostol and sometimes remnants of vaginal tablet may be found in the vagina after hours just like in this study in eight women. Both oral and vaginal routes have drawbacks. Some women found vaginal administration of drug inconvenient and unacceptable and it was more convenient to give a drug by mouth. In a day surgery setting at the same time it was better to avoid oral intake of fluid before operation especially if this was done under general anesthesia.

Sublingual misoprostol can avoid the uncomfortable vaginal application and oral intake of fluid before operation. Patient can take sublingual tablet at home thus reducing the time of hospital admission. Its clinical effectiveness in cervical priming was proven to be same as vaginal misoprostol in this study. Pilot studies reported the successful use of repeated doses of sublingual misoprostol for medical abortion. The sublingual route allows the use of most vascular area in the buccal cavity and the reported dissolving time is about 10-15 minutes. In this study, it was 10-50 minutes.

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**Table 1. Demographic Characteristic of the 70 Women Who Underwent Surgical Abortion**

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<thead>
<tr>
<th></th>
<th>Sublingual (n = 36)</th>
<th>Vaginal (n = 34)</th>
</tr>
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<tbody>
<tr>
<td>Age year (mean)</td>
<td>29.4 years (mean)</td>
<td>28.2 (mean)</td>
</tr>
<tr>
<td>(18-40 year)</td>
<td></td>
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<tr>
<td>Gestation (weeks)</td>
<td>8.7 weeks (mean)</td>
<td>8.5 weeks (mean)</td>
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<tr>
<td>(6-12 weeks)</td>
<td></td>
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<tr>
<td>Parity (P₀-P₆)</td>
<td>3.4 (mean)</td>
<td>3.6 (mean)</td>
</tr>
<tr>
<td>Women with history of surgical abortion</td>
<td>10 (27.77%)</td>
<td>8 (23.52%)</td>
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</tbody>
</table>

**Table 2. Preoperative Side Effects**

<table>
<thead>
<tr>
<th></th>
<th>Sublingual (n = 36)</th>
<th>Vaginal (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>4 (11.11%)</td>
<td>1 (2.94%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Vaginal bleeding scanty</td>
<td>15 (41.66%)</td>
<td>9 (26.47%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Pain (mild-to-moderate)</td>
<td>25 (69.44%)</td>
<td>20 (58.82%)</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>1 (2.77%)</td>
<td>Nil</td>
</tr>
<tr>
<td>Passage of product of conception before operation</td>
<td>Nil</td>
<td>Nil</td>
</tr>
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</table>
This provides a promising route of administering misoprostol avoiding first pass effect with oral route and inconvenience and discomfort to women with vaginal administration. The present study observed that cervical ripening effect and mean time taken by misoprostol were favorable among the sublingual group. Our result were consistent with the observation by various other studies. The mean intraoperative blood loss was less in the vaginal group though statically, it was not significant (value of t-test 0.331). The total duration of surgery was less in the sublingual group that can be explained on the basis of more cervical ripening and dilatation achieved in this group. This finding was consistent with other observations. Intraoperative pain score was found to be significantly lower in sublingual group. Saxena et al, Parveen et al and Tang et al also found significant difference with regard to this parameter. Vaginal bleeding and abdominal pain were the commonest side effects after misoprostol. In this study, very few women complained of severe abdominal pain. In most of the women, bleeding amount was scanty. In this study, there were few shortcomings:

- We did not use tonometer to measure the actual force applied for dilatation
- Surgeon and patient were not blinded to the route of administration
- Number of patients was relatively less.

CONCLUSION

It can be concluded that sublingual misoprostol is an effective and favorable cervical priming agent for first trimester abortion as compared to vaginal route. It can be conveniently self-administered at home thereby decreasing hospital stay and cost. It also has a good patient acceptability rate.

REFERENCES