The Effect of 1000 Microgram Vaginal Misoprostol on Preoperative Cervical Ripening before Diagnostic Hysteroscopy

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Abstract
Objective: To compare the effect of 1000 microgram vaginal misoprostol on preoperative cervical ripening before diagnostic hysteroscopy in premenopausal women with abnormal uterine bleeding.

Methodology: This study was conducted in Gynae/Obs Unit-II, Holy Family Hospital, Rawalpindi, from 22nd of January 2009 to 22 of July 2009. The data were collected from 70 women on a pre-structured proforma admitted to inpatient department for diagnostic hysteroscopy with abnormal uterine bleeding. Inclusion criteria were women above 40 years of age, previously delivered vaginally or by caesarean section and with previous cervical dilation and biopsy. An exclusion criterion was pregnancy, pelvic infection, and cervical cancer. The women were randomized to two groups of 35 each. In group A: women were given 1000mcg misoprostol vaginally 12 hours preoperatively to diagnostic hysteroscopy and in group B: women were taken as controls i.e. they underwent hysteroscopy without any drug for cervical dilatation. The effect of preoperative cervical dilatation was measured by passing Hegar dilators. Cervical dilatation of ≥5 mm was considered as satisfactory and the duration of cervical dilatation and hysteroscopy were noted in both groups.

Results: Among the premenopausal women receiving misoprostol, 88% (n=31) achieved cervical dilatation of >5mm compared with 65% (n=23) in the control group. The mean cervical dilatation in group A was 6.4 mm and 4.8 mm in group B. The mean difference in cervical dilatation was 1.6 mm (95% CI 0.5- 2.7), with a p- value<0.001. The mean time for cervical dilatation was 47 seconds in group A and 68 seconds in group B, with a p-value <0.001. Mean duration of hysteroscopy in minutes, in group A was 15 minutes whereas in group B it was 23 minutes

Conclusion: One thousand micrograms of vaginal misoprostol 12 hours prior to hysteroscopy has a significant cervical ripening effect requiring less instrumentation as compared with control group in premenopausal women. Duration of hysteroscopy is also reduced in women treated with vaginal misoprostol as less instrumentation was required for cervical dilatation.

Vaginal misoprostol 1000 microgram before hysteroscopy is safe, and is highly acceptable by the patient.

Keywords: Misoprostol; Hysteroscopy; Cervical priming; Premenopausal women.

Introduction
Diagnostic hysteroscopy has become a basic investigation in modern Gynaecology and has essentially replaced the time honored D & C (dilatation and curettage). Although hysteroscopy has been described since early 1800s, widespread use by practicing gynecologists did not occur until the 1980s. With improvements in optics, video systems, and distension media, there has been an increased acceptance of hysteroscopy as the gold standard in the evaluation of the uterine cavity and treatment of intracavitary pathology. It can be done as an outpatient procedure, and is an integral component of a one-stop approach to the management of menstrual symptoms. Hysteroscopy provides a virtually instant diagnosis, and is the logical precursor to operative hysteroscopy. The royal college of obstetricians and gynaecologists (RCOG) has recognized the importance of diagnostic hysteroscopy and it is now part of core training in our specialty.

It is estimated that one of the common reason of all outpatient presentation is abnormal uterine bleeding. Abnormal uterine bleeding usually occurs at extreme of reproductive years, that is, under the age of 19 years and over the age of 39 years. Premenopausal transition is associated with greater occurrence of abnormal uterine bleeding. The incidence of menorrhagia is increased after the age of 40 years. A typical finding is menorrhagia in conjunction with oligomenorrhea. This is most commonly seen due to an ovulation in conjunction with increased estradiol levels. The abnormal uterine bleeding is associated with increased chances of endometrial hyperplasia and is associated with increased risk of endometrial carcinoma. Hysteroscopy can predict 40-50% of women with menorrhagia and irregular cycles previously diagnosed as dysfunctional uterine bleeding have sub mucus myomas.
and endometrial polyp. The common complications encountered during hysteroscopy are cervical laceration, uterine perforation, and creation of false tracts. Misoprostol is a synthetic prostaglandin (15-deoxy-16-hydroxy-16-methyl PGE analogue). It is cheap, stable at room temperature, and readily available in our country. It has proved effective for cervical dilatation before suction evacuation in the first and second trimester of pregnancy. Recently, effect of misoprostol for cervical ripening in nonpregnant women to prevent cervical injury during dilatation has been evaluated in many trails. One trial has shown misoprostol to be effective among premenopausal women achieving 88% of cervical dilatation of ≥5mm as compared to 65% in the placebo group. Another study showed misoprostol to be promising but further research is required to identify ideal dose, route, and timing of administration of misoprostol. The mean cervical dilatation of ≥5mm will be considered satisfactory. This study will help to reduce burden on in patient department while performing hysteroscopy as office procedure in our setup as hysteroscopy is not used as office procedure yet in our tertiary care hospital but will have better outcomes in relation to reducing total time of procedure and resistance and force to dilatation thus in future reducing inpatient admission.

Patients and Methods

The present study was conducted in the department of gynecology, Holy family hospital, Rawalpindi, from January to July 2009. The data was calculated by using WHO sample size calculator taking level of significance 5%. Power of test 90%, population proportion P1=88% population proportionP2=65% and sample size (n)=70 (35 in each group). Total of 70 women were admitted to inpatient department for diagnosis hysteroscopy with abnormal uterine bleeding above 40yrs of age, previously delivered vaginally or by caesarean section and with previous cervical dilatation and biopsy, were included in the study. Patients with pregnancy, pelvic infection, and cervical cancer were excluded. Women who were suspected of being in early pregnancy were excluded by urine pregnancy test and patients with genital tract infections were excluded on the basis of history and examination. All routine investigations including blood group, CBC, random blood sugar, urine routine examinations, HBsAg, Anti HCV and pelvic ultrasound were carried out in all women, after informed consent. Preoperative anaesthesia fitness was obtained. The women were either randomized to two groups, 35 premenopausal women in each.

Group A: Women in this group were given 1000mcg misoprostol vaginally 12 hours before diagnostic hysteroscopy.

Group B: Women in this group were taken as controls i.e. they underwent hysteroscopy without any drug for cervical dilatation.

All patients were NPO from midnight. Examination under anaesthesia was done and the effect of preoperative cervical dilatation was measured by passing Hegar dilators. Cervical dilatation of ≥5 mm was considered as satisfactory and the duration of cervical dilatation were noted in both groups. Hysteroscope was then introduced through cervix and uterine cavity was distended with 0.9% normal saline at a rate of 50 ml/min and all these details were entered in pre-structured proforma. All calculations were done by SPSS version 10.

- Mean and standard deviation were calculated for quantitative variables (age, height, weight, BMI and duration of procedure).
- Frequency and percentages were calculated for qualitative variable (number of Hegar dilator).
- Independent sample t-test was used to compare duration of cervical dilatation and hysteroscopy in both groups.
- Chi square test was used to compare cervical dilatation ≥5mm in both groups; p-value <0.001 was considered significant.

Main outcome measures: Preoperative cervical dilatation ≥5mm is the primary outcome and time required for dilatation.

Results

The results of the study are tabulated in Table 1. In group A 18 (51.14%) patients were of age <45 years, 11 (31.14%) patients were between the age range of 45-50 years and 6(17.14%) patients of age >50 years. The mean age in A 23(65.7) patients were of height >5.5 feet and 12 (34.3%) patients were group A was 43 years. In group B 20 (57.14%) patients were of age <45 years, 11 (31.14%) patients were between the age range of 45-50 years and 4(11.14%) patients were of age >50 years. The mean age in A was 42 years, as shown in table 1. Therefore mean height in group A was 5.5 feet. In group B 21(60%) patients were of height >5.5 feet and 14(40%) patients were of height <5.5 feet. While in group B mean height were 514 feet. In group A 2(6%) patients were of weight <50 kg, 29(83%) patients were of weight between 50-80 kg and 4(11%) patients were of weight >80 kg. Hence mean weight of patient in group A was 62 kg. In group B 2(6%) patients were with a weight <50 kg, 27(77%) patients were of a weight between 50-80 kg and 6(17%) patients were of weight >80 kg. The mean weight in group B was 66 kg. In group A, 4(11%) patients had a BMI of <20, 25(71.4%) patients had a BMI 20-30 and 6(17%) patients had a BMI of >30. Therefore Mean BMI in group A was 24 kg/m². In group B 4(11%) patients had a BMI of <20, 23 (66%) patients had a BMI 20-30 and 8(25%) patients had a BMI of >30. Whereas in group B mean BMI was 25±2 kg/m² as shown in table I.
Table 1: Intra-Operative Findings: Distribution of Cervical Dilatation and Time in Two Treatment Groups

<table>
<thead>
<tr>
<th>Condition</th>
<th>Group A (n = 35)</th>
<th>Group B (n = 35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of women achieving cervical dilatation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 mm</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>Cervical dilatation, median (mean ± SD)</td>
<td>6.4 (2.4)</td>
<td>4.8 (2.0)</td>
</tr>
<tr>
<td>Cervical dilatation, range (mean ± SD)</td>
<td>6 (&lt;2-11)</td>
<td>5 (&lt;2-8)</td>
</tr>
<tr>
<td>Mean difference in cervical dilatation (mm)</td>
<td>1.623 (95% CI: 0.52-2.7)</td>
<td></td>
</tr>
<tr>
<td>Mean duration of hysteroscopy (minutes)</td>
<td>15</td>
<td>23</td>
</tr>
</tbody>
</table>

Chi square test was used to compare cervical dilatation in both groups. P-value <0.001 was considered significant. The cervical dilatation in the two treatment groups are shown in Table II. The mean cervical dilatation in group A was 6.4 mm (SD 2.4), whereas in group B was 4.8 mm (SD 2.0). The mean difference in cervical dilatation was 1.6 mm (95% CI 0.5-2.7). Among women receiving misoprostol in group A, 31 (88%) patients achieved a cervical dilatation of >5 mm as compared to group B with 23 (65%) patients who achieved a cervical dilatation of >5 mm. The P-value was <0.001.

Independent sample t-test was used to compare duration of cervical dilatation and duration of hysteroscopy in both groups. The mean time for cervical dilatation was 47 seconds in group A and 68 seconds in group B, with a p-value <0.001. Mean duration of hysteroscopy in minutes, in group A was 1.5 minutes whereas in group B it was 2.3 minutes, with a p-value of <0.001.

Discussion

The study demonstrated that 1000 microgram vaginal misoprostol 12 hrs prior to hysterectomy had a significant cervical ripening effect and also reduced time spending on hysterectomy with the significant difference in the mean duration of hysterectomy between the two groups which tailored toward the primary outcome measures of this study. Misoprostol is marketed for prevention and treatment of gastric ulcer disease. It is very inexpensive and can be kept at room temperature. This drug is being used for many years for pregnancy terminations in our tertiary care hospital, which is of low resources, very successfully. Effect of misoprostol for cervical ripening in nonpregnant women to prevent cervical injury during dilatation is still being evaluated. Misoprostol can be administered by many routes such as orally, vaginally, and rectally. On reviewing the national and international literature for the same topic, there were number of studies on use of misoprostol for preoperative cervical dilatation prior to hysterectomy. A review by Crane and Haley concludes that in premenopausal women, misoprostol appears to be promising as a cervical ripening agent prior to hysterectomy, although further research is needed to identify the ideal dose, route and timing.12 The dosages used in studies have varied from 200 and 1000 micrograms of misoprostol given between 2 and 24 hrs before hysterectomy via oral, sublingual and vaginal routes.13-16. Aronsson et al.17 studied the effect of vaginally and orally administered misoprostol on the local cervical inflammatory response Khan Ru et al.18 showed that vaginal misoprostol is present in the circulation longer than oral misoprostol.

In my study, the premenopausal women receiving misoprostol, the mean cervical dilatation was 6.4 mm (SD 2.4) and 4.8 mm (SD 2.0) in the control group. The mean difference in cervical dilatation was 1.6 mm. Among the women receiving misoprostol (n=31) 88% achieved a cervical dilatation of >5 mm as compared with (n=23) 65% in the control group. Dilatation was less required and quicker in misoprostol group. The mean time for cervical dilatation was 47 seconds in group A (misoprostol group) and 68 seconds in group B (control group), with a p-value <0.001. Mean duration of hysterectomy in minutes, in group A was 1.5 minutes whereas in group B it was 2.3 minutes, with a p-value of <0.001.

There were certain limitations in my study such as the number of patients and mainly involve postgraduate trainees to perform the procedures who are relatively less experienced. The bias regarding expertise can be removed by involving experienced staff. Other limitation were that this regimen was mainly given in different studies to see effect and facilitate cervical dilatation prior to operative hysterectomy which is not being done in our hospital due to less experienced staff. But I choose diagnostic hysterectomy and curettage which is a gold standard technique for premenopausal women with abnormal uterine bleeding who are at risk of endometrial hyperplasia, which is being practiced in our hospital.

Conclusion

Offering this inexpensive and easy-to-use regimen to premenopausal women prior to undergoing hysterectomy facilitates cervical dilatation. Administration of vaginal misoprostol of 1000 microgram the evening before hysterectomy is safe and highly acceptable method for cervical ripening in premenopausal women.

References

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