**ABSTRACT**

**BACKGROUND:** This study was carried out to evaluate the efficacy, safety, advantages and complications, if any, of oral misoprostol as an agent for cervical priming prior to minor uterine procedures. The objective of this study was to answer the question that ‘is the use of oral misoprostol beneficial as an agent for cervical priming prior to minor uterine procedures?’

**MATERIAL AND METHOD:** In this randomized prospective study over a period of three years, all women for minor uterine procedures like Medical Termination of Pregnancy (MTP) by suction evacuation, Dilatation & Curettage (D & C), Hysterosalpingography (HSG) and Office Hysteroscopy were randomly selected as cases or controls. The cases were given 400 μg of oral misoprostol four hours prior to the procedure. All these procedures were performed under sedative medications in both the cases and controls. The need for cervical dilation and the perception of pain on numeric scale were noted in all the groups. Additionally, the amount of blood loss was also noted in the MTP group.

**RESULTS:** The cases that were given oral misoprostol prior to minor uterine procedures required less dilation & experienced less pain than the controls. There was significantly less blood loss during the MTP in cases.

**CONCLUSION:** The results of this study suggest that the use of oral misoprostol as an agent for cervical priming prior to the minor uterine procedures can be efficacious, safe and advantageous.

**Keywords:** Oral misoprostol, Cervical priming, Medical Termination of Pregnancy, Dilatation & Curettage, Hysterosalpingography, Office Hysteroscopy.

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**INTRODUCTION**

Minor uterine procedures like Medical Termination of Pregnancy (MTP) by suction & evacuation, Dilatation & Curettage (D & C), Hysterosalpingography (HSG) and office hysteroscopy are one of the most frequently performed gynecological operations throughout the world. All these procedures require opening up the cervix to introduce one or the other instrument inside the uterine cavity. This first step of dilatation of the cervix carries several risks like pain, injury to cervix, false passage, uterine perforation & bleeding. In this scenario, if a conventional method can be simplified with a use of a newer drug that can reduce pain and help open up the cervix easily, it is likely to be welcome by all involved in providing the abortion care, gynecology care and infertility care.

The development of newer prostaglandin analogues offers more advantages in the management of cases requiring cervical dilatation. Misoprostol is a comparatively newer synthetic 15-deoxy-16-hydroxy-16-methyl analogue of Prosta-glandin E1 (PGE1), originally discovered as a gastro-protective and gastric acid anti-secretory agent. But, it is subsequently found to have uterotonic and cervical ripening effects too. Misoprostol has been widely used for this purpose because of its effectiveness, low cost, ease of administration and dosage, stability in light and hot climate and fewer side effects.

Misoprostol is rapidly absorbed following oral administration and its bioavailability exceeds 80%. Peak plasma concentrations occur in 30 to 60 minutes, following an oral dose of 400 μg, which is higher than the vaginal administration. The oral and sublingual routes are known to have quickest onset of action. The metabolites after oral administration undergo biphasic elimination, where the fast phase lasts for 1.5 hours while the slow phase extends up
Cervical Priming with Misoprostol prior to minor uterine procedures

Oral misoprostol is found to have fewer side effects on the other hand. The optimal dose of misoprostol for cervical priming prior to minor uterine procedures has been considered to be 400 μg in number of other studies. The recommended interval between administration of misoprostol for cervical priming and commencement of actual procedure is at least three hours. Thus, to study these effects, it was decided to use 400 μg of Misoprostol orally 4 hours prior to the intended procedure in the present study.

MATERIAL & METHODS
This was a randomized prospective study for duration of three years. There were four groups under this study, with all the groups having cases and controls. The first group comprised of all those women who underwent voluntary termination of pregnancy in first trimester by suction & evacuation. They were randomly distributed as a case or as a control. The parameters like duration of pregnancy, parity and number of previous caesarean sections were matched. Inclusion criteria were gestational age of 12 weeks or less. Exclusion criteria were gestational age of more than 12 weeks, unsure gestational age, two or more previous caesarean sections, cardio-respiratory disorders, Hemoglobin (Hb) < 8 g/dl. Gestational age was estimated by last menstrual period (LMP) and pelvic examination. Ultrasonography was performed to confirm the gestational duration.

The second group consisted of all non-pregnant patients undergoing D & C for gynecological reasons.

The third group comprised of women undergoing HSG.

The last group consisted of all women undergoing office hysteroscopy.

For all groups, a detailed history was taken, basic investigations were carried out and a written informed consent was obtained.

Considering the pharmacological actions, the dose of 400 μg orally was selected, to be taken in the early morning of the procedure for cases in all the groups. The controls were given placebo instead of misoprostol.

All the subjects were asked to come to the operation theater in the morning at eight. Sedative medications along with systemic analgesics were given to all the subjects prior to the procedure. Anesthesia was not used in any of the cases. The intended procedure was then carried out in a standard manner. In all the controls, routine Hegar’s cervical dilators were used at the beginning of the intended procedure. The effect was objectively noted on different aspects, the cervical dilation prior to commencing the procedure and the perception of pain by the subjects as evaluated after the procedure on the numeric pain scale of 1-10. In the group of MTP, the amount of bleeding during the procedure was also noted. The highest number of Hegar’s dilator that can be easily introduced at the commencement of the procedure was noted for each subject.

For the group of MTP, it was ensured that the suction tubing and the bottle were completely empty at the beginning of the procedure. The termination of pregnancy was carried out with the suction and evacuation method using plastic cannula of appropriate number. Then at the end of the procedure, all material and fluid were passed through the filter and the filtered out blood, free of products of conception, was measured objectively with the jar marked in milliliters. The parameter of bleeding was analyzed only for the group of MTP and not for the other groups. All the subjects were asked about the degree of pain perceived on a numeric pain scale of one to ten with ten being the most severe pain.

All these findings were systematically recorded into SPSS software, version 20.0 and were analyzed with Chi-square test of significance with or without Yate’s correction as per the recommendation.

Table 1 shows the total number of cases and controls, both of which are 250 in this study. They are further divided into three groups as mentioned above. As seen from the table, the distribution of cases and controls in each of these groups are
comparable in terms of gestational age at the time of termination of pregnancy.

RESULTS

Table: 1 Cases & Controls as per the gestational age.

<table>
<thead>
<tr>
<th>No. of Subjects</th>
<th>CASES (n=250)</th>
<th>With Previous C. Section (n=9) (%)</th>
<th>CONTROLS (n=250)</th>
<th>With Previous C. Section (n=9) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=6 weeks</td>
<td>Total (440)</td>
<td>1 (0.40%)</td>
<td>9 (3.60%)</td>
<td>2 (0.80%)</td>
</tr>
<tr>
<td>&gt;6 to &lt;=8 weeks</td>
<td>92 (3.60%)</td>
<td>4 (1.60%)</td>
<td>105 (42.00%)</td>
<td>4 (1.60%)</td>
</tr>
<tr>
<td>&gt;8 to &lt;=10 weeks</td>
<td>89 (35.60%)</td>
<td>3 (1.20%)</td>
<td>88 (35.20%)</td>
<td>5 (2.00%)</td>
</tr>
<tr>
<td>&gt;10 to &lt;=12 weeks</td>
<td>58 (23.20%)</td>
<td>1 (0.40%)</td>
<td>48 (19.20%)</td>
<td>3 (1.20%)</td>
</tr>
</tbody>
</table>

Table: 2 Comparison of Dilation Required in two groups as per Duration of Gestation

<table>
<thead>
<tr>
<th>Duration of gestation &amp; dilation</th>
<th>CASES (n=223)</th>
<th>Dilation not required (n=6)</th>
<th>Dilation required (n=117)</th>
<th>Chi-Square &amp; DF</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=6 weeks</td>
<td>11</td>
<td>4%</td>
<td>6%</td>
<td>28.76 (with Yate’s Correction), at 3 Degrees of Freedom</td>
</tr>
<tr>
<td>&gt;6 to &lt;=8 weeks</td>
<td>90</td>
<td>36%</td>
<td>7%</td>
<td>13.82</td>
</tr>
<tr>
<td>&gt;8 to &lt;=10 weeks</td>
<td>81</td>
<td>32%</td>
<td>8%</td>
<td>19%</td>
</tr>
<tr>
<td>&gt;10 to &lt;=12 weeks</td>
<td>41</td>
<td>16%</td>
<td>17%</td>
<td>19%</td>
</tr>
</tbody>
</table>

Table: 3 Comparison of Blood Loss in two groups.

<table>
<thead>
<tr>
<th>Amount of blood loss</th>
<th>CASES (n=250)</th>
<th>CONTROLS (n=250)</th>
<th>Chi-Square &amp; DF</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 ml</td>
<td>188</td>
<td>75.20%</td>
<td>48.80%</td>
</tr>
<tr>
<td>50-100 ml</td>
<td>34</td>
<td>33.20%</td>
<td>48.80%</td>
</tr>
<tr>
<td>&gt;100 ml</td>
<td>28</td>
<td>18.00%</td>
<td>48.80%</td>
</tr>
</tbody>
</table>

Table: 4 Comparison of Pain Score in two groups.

<table>
<thead>
<tr>
<th>Pain scoring</th>
<th>CASES (n=250)</th>
<th>CONTROLS (n=250)</th>
<th>Chi-Square &amp; DF</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>207</td>
<td>82.80%</td>
<td>60.40%</td>
</tr>
<tr>
<td>4-6</td>
<td>36</td>
<td>14.40%</td>
<td>31.20%</td>
</tr>
<tr>
<td>7-10</td>
<td>7</td>
<td>2.80%</td>
<td>8.40%</td>
</tr>
</tbody>
</table>

The Table 1 also shows the distribution of subjects with previous one caesarean section in each of the groups of cases and controls. As seen form this table, the respective numbers of cases in each gestational age group, are comparable in cases and controls. Thus, this data also supports the standardization of the study. Table 2 compares the need of dilation in cases and controls for the different gestational age groups. As seen here, in <=6 weeks group, none of the cases required dilation, whereas three controls required dilation. In remaining three groups, the procedure was not possible without dilation in any of the controls. Amongst cases, increasing number required dilation as the gestational age increased. These findings were statistically analyzed using Chi-square test with Yate’s correction. At three degrees of freedom and at P= 0.001, the table value of Chi-square is 16.27 which is much less than the obtained Chi-square value of 28.76. Thus, this finding is statistically significant at P=0.001. Thus, the cases that were given oral misoprostol required less dilation than the controls.

Table 3 explains relative blood loss in cases and controls. The blood loss was divided into three groups as <50 ml, 50-100 ml and > 100 ml. There were more subjects with blood loss of < 50 ml in cases than controls. Whereas in the other two groups, this number was higher in controls than cases. The Chi-square test was applied to these results as well. As seen here, at two degrees of freedom and at P=0.001, the Chi-square value of the Probability table is 13.82 which is less than the obtained Chi-square value of 38.53. Thus, this difference of blood loss in cases versus controls is statistically significant at P=0.001.

Table 4 compares the perceived pain score of cases and controls. The pain is categorized as mild, moderate or severe depending on the pain score of 0-3, 4-6 and 7-10 respectively. As seen in the table, there are 207 cases and 151 controls with mild pain. The subjects with moderate and severe pain are 36 & 7 in cases and 78 & 21 in controls respectively. Again analyzing with Chi-square test, at two degrees of freedom, at P=0.001, the table value of Chi-square is 13.82 versus
obtained Chi-square value of 31.23. This shows that the result of pain score is also statistically significant at P=0.001. Hence, the cases with oral misoprostol experienced less pain than their controls without misoprostol. This is because the pain during the minor uterine procedures mainly occurs during cervical dilation. And with the use of misoprostol as an agent for cervical priming, the pain experienced by the cases is significantly less.

Finally, the complications were also compared in the two groups, as shown in table 5. The complications noted were cervical laceration or injury, uterine perforation, scar rupture & incomplete evacuation. The Chi-square test with Yate’s correction was applied to the obtained results. At four degrees of freedom and P=0.5, the table value of Chi-square is 2.37 which is higher than the obtained value of 1.01. Thus, there is no statistically significant difference in the occurrence of complications in two groups. Hence, the use of oral misoprostol prior to termination of pregnancy does not result in the decrease of the complications.

**DISCUSSION**

Present study was conducted to find out efficacy, safety, advantages and complications, if any, of oral misoprostol as an agent for cervical priming prior to minor uterine procedures. The use of oral misoprostol decreases the requirement of cervical dilation at the beginning of minor uterine procedures. This is because of the established ripening effect of this drug on the cervical tissue leading to significant cervical dilation. Similar results are also obtained in studies conducted earlier by More B, Radulovic N et al and Claudio C et al.

The blood loss during the procedure is also found to be less in the cases with the prior use of misoprostol. This can be explained on the basis of uterotonic effect of misoprostol that causes better separation of the placenta and allows placental bed to contract avoiding extra bleeding which would otherwise occur from open sinuses of placental bed. This finding is also supported by other studies by Tang OS et al and Fiala C et al.

And finally, the perception of pain is significantly less with the use of misoprostol as a cervical priming agent. With the use of misoprostol, the stretching of the cervix by the cervical dilator would be avoided in many cases or would be needed to a very lesser extent. Thus, the overall perception of pain will be significantly less. The reduced perception of pain is also reported in studies carried out by Fiala C et al and Gemzell Danielsson K et al.

The number of complications remains the same with the use of oral misoprostol in our study. However, in one such similar study by Fiala C et al, the complications are found to be less with the use of misoprostol. Possibly, a larger sample size is required to establish this observation.

**CONCLUSION**

From this randomized prospective study, it can be concluded that the use of oral misoprostol as an agent for cervical priming prior to the minor uterine procedures can decrease the need of mechanical cervical dilation, can reduce the pain and the amount of bleeding. Cervical Priming with Misoprostol prior to minor uterine procedures.

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Cervical Priming with Misoprostol prior to minor uterine procedures


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