ABSTRACT

Background: Difficulty in cervical dilatation is a hard situation during the procedure of diagnostic dilatation and curettage in some cases. This study was performed to evaluate the effect of vaginal misoprostol for cervical priming before diagnostic dilatation and curettage. Methods: In this study 56 women were selected as the candidates for dilatation and curettage. The study was double blind and was performed for two parallel groups. One misoprostol tablet (200 μg) was administered in posterior fornix of vagina 2-4 hr before operation in 28 patients whereas in other 28 patients, placebo (VitB6) was used. Then, the two groups were compared according to the patency of the cervix measured by No. 5 Hegar dilators and the duration of dilatation and curettage procedure as well. Chi-square test, t-test, and Mann-Whitney U test were used for comparing two groups, and a p-value less than 0.05 was considered as statistically significant. Results: Before the procedure of dilatation and curettage, the patency of the cervix was measured by passing Hegar dilator number 5 through the cervical canal in fifteen (53.6%) patients in the misoprostol group and 8 patients (28.6%) in the placebo group (p=0.05) which their difference was statistically significant. The effect of misoprostol was not significant in nulliparous women and postmenopausal period either. Conclusion: Vaginal misoprostol is a useful drug for ripening and dilating the cervix. It also facilitates the procedure of dilatation and curettage in premenopausal and multiparous women. Misoprostol was less effective in nulliparous women and in postmenopausal period.

KEYWORDS: Cervical ripening, Curettage, Dilatation, Misoprostol.
INTRODUCTION
abnormal uterine bleeding is a common problem that gynecologists encounter and most of the patients have benign disease, but need more evaluation especially after the age of 35.[1]

Difficulty in dilating the internal cervical os is a common problem in performing curettage. The complications related to this problem include cervical trauma, creation of false tract and uterine perforation.[2] Ripening the cervix before curettage reduces commonness of these complications. A few studies are available on the use of misoprostol for ripening the cervix prior to gynecological procedures on women. Nowadays misoprostol has become a desirable agent due to its beneficial effects on cervical ripening on nonpregnant women.[3-5]

Originally, misoprostol as a synthetic prostaglandin
E1 analogue was administered for prevention and treatment of gastric ulcer diseases. One of the effects of this agent has been dilatation of cervix which is used in gynecology because of its effectiveness and ease of administration.[6,7] After oral administration, misoprostol is rapidly absorbed. The half life of this agent is about 20 to 40 minutes.[7] Adverse effects of misoprostol after oral administration are nausea, vomiting, diarrhea, abdominal cramps, and fever which are dose dependent. Gastrointestinal side effects are decreased if the tablets are administered vaginally.

Vaginal application of misoprostol, results in a slower increase in plasma but overall exposure to the drug is increased.[8] This study was conducted in order to evaluate effectiveness of misoprostol on ripening the cervix before dilatation and curettage.

MISOPROSTOL
Misoprostol is a synthetic prostaglandin (PG) E1 analogue. Naturally occurring PGE1 is not orally sustainable, as it is unstable in acid media and is also not suitable for parenteral use because of its rapid degradation in the blood. Misoprostol, the synthetic PGE1 analogue, is produced by bringing about an alteration in the chemical structure of the naturally occurring compound, thereby making it orally stable and clinically useful. Misoprostol is otherwise called alprostadil and its chemical formula is C22H38O5 ((13E)-methyl(13E)-11,16-dihydroxy-16-methyl-9-oxoprost-13-enoate), as shown in Figure 13. Misoprostol is manufactured as oral tablets of 200 μg scored and 100 μg unscored. It possesses three major advantages – stability at ambient temperature, long shelf-life and low cost – that have made it a central focus of research in obstetrics and gynecology for the past 25 years4. Misoprostol is
rapidly absorbed via the oral route and, although not formulated for parenteral use, can also be administered sublingually (buccally), rectally and vaginally.\textsuperscript{[5–7]}

**Pharmacokinetics, physiology and teratogenicity profile**

Misoprostol is extensively absorbed and undergoes rapid de-esterification to misoprostol acid; this latter compound is responsible for its clinical activity and, unlike the parent compound, it is detectable in plasma. After oral administration, the peak level of misoprostol acid is reached within 9–15 min, with a terminal half-life of 20–40 min. Plasma levels of misoprostol acid vary considerably between and within studies, but mean values after single doses show a linear relationship with the dose over the range of 200–400 mg. No accumulation of misoprostol acid was noted in multiple dose studies and a plasma steady state was achieved within 2 days. The bioavailability of misoprostol is decreased when administered with food or antacids.\textsuperscript{8} Misoprostol is primarily metabolized in the liver, and less than 1% of its active metabolite is excreted in the urine.\textsuperscript{9} Patients with hepatic disease should receive smaller doses, whereas dose adjustment is not necessary for patients with renal disease not requiring dialysis. Misoprostol has no known drug interactions and does not induce the hepatic enzyme systems.\textsuperscript{[9]}

Pharmacokinetic studies of misoprostol in pregnant women show that sublingual and oral doses used for first-trimester termination of pregnancy produce earlier and higher peak plasma concentrations than vaginal or rectal doses, resulting in earlier, more pronounced uterine tonus (oral misoprostol 7.8 ± 3.0 min vs. vaginal misoprostol 20.9 ± 5.3 min).\textsuperscript{[6,7,10]} These findings also have been validated in women after delivery.\textsuperscript{[11]} The effects of misoprostol on the reproductive tract are increased and gastrointestinal adverse effects are decreased when it is administered vaginally.\textsuperscript{[10,12,13]}

When misoprostol tablets are placed in the posterior fornix of the vagina, plasma concentrations of misoprostol acid peak in 1–2 h and then decline slowly (Figure 2).\textsuperscript{5} Vaginal application of misoprostol results in slower increases and lower peak plasma concentrations of misoprostol acid than does oral administration, but overall exposure to the drug is increased (indicated by the increased area under the curve in Figure 2).\textsuperscript{5} The peak plasma levels of misoprostol are sustained for up to 4 h after vaginal administration (Figure 2). Among women who were 9–11 weeks pregnant and given misoprostol before a surgical termination of pregnancy, intrauterine pressure began to increase an average of 8 min after oral and 21 min after vaginal administration.
Pressure was maximal 25 min after oral administration and 46 min after vaginal administration. Uterine contractility initially increased and reached a plateau 1 h after oral administration, whereas it increased on a continuous basis for 4 h after vaginal administration. Maximal uterine contractility was significantly higher after vaginal administration. Maximum serum concentration was achieved 23 min later in rectal administration, and peak levels were lower compared with oral administration of misoprostol (Figure 2). In the pharmacokinetic study by Tang and colleagues, the peak plasma level of misoprostol acid was highest and earliest after administration of misoprostol by the sublingual route. Misoprostol tablets dissolved in water and taken orally also have been shown to produce a faster onset and stronger uterotonic effect than either oral or rectal tablet administration. However, no significant difference was present when misoprostol was used in the form of moistened compared with dry tablets for first-trimester termination of pregnancy.

ADVERSE EFFECTS

Common side-effects of misoprostol include shivering, diarrhea and abdominal pain. Less common side-effects include headache, abdominal cramps, nausea and flatulence, chills and fever, all of which are dose dependent. Interestingly, before its use in pregnant women, chills, shivering and fever were not commonly reported side-effects, suggesting that these are dose dependent.

Package warnings prepared by the manufacturer and based on the original indication for which this drug was marketed clearly state that misoprostol is not to be taken by pregnant women, and that nonpregnant women should use contraceptives while taking misoprostol and should be warned about the effects of misoprostol if taken by pregnant women. Misoprostol should also be avoided in nursing mothers because of concern over causing diarrhea in the baby.

Congenital anomalies sometimes associated with fetal death have been reported subsequent to the unsuccessful use of misoprostol for termination of pregnancy, but the drug’s teratogenic mechanism has not been elucidated. Several reports associate the use of misoprostol during the first trimester of pregnancy with skull defects, cranial nerve palsies, facial malformations (Mobius syndrome) and limb defects.
Misoprostol is listed as a pregnancy category X drug. Toxic doses of misoprostol have not been determined; however, pregnant women have tolerated cumulative doses up to 2200 µg administered over a period of 12 h without any serious adverse effects. A dose of 6000 µg of misoprostol (which is far greater than necessary), taken orally to induce termination of pregnancy (with trifluoperazine), resulted in abortion with hyperthermia, rhabdomyolysis, hypoxemia and a complex acid–base disorder. Induction of labor after fetal death.

Misoprostol is an ideally suited agent for induction of labor after fetal death, as there is no concern about the adverse effects of uterine hyperstimulation on the fetus. For fetal death at term, a dose as low as 50 µg every 12 h may be adequate for induction of labor, whereas higher doses are necessary in patients with fetal death in the second trimester and early in the third trimester. It is safer to use the lowest effective.

METHODS
This study was performed over a period of six months between October 2018 and April 2019 at hospital in iraq with random allocation followed by a double blind design for two parallel groups.

56 nonpregnant women admitted for diagnostic dilatation and curettage due to abnormal uterine bleeding were the participants of this study. After counseling with the patients in clinic, the patency of the cervix was as closed as to prevent passage of hystrometer were included. Patients who had history of cervical surgery, cervical incompetency, and current pregnancy were not included. The patients who had any contraindications for use of misoprostol, such as history of asthma, hypertension, and glaucoma, were not included.

Age, menopausal status, parity, and cervical patency were recorded. Initially, 102 patients were enrolled for this study. 46 patients were excluded from the study either due to not meeting the inclusion criteria (n=38) or due to refusal (n=8). Fifty six women scheduled to have diagnostic dilatation and curettage due to abnormal uterine bleeding were included in this study after going through inclusion and exclusion criteria. The patient were randomly allocated to two parallel groups (A and B) having 28 patients in each of the two arms using computer generated randomization protocol.
All the patients were admitted on the day before operation and undergone detailed history taking and clinical examination. Routine baseline investigations were also performed.

The patients in the study group (Group A) received 200 μg misoprostol (Searle & Company (now Pfizer) under the trade name Cytotec, USA) in posterior fornix of vagina, 2-4 hr prior to the operative procedures and the patients in the control group (Group B) received vitamin B6 (Kimia Daroo, Iran) in posterior fornix of vagina 2-4 hr prior to the operative procedures.

Selection of vitamin B6 tablet as a placebo is due to the fact that it doesn’t have any significant systemic effects by vaginal administrations. Also there was no report of its effects on cervical tissue or uterine.\[4,6\] We had used both the misoprostol and vitamin B6 tablets in round compressed shape (white in color), and the smaller size of vitamin B6 tablet was the only difference. For having double blinded study, both of the drugs were in identical sealed envelope. The duty Resident doctor, just before application of the drugs, opened the sealed envelope and applied them in posterior fornix of the patients. The investigators did not have any information about the agents that were administered.

To determine the cervical width, a No. 5 Hegar dilator was first applied to the cervical canal. Upon passage of Hegar dilator, curettage was successfully completed. If not passed, progressively smaller sizes of Hegar dilator were applied. Cervical response was assessed by the largest size hegars dilator that could be inserted without resistance at the beginning of the surgical procedures. Other outcome measures were needed for further cervical dilatation (larger than No. 5 Hegar dilator).

Development of any pre-operative side effects, such as nausea, vomiting, abdominal cramp, vaginal bleeding, pyrexia of significance, loose motions, etc. were also noted.

Per-operative complications, if any were also taken into consideration.

The data was analyzed using SPSS 14 statistical software. To compare the outcomes between the study group and the placebo group for statistical analysis, Chi-square test, t-test and Mann-Whitney U test were used. A p-value less than 0.05 was considered as statistically significant.
RESULTS

The average of age of participants was 50.7±9 years in misoprostol group and 50.4±9 years in the control group. Eleven patients in misoprostol group and 7 in placebo group were nulliparous.

There were 9 menopausal patients in misoprostol group and 7 in the control group. There was no significant difference in the clinical characteristics (age, weight, parity, and menopause status) between misoprostol and control groups either (Table 1). With an increase in age, misoprostol was less effective (p=0.008) but body weight of the patients did not have any correlation with misoprostol dose (p=0.5).

In fifteen patients (53.6%) of misoprostol group and 8 patients (28.6%) in the placebo group, the Hager dilator number 5 could pass the cervix. This result was statistically different between two groups (p=0.05). The use of vaginal misoprostol facilitated dilatation and curettage. Cervical os was wider in misoprostol group (4.8±1 mm) than in control group (4.0±1 mm), p=0.01. Operative procedures undertaken in both groups were also comparable. Procedural time (minutes) from the beginning of procedures through the external cervical was significantly shorter in misoprostol group (13.5±1.4 min) than in placebo group (19.4±0.9 min) (p<0.001). Requirement of further cervical dilatation and the time required for that was also significantly less in the study group (Table 2).

In premenopausal women, the cervical width (based on number of Hegar dilator) before dilatation and curettage was 5.0±0.9 mm in misoprostol group versus 3.9±1 mm in placebo group (p= 0.003). In postmenopausal women, the cervical width before dilatation and curettage was 4.3±1.3 mm in misoprostol group versus 4.1±1 mm in control group (p=0.86). The difference between the two groups in postmenopausal patients was not significant. Requirement of further cervical dilatation for that in premenopausal patients was also significantly less in the study group. The number of post menopause cases was too low to evaluate distinctively (Table 3).

In nulliparous patients, the cervical width before dilatation and curettage was 4.8±1.2 mm in misoprostol group versus 3.6±1.5 mm in control group (p=0.066). Therefore, there was no significant difference in cervical width between groups. Moreover, there was no difference in requirement for further cervical dilatation (Table 3).
Misoprostol had minor and transient side effects; nausea was reported in three patients, abdominal pain in two patients (25%), diarrhea in two patients (25%), and no cases of fever or vomiting were reported. These side effects were also not significantly higher than the placebo group. There was a case of vaginal bleeding related to misoprostol use.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Misoprostol (n=28)</th>
<th>Placebo (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age * (year)</td>
<td>50.7±9.3</td>
<td>50.4±9.1</td>
<td>0.908 **</td>
</tr>
<tr>
<td>Weight * (kg)</td>
<td>69.8±9.5</td>
<td>69.9±9.2</td>
<td>0.977 **</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>11(39.3%)</td>
<td>7(25%)</td>
<td>0.252 ***</td>
</tr>
<tr>
<td>Multiparity</td>
<td>17(60.7%)</td>
<td>21(75%)</td>
<td>0.39 **</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>9(32.1%)</td>
<td>7(25%)</td>
<td>0.554 ***</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>19(67.9%)</td>
<td>21(75%)</td>
<td>0.76 ***</td>
</tr>
</tbody>
</table>

* Means=SD, ** t-test, *** Chi-square test

<table>
<thead>
<tr>
<th>Cervical Status before dilatation</th>
<th>Misoprostol (n=28)</th>
<th>Placebo (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical width * (mm)</td>
<td>4.8±1.1</td>
<td>4.0±1.1</td>
<td>0.01 **</td>
</tr>
<tr>
<td>Duration of operation * (min)</td>
<td>13.5±1.4</td>
<td>19.4±1.9</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>No. 5 Hegr passed</td>
<td>15(53.6%)</td>
<td>8(28.6%)</td>
<td>0.05 ***</td>
</tr>
<tr>
<td>No. 5 Hegr did not pass</td>
<td>13(46.4%)</td>
<td>20(71.4%)</td>
<td>0.057 ***</td>
</tr>
</tbody>
</table>

* Means=SD, ** Mann-Whitney U test, *** Chi-square test

<table>
<thead>
<tr>
<th>Menopausal status</th>
<th>Postmenopausal</th>
<th>Premenopausal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Misoprostol</td>
<td>Placebo</td>
</tr>
<tr>
<td>Cervical width pre-procedure * (mm)</td>
<td>4.3±1.3</td>
<td>4.1±1.1</td>
</tr>
<tr>
<td>No. 5 Hegr passed</td>
<td>1(11.1%)</td>
<td>3(42.9%)</td>
</tr>
<tr>
<td>No. 5 Hegr did not pass</td>
<td>8(88.9%)</td>
<td>4(57.1%)</td>
</tr>
</tbody>
</table>

* Means=SD, ** Mann-Whitney U test, *** Chi-square test

<table>
<thead>
<tr>
<th>Parity</th>
<th>Nulliparous</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Groups</td>
</tr>
<tr>
<td>Cervical width before dilatation * (mm)</td>
<td>4.8±1.2</td>
</tr>
<tr>
<td>No. 5 Hegar dilator passed</td>
<td>6(54.5%)</td>
</tr>
<tr>
<td>No. 5 Hegar dilator did not Pass</td>
<td>5(45.4%)</td>
</tr>
</tbody>
</table>

* Means=SD, ** Mann-Whitney U test, *** Chi-square test
DISCUSSION
1. Our findings showed that misoprostol is effective in cervical priming for dilatation and curettage in premenopausal women. Procedures such as dilatation and curettage are frequently performed for different gynecological problems in both pre and postmenopausal women either for diagnostic or for therapeutic purposes. Cervical dilatation is difficult part of the procedure. Cervical ripening prior to operative procedures makes the operation easier and decreases the risk of cervical injury and uterine perforation which are often associated with mechanical cervical dilatation. Laminaria and prostaglandin agents are usually used for this purpose.\[9\]

Discomfort and complications due to cervical dilatation despite local anesthesia and precise techniques are serious problems in those women. Cervical narrowing or stenosis, the frequently encountered condition during these procedures is a major cause of these undesirable effects. Misoprostol, a prostaglandin E1 analogue was used in obstetrics because of its uterotonic and cervical ripening effects in different studies.\[7,10\] Ngai et al. had reported that oral misoprostol was effective for cervical ripening in nulliparous woman\[8\] but it was not proved in the present report. Cervical incompetency usually accompanies uterine anomalies except arcuate uterus\[11\]; therefore, misoprostol is likely to be applicable to dilate the cervix in arcuate uterus cases as well.

Mathlouthi et al. reported that there is no significant difference between two groups (placebo and misoprostol) in cervical width prior to curettage. Their result is different from our findings.\[12\] It might be due to route of misoprostol administration; in our study administration was vaginal, while in their study was sublingual. Sublingual administration has lower effect on cervix and uterine.\[7\]

However, some studies reported that preoperative use of vaginal misoprostol did not reduce the cervical resistance particularly when used in postmenopausal women.\[13,14\] It might be due to hypoestrogenic state in postmenopausal women. Oppegaard et al. reported that after 2 weeks of using vaginal estrogen in postmenopausal women, 1 mg misoprostol 12 hr before curettage reduces the cervical resistance.\[15\] Bisharah et al. also reported that misoprostol did not produce cervical priming effect when used in hypoestrogenic state cases through leuprolide acetate injection.\[16\] In the present study, by increasing age, the efficacy of misoprostol declined probably due to estrogen deficiency.
Preoperative use of vaginal misoprostol reduced the need of higher cervical dilatation in many patients. Dilatation of the cervix was also easier in the cases. Ripening of the cervix by vaginal misoprostol reduces the pain during cervical dilatation. Saving the operation time and using lower dose of anesthesia drugs are other advantages. There are other studies which reported the same results in premenopausal patients. Cervicouterine injury during operation was very rare (only a single case of cervical injury out of 28 women) in the misoprostol group. Although vaginal use of misoprostol produced mild abdominal discomfort and slight vaginal bleeding in some women, there were no serious side effects seen in patients.

The only limitation of vaginal use of misoprostol tablets is the requirement for prior hospitalization of patients. Sublingual route of misoprostol may be the solution in this case.

The limitations of our study were performing the procedure by several resident doctors and variation in anesthesia for the patients. History of vaginal delivery is also likely to have an effect on cervical patency as well. Future studies are needed to be carried out for limiting the effects of these variables.

2. Dilation and curettage is frequently performed for different gynecological problems either for diagnostic or for therapeutic purposes. Cervical dilatation is the most unpleasant part during these procedures. Cervical priming before operative procedures facilitates the operation and reduces the risk of complications of mechanical dilatation such as cervical laceration, creation of a false passage, and uterine perforation. Agents commonly used for this purpose include laminaria tents and various prostaglandin preparations.[14]

The present study used a randomized double-blind protocol to compare the effectiveness of vaginal misoprostol with that of the placebo for cervical priming before dilatation and curettage in premenopausal and postmenopausal women. We found that vaginal misoprostol was more effective than the placebo for cervical dilatation; there was a significant difference between the study and control groups in both premenopausal and postmenopausal women with respect to cervical dilatation, as determined by the increased basal cervical width in the misoprostol group.

Ngai et al.[15] had reported that oral misoprostol was effective for preoperative cervical dilatation in nonpregnant women. Following this study, many reports supported this beneficial effect of misoprostol, used either vaginally or orally.[16–18]
The present study was in accordance with the studies by Thomas et al.\cite{11}, Kant et al.\cite{18}, Oppegaard et al.\cite{19}, and Gkrozou et al.\cite{20}, who showed that vaginal misoprostol has a significant effect on cervical dilatation in the total population of premenopausal and postmenopausal women to a statistically significant extent.

However, Gkrozou et al.\cite{20} concluded that there is insufficient evidence to recommend the routine use of misoprostol before every hysteroscopy. Our findings were inconsistent with the results reported by Perrone et al.\cite{21} They found no evidence of an effect on cervical resistance, on the success rate of obtaining a biopsy, and on the ease of performing a biopsy.

This may be because of the shorter interval between administration of misoprostol and analysis of results in their study (3 vs. 12 h in the present study). Other studies also reported that preoperative use of vaginal misoprostol did not reduce the cervical resistance, particularly in postmenopausal women\cite{10,22,23}\ This might be because of the hypoestrogenic state postmenopausal women. Bisharah et al.\cite{23} had reported that misoprostol did not produce a cervical priming effect when used in women in the hypoestrogenic state induced by leuprolide acetate injection.\cite{23}

In premenopausal women, studies have found 200, 400, or 1000 mg of vaginal misoprostol or 400 mg of oral misoprostol administered at least 9–12 h preoperatively to be superior to placebo.\cite{15,23–25} Other studies showed that vaginal misoprostol administered for shorter intervals (4–6 h preoperatively) had no effect.\cite{4,26}

Therefore, the time to adequate cervical ripening may be different for pregnant and nonpregnant women and for premenopausal and postmenopausal women. In the present study, misoprostol was administered at a dose of 400 mg 10–12 h before the procedure. Batukan et al.\cite{27} compared vaginal versus oral misoprostol and showed that vaginal administration of misoprostol is more effective than the oral route for preoperative cervical ripening in premenopausal women.

Inconsistent with these findings, Lee et al.\cite{28} found no favorable effect of vaginal misoprostol over sublingual or oral misoprostol.

A review of seven randomized controlled trials reported that current evidence does not support the routine use of preoperative misoprostol in operative hysteroscopy.\cite{29}
In the present study, the most common side effects observed in the misoprostol group were mild vaginal bleeding (20% of both premenopausal and postmenopausal women) and mild abdominal cramps (10% of postmenopausal and 12% of premenopausal women).

Inconsistent with our findings, Thomas et al.\textsuperscript{[11]} reported a significant difference in the incidence of side effects between the misoprostol-administered groups and the control group. No statistically significant difference was reported between premenopausal and postmenopausal women using misoprostol with regard to the incidence of complications. The reported complications included cervical injury, uterine perforation, and false passage, with incidence ranging from 2 to 8%. Unlike our findings, uterine perforation was reported in two patients of the vaginally administered misoprostol group in the study by Bunnasathiansri et al.\textsuperscript{[30]}, whereas no uterine perforation was reported in the placebo group. In the study by Thomas et al.\textsuperscript{[11]}, four cases of cervical lacerations and two cases of uterine perforation were reported in the orally administered misoprostol group and the placebo group, respectively. In the study by Bisharah et al.\textsuperscript{[23]}, one patient with cervical injury was reported in the misoprostol group, whereas no complications were reported in the placebo group.

CONCLUSION
We have found that vaginal misoprostol has a promising significant benefit when used for cervical priming in premenopausal and postmenopausal women with tolerable minor side effects.

1. It was found that vaginal misoprostol applied in nonpregnant premenopausal women before dilatation and curettage facilitates the cervical dilatation and minimizes cervical or uterine injuries. The effect is not significant in nulliparous or postmenopausal women.

2. Misoprostol is one of the most important medications in obstetric practice. As of the time of writing, its use in pregnant women remains unapproved by the US FDA, except in conjunction with mifepristone (or, in some cases, methotrexate) for first-trimester medical termination of pregnancy. Despite this, the international literature is replete with innumerable favorable reports in many languages of off-label uses. For example, there is strong and consistent evidence to support the use of misoprostol for cervical ripening before surgical abortion in the first trimester and for induction of labor in the second and third trimesters. Whereas lower dose and strict vigilance are required for use of misoprostol for induction of labor with a live fetus,
REFERENCES


17. Cervical Priming by Misoprostol before Diagnostic Dilatation and Curettage: A Randomized Clinical Trial Shima Mohammadian 1, Anahita Tavana 2, Shahrzad Tavana 2, Aida Mohammadian 3, Masoumeh Fallahian 4*
