



Prospective study of laminaria, vaginal misoprostol, and mechanical dilator applications before surgical intervention in first-trimester pregnant women with missed abortion

ORIGINAL
INVESTIGATION

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ABSTRACT

Objective: We aimed to compare the efficacies of laminaria, vaginal misoprostol, and mechanical dilator applications before surgical intervention with regard to the optimal cervical dilation and severity of pain in first-trimester pregnant women with missed abortion.

Materials and Methods: The prospective study included a total of 103 patients with a diagnosis of missed abortion in the sixth-tenth gestational week randomly divided into 3 groups of 400 µg vaginal misoprostol, laminaria, or mechanical dilator applications for the dilation of the cervix before surgical intervention. The effects of laminaria and vaginal misoprostol on the cervical ripening for surgical intervention were evaluated using the Hegar test. Visual analog scale (VAS) values were evaluated during the first application, throughout the period of their applications, and after the surgical intervention.

Results: The cervical dilation was found to be similar in the laminaria and vaginal application groups ($p=0.64$). During the first application, laminaria caused more pain than misoprostol but the difference was not statistically significant ($p=0.28$). Throughout the period of application and after the surgical intervention, although there was less pain with respect to VAS values after laminaria application, this was not statistically significant ($p=0.11$). The VAS values after the surgical intervention was determined to be statistically higher after mechanical dilatation compared to other procedures ($p=0.001$).

Conclusion: Laminaria provides cervical preparedness similar to intracervical misoprostol without increasing the side effects in the management of first-trimester pregnant women with missed abortion.

Keywords: Cervical ripening, laminaria, intravaginal misoprostol, missed abortion

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INTRODUCTION

Missed abortion is defined as the loss of the embryo or fetus in the early stage of pregnancy when the cervix is closed. Miscarriage is the most common complication of early pregnancy (1). The rates of miscarriage have been reported to be approximately 10%-20% in known pregnancies and 30%-40% of all fertilizations (2-4). Various surgical and medical methods are used in the treatment of missed abortion (5). When applying surgical methods, cervical preparation is very important to reduce cervical and uterine complications (6). To obtain cervical dilation, several alternatives, including mechanical dilators, intracervical osmotic dilators, mifepristone, and misoprostol can be used (7-9). Misoprostol can be administered before the surgical procedure via the vaginal, rectal, oral, sublingual, or buccal routes (10-12), although the side effects of cramping, nausea, and pain have been reported (13).

For many years, natural and synthetic osmotic dilators have been used in gynecological and obstetric procedures for cervical preparation. Compared to mechanical dilation or surgical intervention, these cause a gradual softening and dilation of the cervix, with a reduced risk of stretch injuries or perforation, thus providing the advantage of slowly increasing the cervical diameter. As there are minimal local and no systemic side effects, natural osmotic dilator is a desirable natural material to be used for cervical preparation before dilation and curettage (D&C) (14). Although mechanical dilators have been in use for many years, they are less preferred currently because of cervical and uterine complications (5).

The aim of cervical preparation is to soften and open the cervix and thus provide safe entry of instruments into the uterine cavity. Several buccal, oral, vaginal, and intracervical methods have been attempted at different dosages and conflicting results have been obtained. No consensus has been attained yet on the method, the drug, and the drug dosage, and there are many ongoing discussions on this subject (15, 16). The aim of this prospective study was to assess the efficacies of laminaria, vaginal misoprostol, and mechanical dilator applications before surgical intervention with regard to the optimal cervical dilation and severity of pain in first-trimester pregnant women with missed abortion.

MATERIALS and METHODS

Approval for the study was granted by the Human Research Ethics Committee of our university. Informed consent was obtained from the study participants. This was a prospective study of first-trimester pregnant women with missed abortion who were admitted to the Gynecologic Surgery Unit at the university hospital between January 2015 and January 2016. Patients were excluded from the study if they had undergone previous cervical cone biopsy or surgery requiring cervical tissue removal; cervical incompetence; a history of cervical laceration repair during vaginal birth; cervical stenosis; contraindications for the use of misoprostol (history of severe asthma, glaucoma, pre-existing cardiac disease, hypertension, or renal failure); or significant uterovaginal prolapse precluding the administration of vaginal tablets.

All the study subjects were admitted to hospital one day before the D&C procedure. Based on a random selection by a staff member, patients were assigned to one of the study groups: laminaria, misoprostol, or the control. A full history was obtained from all the subjects, detailed general and pelvic examinations were performed, and the gestational week was evaluated using a transvaginal ultrasound (US). A diagnosis of missed abortion was made for all the patients. In the misoprostol dilation group, patients were administered with 400 µg intravaginal misoprostol (Cytotec 200 mcg tablets, Ali Raif, Istanbul, Turkey) into the posterior fornix under direct visualization with a vaginal speculum prior to D&C (2 misoprostol tablets at 2-hour intervals). In the laminaria group, using a vaginal speculum, the cervix was cleansed with a vaginal antiseptic solution, a local anesthetic was topically applied to the ectocervix, then a tenaculum was placed, and a single 3-mm laminaria (MedGyni Lombard, IL, USA) was inserted into the cervical canal under and abdominal US guidance. The laminaria was removed aseptically before the D&C.

Before the administration of misoprostol and luminaria and in all groups at the beginning of the operative D&C, the width of the cervix was measured using a transvaginal US. For the patients in the misoprostol and laminaria groups, in the operating room, a single-tooth tenaculum was used to grasp the anterior lip of the cervix and the degree of baseline cervical dilation was measured using Hegar dilators. This was achieved by introducing Hegar dilators into the uterine cavity in an ascending size, and the maximum caliber that was not met with resistance was accepted as the baseline cervical dilation. A complications related to the administration of the dilating agents were recorded. Pain during the first application of misoprostol and laminaria, throughout the period of use, and after the intervention was evaluated using a visual analog scale (VAS). The cervical dilation limit was determined as 11 mm in all groups. Before the surgical intervention, cervical dilation was measured using Hegar test. If the cervical dilation was less than 11 mm, the cervix dilated to 11 mm using a Hegar dilator and the time to dilation limit was noted. In the control group, patients received no cervical preparation and the cervical canal was dilated using Hegar dilators. In all the groups, after the completion of cervical dilation, under light sedation, the curettage procedure was completed. Side effects, such as feeling an increase in body temperature, headache, nausea and vomiting, diarrhea, abdominal pain in the lower quadrant, and vaginal bleeding were noted (9).

Statistical Analysis

The data obtained in the study were analyzed using the Statistical Package for Social Sciences (SPSS) version 22 (IBM Corporation, Armonk, NY, USA). Descriptive statistical results of the variables were presented as mean±standard deviation (SD), median (min-max), or percentage (%) as appropriate. Comparisons of age, body mass index (BMI), uterine and cervical length, cervical width, and VAS values of the patients in the laminaria, misoprostol, and control groups, were performed with the ANOVA test using the post hoc Tukey test. The comparisons of parameters of obstetric history, and duration of application were analyzed using the Kruskal-Wallis ANOVA with the post hoc Mann-Whitney test. Categorical variables were compared using the Chi-square test. A p value of <0.05 was accepted as statistically significant.

RESULTS

A total of 114 patients were initially enrolled and as 11 did not meet the inclusion criteria, the study was completed with 103 participants randomly assigned to the laminaria (n=38), misoprostol (n=33), and control (n=32) groups. In the cervical preparation groups, laminaria and misoprostol were administered successfully to all patients. All participants completed the study.

The demographic and clinical parameters of the laminaria, misoprostol, and control groups are summarized in Table 1. BMI, gravida, parity, D&C, previous miscarriage, gestational week, and the duration of application values were determined to be similar among the study groups (from p=0.20 to p=0.84), except the age that was significantly lower in the laminaria group (p=0.02). No significant difference was determined between the study groups with respect to baseline cervical width (p=0.64) and cervical width after treatment (p=0.31).

The percentage of patients with vaginal bleeding and vomiting in the misoprostol group was significantly high compared to the laminaria and control groups (p=0.04). No statistically significant difference was determined between the laminaria and control groups with respect to the percentage of patients with vaginal bleeding (p=0.43) and vomiting (p=0.46). There was no significant difference between the laminaria and misoprostol groups with respect to diarrhea (p=0.16). No significant difference was determined between the laminaria, misoprostol, and control groups with respect to headache and nausea (from p=0.29 to p=0.47).

The Hegar test values of the study groups are presented in Figure 1. The Hegar test values after treatment in the laminaria and misoprostol dilation groups were significantly higher than that of the mechanical dilation group (p=0.001); however, there was no significant difference between the laminaria and misoprostol groups with respect to the Hegar test value (p=0.06). There were no significant differences between the study groups with regard to the baseline Hegar value (p=0.10).

The VAS values of the study groups are shown in Figure 2. During the first application, luminaria was determined to have caused more pain compared to the misoprostol group, but not statistically significant (p=0.28). Throughout the period of use, there were no statistically differences between groups with respect to pain, but misoprostol caused more pain than luminaria (p=0.56). After the

Table 1. Selected clinical parameters of study groups

	Laminaria (n=38)	Misoprostol (n=33)	Mechanical dilator (n=32)	p value
Age (y)	28.1±7.1 ^a	30.4±7.8	33.5±7.4	0.02
BMI (kg/m ²)	25.1±4.3	25.6±5.1	27.1±5.3	0.20
Obstetric history				
Gravidity	3.0 (0–6)	3.0 (1–8)	3.0 (0–7)	0.84
Parity	1.0 (0–4)	1.0 (0–6)	2.0 (0–5)	0.23
D&C	0.0 (0–3)	0.0 (0–6)	0.0 (0–1)	0.82
Previous miscarriage	0.0 (1–3)	0.0 (0–6)	0.0 (0–1)	0.68
Gestational week	9.0 (7–10)	8.5 (6–10)	9.0 (6–10)	0.60
Cervical width (mm)				
Baseline	29.2±6.1	30.2±5.6	30.1±5.4	0.64
After treatment	33.0±8.0	33.6±5.5		0.31
Duration of application (h)	16.5 (10–24)	16.0 (12–24)		0.29
Hegar test (mm)				
Baseline	3.0 (2–3.5)	3.0 (2–3.5)	3.0 (2.5–3.5)	0.10
After treatment	9.5 (6–11.5)	9.0 (4–12)		0.06
Side effects				
Headache	7 (18.4%)	4 (12.1%)	2 (6.3%)	0.29
Vomiting	3 (7.9%)	6 (18.2%) ^b	0	0.35
Nausea	4 (10.5%)	5 (15.2%)	2 (6.3%)	0.47
Vaginal bleeding	5 (13.2%)	8 (24.2%) ^c	1 (3.1%)	0.04
Diarrhea	0	2 (6.1%)	0	
Increase in body temperature	0	2 (6.1%)	0	

Data are presented as mean±SD, median (min–max), and percentage as appropriate
 BMI: body mass index; D&C: dilation and curettage; SD: standard deviation
^ap<0.05 vs. misoprostol and mechanical dilation
^{b,c}p<0.05 vs. laminaria dilation

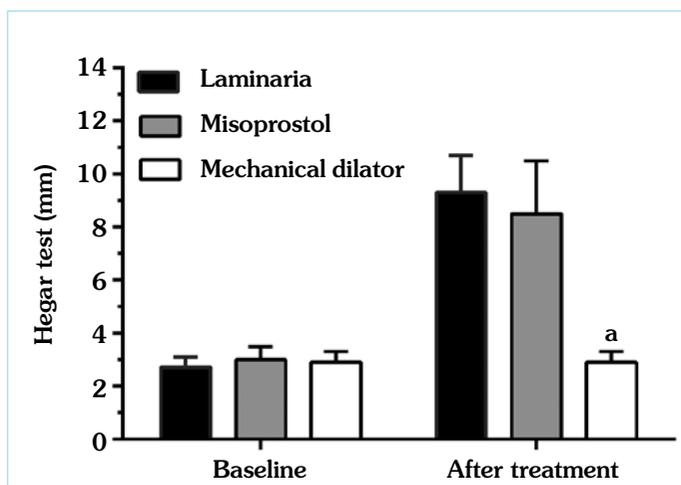


Figure 1. Hegar test in laminaria (n=38), misoprostol (n=33), and mechanical dilator (n=32) groups at baseline and after treatment. Data are expressed as mean±standard deviation (SD); ^ap<0.05 mechanical dilator vs. laminaria and misoprostol dilation groups

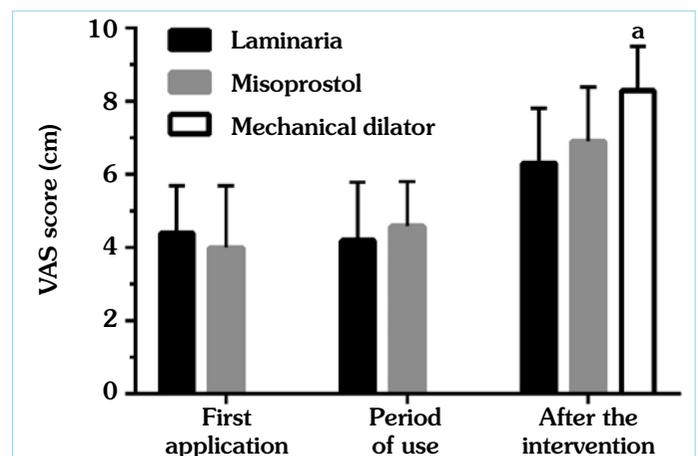


Figure 2. Visual analog scale (VAS) values in the laminaria (n=38), misoprostol (n=33), and mechanical dilator (n=32) groups at first application, period of use, and after the intervention. Data are expressed as mean±standard deviation (SD); ^ap<0.05, mechanical dilator vs. laminaria and misoprostol dilation groups

intervention, there was no significant difference between the laminaria and misoprostol dilation groups ($p=0.11$); however, in the mechanical dilator group, the VAS value was significantly higher compared to the other groups ($p=0.001$).

The time required for the dilation of the cervical canal up to 11 mm was significantly higher in the mechanical dilation group compared to the other groups ($p=0.001$). This value was significantly higher in the misoprostol group compared to the laminaria group ($p=0.01$).

In the laminaria dilation group, the string holding the laminaria broke in 3 patients and the laminaria was surgically removed. In the misoprostol group, 1 patient had posterior wall uterine perforation, which was surgically repaired and the patient was discharged with full recovery. Curettage was reapplied with a diagnosis of retained placenta to 2 patients in the laminaria group, 1 in the misoprostol group, and 1 in the control group.

DISCUSSION

From a general perspective, the results of the laminaria, misoprostol, and mechanical dilator groups in this study were found to be comparable when evaluated with respect to selected clinical parameters. The application times of laminaria and vaginal misoprostol for cervical preparedness were determined to be similar. Although some of the side effects of vaginal misoprostol were greater in general; overall, there were no cervical dilation procedures with meaningfully increased side effects. The value of cervical dilation using the Hegar test was similar at baseline in the three cervical dilation techniques, although the dilation value was significantly increased with laminaria application.

According to the VAS values recorded in the study, although laminaria was more painful than misoprostol during the first application, no difference was determined between the two groups throughout the period of use. In the evaluation of the VAS values in the laminaria, misoprostol, and mechanical dilator applications after the intervention, the VAS value after the mechanical dilator application was determined to be higher compared to other applications. Although the VAS value related to the use of laminaria was lower than that of intravaginal misoprostol, the difference was not statistically significant. When main findings of current study were considered, overall, the laminaria application before surgical intervention in first-trimester missed abortion cases could provide similar efficacy as intravaginal misoprostol application. We thought that according to our findings of not reaching statistical significance related to the success of laminaria, in further studies with an adequate sample size, laminaria application can be more effective than intravaginal misoprostol. There is also a possibility of obtaining adequate and controlled cervical dilation with laminaria sticks fabricated for different cervical dilation needs.

Providing cervical preparedness is very important to reduce complications and facilitate the surgical intervention for missed abortion, which can be seen in many pregnancies. This maturity can be provided by many different methods, such as laminaria, misoprostol, and mechanical dilators (8, 9, 17). The application of misoprostol, a synthetic prostaglandin analog, before surgical treatment improves cervical preparation by lowering the resistance of the cervix to dilation and increasing the baseline cervical dilation, although

the extent is difficult to predict (18). Although prostaglandin analogs are established cervical priming agents, osmotic dilators have been significantly used in cervical preparation. Osmotic dilators of both natural and synthetic types have unique properties (19, 20). The natural laminaria dilator is produced from the stems of *Laminaria japonica* or *Laminaria digitata*. The laminaria dilator increases its diameter by more than 3-fold through the absorbance of water, which provides the significant advantage of more rapid and gradual cervical dilation (19). Previous reports in literature have compared pharmacological and mechanical cervical preparation (9, 17, 21).

In a study by Borgatta L et al. (21), patients with a diagnosis of missed abortion at 14–16 weeks of the pregnancy were administered with intracervical osmotic dilator or 200 mg oral mifepristone for cervical preparation 24 hours before surgical intervention. It was determined that the abortus time was shorter in the osmotic dilator group as there was a lesser requirement for additional cervical dilation. However, mifepristone was preferred as pain levels were lower than that with the use of osmotic dilator.

Goldberg AB et al. (17) compared two groups of pregnant patients diagnosed with abortus; for cervical preparation, one group was applied with overnight laminaria and the other was administered 400 µg vaginal misoprostol 3–4 hours before the intervention. Cervical dilation was determined to be greater in the laminaria group than in the misoprostol group. However, although cervical preparation took longer time in the misoprostol group, it was more preferred.

In another recent study, Karakus S et al. (9) compared laminaria, vaginal misoprostol, and mechanical dilators in cervical preparation before operative hysteroscopy. It was reported that laminaria should be suggested as the first option for cervical preparation before operative hysteroscopy. In the current study, although laminaria was somewhat more effective than vaginal misoprostol with respect to cervical ripening, but this difference did not reach statistical significance.

Different views have been reported in previous studies on the pain in the application of laminaria and misoprostol (7-9, 17, 21). It has been shown that pain develops in patients during the first application and throughout the period of use of laminaria and misoprostol (7-9, 21). During the first application, laminaria has been shown to cause more pain than misoprostol (8, 9, 21). However, in another study, no statistically significant difference between misoprostol and laminaria with respect to pain severity during the intervention was observed (17).

In the current study, although no statistically significant difference was determined between misoprostol and laminaria on first application and throughout the period of use, misoprostol was seen to be more painful than laminaria. Following the intervention, the VAS value of the mechanical dilator group was determined to be higher than that of the laminaria and misoprostol groups, but no significant difference was determined between the laminaria and misoprostol groups. Hence, the etiology of the pain following the cervical preparation procedure could be considered an important parameter. Providing cervical preparation before the intervention could ensure that patient experiences less pain.

This study has several limitations mainly related to the low sample size, no stratification according to the history of D&C, and the number of previous miscarriages, and vaginal birth. These factors have a potential to affect the conditions of the current study. Despite the randomization of the participants, the subjects in the mechanical dilator group were slightly older than those in the other groups. However, there was no difference in parity between the three groups.

In conclusion, laminaria application provides cervical ripening as intracervical misoprostol without increasing the side effects in the management of first-trimester pregnant women with missed abortion. Considering the possibility of available laminaria sticks for different needs of cervical dilation, further studies with adequate sample size can determine the value of laminaria in the armamentarium of gynecologic surgeons.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Cumhuriyet University Clinical Research (13.01.2015/Decision no: 2015-01/05).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Conceived and designed the experiments or case: SK., SOG., BO., GS., AC. Performed the experiments or case: SK., GS. Analyzed the data: SK., SOG., CY. Wrote the paper: SK., SU., AC.

All authors have read and approved the final manuscript.

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