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Research Article

The Effect of Uterocervical Angle on Treatment Efficacy in First-Trimester Pregnancy Terminations

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Abstract

Aim: We aimed to evaluate the effectiveness and usability of the uterocervical angle, which we examined ultrasonographically before misoprostol treatment, which we used in first-trimester pregnancy terminations, and its relationship with the abortion time.
Material and Method: This prospective study includes 207 pregnant women diagnosed with an ex-fetus in utero hospitalized for medical termination in a single center. These patients were divided into two groups patients whose treatment was completed in the first cycle and who needed additional cycles. The characteristics of all pregnant women, abortion times, and misoprostol doses used were compared with uterocervical angle and cervical length and analyzed between groups.
Results: The mean age of the patients in the entire study group was 30.1±6.3, the median uterocervical angle was 112 degrees, and the cervical length was 36 mm. Increasing cesarean number and increasing uterocervical angle degree were positively correlated with increasing abortion time. The number of cesarean sections and the degree of uterocervical angle differ significantly between the group whose treatment was completed in the first cycle and the groups that needed additional cycles. In the treatment groups with elevated uterocervical angle degrees, the first cycle was higher than the successful group. Additional dose and cycle requirements arise if the uterocervical angle is >110 degrees.
Conclusion: Evaluation of the uterocervical angle in first-trimester medical terminations may guide the clinician in the early completion of treatment. With this evaluation before medical treatment, the duration of hospitalization can be shortened, and the need for surgical intervention for patients can be reduced.

Keywords: Pregnancy, first trimester, prenatal diagnosis, misoprostol, abortion missed

INTRODUCTION

Abortion is among the most common complications in pregnancy. It is the most common cause of vaginal bleeding in the first and second trimesters (1). It can be evaluated into two groups spontaneous or induced abortion according to how it occurs. According to the World Health Organization (WHO) definition in 1977, The expulsion of a fetus and its appendages before the 20th gestational week or less than 500 grams out of the uterine cavity is abortion (2).

In clinical pregnancy follow-up, measurement of β-hCG and progesterone levels, abdominal/transvaginal ultrasound (tvusg) evaluation is performed. The threshold level of β-hCG, at which the intrauterine gestational sac should be strictly monitored, is called the "differential zone" (3). For transvaginal ultrasonography, β-hCG is 2000-3000 mIU/mL, while intrauterine gestational sac monitoring is expected (4). With transvaginal ultrasonography, the embryonic pole is seen from the sixth week. Crown-rump length (CRL) is the measurement of the echogenic area between the embryonic head and rump poles. CRL increases by an average of 1 mm per day (5).

Spontaneous abortion, which has a wide range, is around 15-40%, and most of them occur before the 12th gestational week. Approximately 30-50% of conceptions and approximately 15% of clinically diagnosed pregnancies

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result in miscarriage. Chromosomal abnormalities are present in 70 percent of pregnancy losses before 20 weeks (6,7). Medical abortion is the termination of pregnancy by using pharmaceuticals to induce a process similar to a miscarriage. Mifepristone (8), misoprostol (9), or combinations are frequently used globally in the medical approach.

In our clinical experience, we have applied a misoprostol regimen following the International Federation of Gynecology and Obstetrics (FIGO) guidelines for many years, and we standardize the treatment protocols (10,11). The efficacy of misoprostol is affected by many factors such as gestational age, route of administration, dose, and dose range (12-15).

It is still controversial to apply direct dilatation & curettage or to wait for the medical treatment process in cases of missed abortion in the first trimester and early weeks. In this study, we aimed to measure the uterocervical angle (UCA) ultrasonographically to evaluate the effectiveness of misoprostol treatment for the termination of fetuses diagnosed in utero ex during the first trimester of pregnancy. With this pre-treatment evaluation, we can avoid possible side effects of the drug (diarrhea, vomiting, headache, fatigue, breast tenderness, and fever) and unnecessary medical treatment and increase patient comfort by reducing possible complications and length of hospital stay.

In this way, we aimed to evaluate the reliability and usability of the UCA and its relationship with the abortion time.

MATERIAL AND METHOD

This research article was a prospective study at the Health Sciences University Bursa Yüksek İhtisas Training and Research Hospital Gynecology and Obstetrics department. Approved by the local ethics committee with the decision number 2011-KAEK-25 2020/09-06, it covers 207 pregnant women diagnosed with intrauterine ex fetus between 01 November 2020 - 30 April 2021 for a medical termination. Both written and verbal consent was obtained from all of our patients.

First trimester (under 13 weeks), pregnant women aged 20-40 years were included in the study. Under 20 and over 40 years of age, with any comorbidity (diabetes mellitus, hypertension, malignancies, impaired bleeding diathesis, etc.), with a history of uterine anomalies with signs of acute infection, and a fetus with anomaly were out of the study.

We added cervical length and UCA measurements in addition to traditional ultrasonographic measurements (gestational week, gestational sac, crown-rump Length, fetal cardiac activity, location of gestational sac, placentation measurements). The UCA is the segment measured between the lower uterine part and the cervical canal, generating a measurable angle as in the literature (16). The calipers were placed where the anterior and posterior lips of the cervix connect the internal and external os along the endocervical canal. The first line was from the internal os to the external os. If the cervix was curved, the first line was also drawn from the internal os to the external os straight. Then, a second line was drawn to delineate the lower uterine segment. This line was traced up the anterior uterine segment to a distance allowed by the preloaded image. Ideally, the second line would reach 2-3cm up the lower uterine segment to show an adequate measurement. The anterior angle in between the two lines was measured with a protractor.

During the measurement, the patients were standardized, and the measurements were made on the same gynecological examination table and with the same ultrasound device. All dimensions were applied by an experienced sonographer (A.Y.H.) on the same ultrasound with a 5-MHz transabdominal transducer (Ultrasound System Voluson S6; Europe - EAGM). At the same time, the bladder and rectum were empty.

Misoprostol (200 micrograms per tablet) therapy is standardized and routinely used in our department, as well as recommended in World Health Organization (WHO) and FIGO 2017 clinical guidelines (10,17). Four tablets vaginal misoprostol were applied to the group without a previous cesarean section, three vaginal misoprostol was applied to those who had a previous cesarean section, and two vaginal misoprostol was administered to those who had a previous cesarean section. The first dose of misoprostol, determined after the ultrasonography procedure was completed, was applied to the patients on the gynecological examination table. Repeated doses were administered vaginally in the patient's bed to patients who did not abort within the first 8 hours.

The amount and doses of misoprostol used after the patients aborted were recorded in the case report forms and the hours from the patient orders. Curettage procedures were performed under sterile conditions and anesthesia by carmen cannulas for the patients who had an incomplete abortion in the control tvusg. After the procedure, the patients were discharged in good general condition and had no bleeding. The patient group included in the study was divided into 2. The first group of patients whose treatment was completed during the first 8 hours of treatment; The patients who needed additional cycles for treatment constituted the second group. Then, following the treatment protocol, the patients were divided into three groups according to the aborted cycle at 8-hour intervals and reevaluated.

Statistical Analysis

Windows-based SPSS 24.0 statistical analysis program (SPSS Inc., USA) was used for appropriate statistical analysis. Variables were analyzed using visual (histograms, probability graphs) and analytical methods (Shapiro-Wilk and Kolmogorov-Smirnov) to determine whether the data showed a normal distribution. Variables mean±standard deviation (X±SD), mean difference between groups, 95%

confidence interval (95% CI), median (min-max), frequency (n) and percentage (%). Mann-Whitney U test was used to compare non-normally distributed variables in a two-group analysis. Variables containing more than two groups were analyzed with Kruskal Wallis tests, as they did not show normal distribution. Spearman tests were performed to show the correlations between non-normally distributed variables. In the first cycle of successful prediction, binary logistic regression analysis analyzed independent predictors of misoprostol treatment. Model compatibility was found to be significant at $p<0.05$. The degree of UCA was found to have a higher predictive effect than the number of vaginal delivery parameters, and receiver curve characteristic analysis (ROC analysis), which could determine the cutoff value, was applied. However, we divided the volunteers into three groups according to their aborted cycle at 8-hour intervals. By multinomial regression analysis, the degree of UCA was significantly predictive in the groups that aborted in the first 8 hours compared to the groups that aborted after 16 hours.

RESULTS

The descriptive analysis showing the demographic and clinical characteristics of cases terminated with Misoprostol in first trimester pregnancies is shown in Table 1. The mean age in the entire study group was 30.1±6.3. According to the head-rump distance, the median number of pregnancies in the study group was 3, and the median gestational age was 55 days. The median value of the UCA degree, which we evaluated ultrasonographically, was 112 degrees and the cervical length was 36 mm, while the median abortion time of the patients was 10.4 hours. While the number of patients who aborted in the first 8-hour treatment cycle was 86 (40%), The number of patients whose treatment was not completed in the first two cycles and who required additional treatments was determined as 59 (28.5%). All of the findings are shown in Table 1.

Table 1. Analyzes of demographic and clinical characteristics of the participants included in the study

Characteristics of pregnant women and clinical findings	Participants (n=207)
	Median (min-max)
Age (years)	30.1±6.3
Body mass index	26.2 (17.1-43)
Parity	2 (0-9)
Gestational sac diameter (mm)	33.5 (10-81)
Crown-rump length (mm)	15 (2-63.1)
Gestational age according to crown-rump length (days)	55 (40-90)
Cervical length (mm)	36 (10-52)
Uterocervical angle (degrees)	112 (32-172)
Misoprostol dosage (tablets)	6 (2-16)
Time to miscarriage (hours)	10.4 (2.5-30.1)
First cycle abortion (n; %)	86 (41.5%)
Abortion in the second cycle (n; %)	62 (30%)
Abortion in other cycles (n; %)	59 (28.5%)

mm: millimeter, n: number, min: minimum, max: maximum

First-trimester pregnant groups terminated with Misoprostol were divided into two groups according to the abortion time and analyzed in Table 2. Accordingly, the first group of the groups whose treatment was completed during the first 8-hour treatment period; The groups that needed additional cycles for treatment formed the second group. Accordingly, the number of cesarean section deliveries (p=0.004) and the degree of UCA (p=0.002) differed significantly between the two groups. As the degree of UCA increases, the need for additional misoprostol cycles increases statistically and clinically.

Table 2. Comparison of clinical findings according to additional dose misoprostol requirement

	First cycle successful group (n=86)	Group requiring additional doses (n=121)	
	Median (min–max)	Median (min–max)	p
Age (years)	29±4.8	31±5.3	0.32
Body mass index	26.6 (17-43)	25.6 (18.5-39.4)	0.31
Parity	2 (0-9)	2 (0-8)	0.81
Number of vaginal births	1 (0-8)	1 (0-8)	0.09
Number of cesarean births	0 (0-2)	0 (0-2)	0.004
Gestational sac (mm)	34 (15-81)	32.8 (10-81)	0.43
Crown-rump length (mm)	16 (2-63)	14 (2.4-63.1)	0.52
Gestational age (days)	57 (40-90)	55 (40-89)	0.47
Cervical length (mm)	36 (10-46)	35 (21-52)	0.31
Uterocervical angle (degrees)	110 (32-172)	115 (50-160)	0.002

Descriptive analyzes are presented using mean±SD, median (min-max) and (n;%) for normally, non-normally distributed and categorical variables, respectively. Student's t test and Mann-Whitney U test $p<0.05$ was considered significant. mm: millimeter, n: number, min: minimum, max: maximum

Binary logistic regression analysis was evaluated between the two groups to determine the most compatible independent variable that could predict termination success in the first treatment cycle. Accordingly, the first-dose misoprostol successful group was accepted as the reference category. The UCA was significantly higher in the repeated dose groups than in the reference group (p=0.009). Each 1-degree increase in the UCA increases the need for additional cycles 1.02 times (Table 3).

Receiver operating characteristic curves (ROC curves) were created for the degree of UCA, which predicted successful termination with Misoprostol. The area under the curve (AUC), sensitivity (sen.), specificity (spe.), and Youden index were calculated. According to the first dose successful group, a cut-off value was determined for the UCA. Accordingly, if the UCA of the patient, which we evaluated ultrasonographically, is >110 degrees, additional dose and cycle requirements arise with a probability of 63%, a sensitivity of 60%, and a specificity of 55.5% (Table 4, Figure 1)

Table 3. Logistic regression model for additional dose misoprostol requirement

	B	Wald	Odds ratio	95% CI	p
Additional dose misoprostol requirement	0.018	6.850	1.018	1.005-1.032	0.009
	-0.151	2.539	0.860	0.714-1.035	0.111

CI (95%); confidence interval, Wald: test statistic value. Binary logistic regression was used because the dependent variable consisted of 2 groups. Enter method is used. The first cycle successful group was taken as the reference category. Variables that were found to be significant in the previous analysis and with a type 1 error margin level close to 0.05 were included in the analysis. Hosmer-Lemeshow model fit was found p<0.05

Table 4. ROC analysis table of uterocervical angle degree in terms of additional cycle needs in misoprostol treatment success

Area under ROC curve (95% CI)	P	Cut-off (Youden)	Sensitivity	Specificity	PPV	NPV
0.633 (0.558–0.709)	0.001	110	60%	55.5%	55.6%	46.1%

CI: confidence interval, PPD: positive predictive value, NPV: negative predictive value

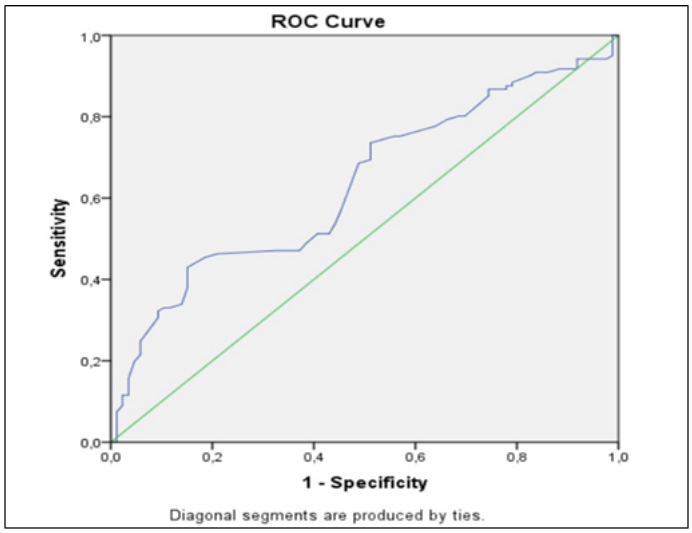

Figure 1. ROC analysis curve of uterocervical angle degree in terms of prolonged treatment in misoprostol treatment success

DISCUSSION

This study examined patients who were administered misoprostol for medical abortion. Our evaluations found that as the degree of UCA increased, higher doses of misoprostol were needed, and a more extended treatment period was required. The number of pregnancies and the number of previous cesarean sections were associated with the degree of UCA. It is seen that the UCA decreases as the gestational sac size and cervical length increase. Increasing cesarean section number and increasing UCA degree were positively correlated with increasing abortion time.

Epidemiologically, about 90% of recurrent pregnancy losses are experienced in the first trimester. Among the causes of abortion, there are many reasons such as medical disorders, environmental factors, uterine or cervical anatomical problems (18).

The cervical length is the most commonly used ultrasonographically used parameter that gives information about the cervix. However, in recent years, the angle measurement between the lower uterine segment and the cervical canal has become popular in many subjects, especially in predicting birth and preterm labor (16,19).

The angulation (UCA) between the uterus and cervix during pregnancy due to structural changes and pressure can give information about labor. This measurement plays a decisive role in estimating the abortion period of the patients.

Depending on the angle of inclination in the pregnant uterus, the cervical canal closes with pressure at a narrow angle or opens with compression in case of a wide-angle (20). The relationship between this change in cervical angle and preterm birth may also be valuable for predicting first trimester abortions.

In a study conducted on multiparous women in the literature, UCA and cervical length were measured by transvaginal ultrasonography before treatment in second-trimester pregnancy terminations. Later, an intracervical Foley catheter was placed in the patients, and then an oxytocin infusion was given. After the patients were aborted, the termination times were compared. It was found that the UCA had a significant effect in patients who aborted in the first 24 hours compared to those who

aborted in the first 48 hours (19).

In another study conducted on primiparous women, transvaginal ultrasonography before treatment in second-trimester pregnancy terminations measured UCA and cervical length. Then, misoprostol treatment was applied to the patients, and the abortion times of the patients were compared. Patients who aborted in the first 24-hour period had higher UCAs than those who aborted late. In this study, groups with UCA >105 were given a shorter-term misoprostol treatment. Therefore, less medication was required, and it was shown that they aborted in a shorter time (21).

The fact that both cervical length and UCA can be measured with the same method or even from the same ultrasound image allows both to be evaluated simultaneously. Many studies on the advantages of UCA measurement have been published recently and continue to be published.

In a study by Pruksanusak et al.; The reliability of UCA and cervical length measurements were compared. The UCA and cervical length were measured separately by three specialists for the 16-24 weeks of pregnant women who participated in the study. Accordingly, UCA measurements showed less variability compared to cervical length measurements. It was stated that UCA measurement is more reliable than cervical length measurement (22).

In a prospective controlled study in which Sallam et al. investigated the measurement of UCA before embryo transfer, measuring the UCA with ultrasound prior to embryo transfer improves clinical pregnancy and implantation rates in patients undergoing in-vitro fertilization and intracytoplasmic sperm injection (23).

In a retrospective case-control study by Sochacki et al., UCA measurement was made and statistically evaluated in the first and second trimesters. A significant difference was found between the median UCA of women who gave birth preterm and the UCA of women who gave birth at term. It was observed that the probability of spontaneous preterm delivery increased in those with a wider angle, and the UCA increased as the gestational week progressed. Despite the limitations of this study, it showed that UCA measured in the first trimester might be a predictive parameter for spontaneous preterm delivery (20).

Our study has some limitations. The first of these is that the study was single-centered. The other one is interobserver variability, which cannot be evaluated because a single clinician performed ultrasonography during the study.

We excluded pregnant women with chronic diseases, uterine anomalies, signs of acute vaginal or cervical infection, previous pelvic surgery, and fetuses with anomalies. The fact that we excluded all pregnant women with non-standardization findings from the study constituted the study's strengths. At the same time, to standardize all patients, they were evaluated with the same ultrasound device on the same gynecological table while the bladder and rectum were empty. The relationship between UCA and abortion duration in second-trimester medical terminations has been investigated, and no comprehensive research has yet been conducted to evaluate UCA in first-trimester medical terminations. In this respect, our work is a candidate to be a valuable and preliminary work.

CONCLUSION

In conclusion, evaluating the UCA for first-trimester medical terminations may guide the clinician, especially in terms of early completion of the treatment. With this evaluation before medical treatment, the duration of hospitalization can be shortened, and the need for surgical intervention for patients can be reduced. Evaluating UCA before medical treatment may be valuable for patients, we plan to terminate with misoprostol treatment.

In order to understand the clinical importance and role of the UCA and obtain more precise data, studies with larger patient groups are needed to support this study.

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