







Evaluation of Methods For Late-Term Abortion, Results of A Tertiary Center

Geç Gebelik Terminasyonu İçin Kullanılan Metodlarının Değerlendirilmesi, Tersiye Merkez Sonuçları

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ÖZET

Amaç: Fetosid, gebeliğin geç 2. ve 3. trimesterinde fetal kardiyak asistoliye neden olmak için potasyum ve digoksin gibi maddelerin kalp içi, intraamniyotik sıvı veya kordona enjekte edilmesi işlemidir. Bu çalışmada, Türkiye'de Etlik Şehir Hastanesi'nde yapılan fetosid sonrası gebelik terminasyonlarının yöntemlere bağlı komplikasyonları ve sonuçları değerlendirildi.

Gereçler ve Yöntemler: 2022 Ekim ve 2024 Şubat ayları arasında, 22 hafta üzeri fetal anomali tanısı almış gebelik terminasyonları retrospektif olarak incelendi. Fetosid için intrakardiyak potasyum klorür (KCI) kullanıldı. Terminasyon yöntemleri arasında misoprostol, foley katater ve sezaryen değerlendirildi. Hastalar, yonteme göre üç gruba ayrıldı ve demografik verileri, hastanede kalış süreleri, komplikasyonlar ve hemoglobin (Hb) ile hematokrit (Hct) değerleri kaydedildi.

Bulgular: Çalışmaya 92 hasta dahil edildi. Misoprostol uygulanan grupta hastanede kalış süresi diğer gruplardan anlamlı olarak daha kısaydı. Hb ve Hct değerlerindeki değişim açısından gruplar arasında anlamlı fark bulunmadı. Misoprostol uygulanan grup en genç yaş ortalamasına sahipti ve bu grupta parite ve yaşayan çocuk sayısı da diğer gruplardan düşüktü. Terminasyon nedenleri arasında istatistiksel olarak anlamlı fark izlenmedi. Komplikasyon oranları ve Hb düşüşü açısından gruplar arasında anlamlı fark bulunmadı.

Tartışma: Çalışmamızda, misoprostol kullanılan grupta hastanede kalış süresi diğer gruplara göre daha kısa bulundu. Hb ve Hct değerlerindeki değişim istatistiksel olarak anlamlı değildi. Misoprostolün güvenli ve maliyet etkin bir yöntem olduğu, ancak sezaryen ve foley katater yöntemlerinin de güvenli olduğu gözlemlendi. Literatürle uyumlu olarak, uterus skarı olan hastalarda misoprostol kullanımının güvenli olduğu desteklenmektedir.

Sonuç: Misoprostol, geç gebelik terminasyonunda güvenli ve etkili bir yöntemdir. Ancak sezaryen ve foley katater yöntemlerinin de güvenli olduğu ve komplikasyon riskinin düşük olduğu gösterilmiştir. Klinisyenler, hasta durumuna göre bu yöntemleri güvenle kullanabilirler.

Anahtar Kelimeler: Fetosid, misoprostol, geç dönem gebelik terminasyonu, terminasyon yöntemleri

ABSTRACT

Objective: To evaluate the complications and outcomes associated with different methods of late-term abortion following fetocide in a tertiary care setting.

Materials and Methods: This retrospective study reviewed the data of 92 patients who underwent fetocide and subsequent abortion induction due to fetal anomalies at Etlik City Hospital between October 2022 and February 2024. Patients were categorized into three groups based on the method of termination: misoprostol, Foley catheter, or cesarean section. Key variables such as maternal age, parity, duration of hospitalization, hemoglobin and hematocrit levels, and complications were analyzed using appropriate statistical methods.

Results: The mean age of patients was significantly younger in the misoprostol group compared to the Foley catheter and cesarean section groups (27±4.8 vs. 31±6.7 and 33±4.9, respectively; p=0.026). The misoprostol group also had significantly lower parity and number of living children (p=0.044 and p=0.047, respectively). The duration of hospitalization was shortest in the misoprostol group (p=0.05). No statistically significant differences were found in hemoglobin and hematocrit levels, duration of abortion, or type of fetal anomaly across the groups.

Conclusion: Misoprostol is a safe and effective method for inducing abortion after fetocide, offering the advantage of a shorter hospital stay. Although concerns remain regarding its use in patients with previous uterine surgeries, our findings support its safety. Methods such as Foley catheter and cesarean section also do not significantly increase complications or affect hemoglobin and hematocrit levels. These findings provide reassurance to clinicians regarding the choice of termination method based on patient and clinical circumstances.

Keywords: Fetocide, misoprostol, late-term abortion, termination methods

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INTRODUCTION

Fetocide refers to the deliberate administration of chemicals, such as potassium and digoxin, directly into the heart, amniotic fluid, or umbilical cord. This procedure is performed during the late stages of the second and third trimester of pregnancy to induce fetal cardiac asystole (1). In our country, similar to many other nations, there are no legal restrictions on abortion during any week if there are physical and mental problems in the infant that would result in significant handicap (2). However, the number of live births increases beyond this point, making fetocide a prominent option for termination (2). There are several reasons to perform fetocide before abortion. The utmost priority is to avert the occurrence of a newborn, which has the potential to cause excruciating and distressing experiences (2). Furthermore, there is evidence indicating that the duration of the abortion or delivery procedure is reduced following a successful fetocide (3,4). The Royal College of Obstetricians and Gynecologists (RCOG) advises the utilization of fetocide for abortions that exceed 21 weeks and 6 days. Various techniques are employed worldwide for the purpose of fetocide. The most frequently employed approach is the intracardiac delivery of potassium chloride (KCL), as recommended by the RCOG, which guarantees fetal asystole (5).

Women who have serious congenital defects should be given the opportunity to choose abortion when the condition is diagnosed, and their family should be notified. Abortions performed on fetuses with congenital deformities can result in bleeding, infection, uterine and cervical damage. The risk of these consequences tends to rise as the pregnancy progresses (6). Misoprostol is the preferred method for inducing abortion in Turkey. Misoprostol is a pharmaceutical compound that has been employed for the purpose of inducing abortions throughout the second and third trimesters of pregnancy since 1997. It is an analog of prostaglandin E1 (7). Misoprostol has several benefits, including its ease of use, cost-effectiveness, and availability in several forms. Nevertheless, the utilization of this treatment may be restricted due to the low adherence of patients and the occurrence of adverse effects, which can reach a rate of up to 30% (8). In addition to this, antiprogestins such as mifepristone, cervical osmolytic dilators, Foley catheters, and oxytocin are alternative techniques for inducing medical abortion during pregnancy or labor (9). Another favored approach is the utilization of an intracervical Foley catheter in conjunction with misoprostol. While certain research indicate that this combination results in a shorter abortion length, other studies have shown no discernible difference (10–12). In this study, as a tertiary center, we evaluated the complications of the procedure and the results depending on the method in patients who underwent abortion after fetocide.

MATERIALS & METHODS

In this study, the data of patients who were diagnosed with fetal anomaly based on ultrasound findings, genetic examinations or both, who underwent fetocide for the purpose of termination of pregnancy over 22 weeks and

who subsequently underwent induction of labor were retrospectively examined in the Perinatology Clinic of Etlik City Hospital between October 2022 and February 2024. Approval of the Ethics Committee AEŞH-EK1-2023-680.

In all of our patients, intracardiac KCl was delivered as a way to induce fetal death. During this treatment, a volume of 2-3 ml of potassium chloride was introduced using ultrasound guidance. The fetal heartbeat was observed for around 5 minutes until it stopped and the loss of the fetal heartbeat was confirmed by Doppler flow. Following the termination of the fetus, the patients were provided with comprehensive information regarding the available alternatives, including misoprostol, Foley catheter, and cesarean delivery. Patients were granted the autonomy to select among the available alternatives. Subsequently, for the patients who agreed to take misoprostol, the suitable protocol was implemented in accordance with the misoprostol guidelines established by the International Federation of Gynecology and Obstetrics (FIGO), taking into consideration the patient's gestational age (13). Labor induction was performed in those who chose a Foley catheter by placing the catheter into the cervix and inflating it to a volume of 40-60 cc. Patients with medical indications for cesarean delivery under suitable conditions underwent cesarean delivery. The patients were categorized into three groups based on their chosen method: group 1 consisted of those who utilized misoprostol, group 2 included those who underwent a Foley catheter, and group 3 comprised those who underwent a cesarean section. Following the initiation of the abortion procedure, we noted the duration of labor, length of hospital stay, any difficulties that arose, the mode of delivery, as well as the hemoglobin (HB) and hematocrit (HTC) levels before and after birth. In addition, the demographic data of the patients, the weeks of pregnancy and the genetic results, if available, were evaluated.

Statistical Analysis

All statistical analyzes were performed using the RStudio to analyze the data. The variables were investigated using visual (histogram, probability plots) and analytic methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to determine whether or not they are normally distributed. Levene test was used to assess the homogeneity of the variance. Descriptive analyses were presented using means and standard deviation for normally distributed variables. One-way ANOVA was used to compare this parameter among the groups. For the non-normally distributed numerical data, descriptive analyses were presented using medians and quartiles (Q1-Q3). Kruskal-Wallis tests were conducted to compare these parameters among the antenatal corticosteroid treatment groups. The Dunn test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. For the categorical variables, descriptive analyses were presented using frequency and percentage. Relationships between categorical variables were analyzed with the Chi-square test or Fisher's exact test (when chi-square test assumptions do not hold due to low expected cell counts). An overall 5% type-I error level was used to infer statistical significance. A p-value of

less than 0.05 was considered to show a statistically significant result.

RESULTS

The study comprised 92 patients who had abortion with feticide. The mean age of the mothers was 27 ± 4.8 in the misoprostol group, 31 ± 6.7 in the Foley catheter group, and 33 ± 4.9 in the cesarean section group. It was found that the misoprostol-treated group was significantly younger than the other groups in terms of age ($p = 0.026$, Table 1). Parity and the number of living children were also significantly lower in the misoprostol group ($p=0.044$ and $p=0.047$, Table 1).

We assessed many factors in the patients, including their history of previous abortions, gestational age, body mass index (BMI), abortion duration, hemoglobin and hematocrit levels at admission, as well as the percentage change in hemoglobin and hematocrit levels following the abortion. There was no statistically significant disparity observed between the groups, as indicated in Table 1.

When comparing the duration of hospitalization (in hours) across the groups who received misoprostol, Foley catheter, and cesarean surgery, the group that received misoprostol had a substantially shorter hospital stay ($p = 0.05$, Table 1). No statistically significant difference was observed between the Foley catheter and cesarean section groups ($p = 0.911$, Table 1). The majority of abortions were performed due to fetal

abnormalities. Out of them, there were 22 syndromes, 22 central nervous system anomalies, and 16 cardiac anomalies. No statistically significant difference was found between the indications ($p = 0.206$, Table 2). The genetic diagnosis of these patients was determined using amniocentesis (AS) in 52 cases, chorionic villus sampling (CVS) in 2 cases, and umbilical cord blood sample in 4 cases. Genetic diagnosis was not established in 28 cases, as indicated in Table 2. The ultrasound results in these cases indicated significant structural abnormalities in the fetus.

The majority of our indications for prenatal genetic tests were determined by ultrasound findings, accounting for 58.6% of cases. Only 8 patients (8.6%) underwent invasive procedures for genetic testing, as the prevalence of prenatal screening was high. No genetic diagnosis was made in 28 patients. When we analyzed these groups according to the termination method, no statistically significant difference was found between them (Table 2).

Uterine rupture occurred as a complication in the misoprostol group among the patients included in our study and this case had emergency surgery for this reason.

DISCUSSION

In our study, we investigated the termination methods after feticide in the 2nd trimester, the duration of hospitalization and the changes in the patient's HB and HTC levels. The length

Table 1. Maternal Characteristics of the Pregnant Womans Included in the Study

	Group I (Misoprostol) (n=48)	Group II (Foley Catheter) (n=30)	Group III (Caesarean Section) (n=14)	p
Maternal age(year)	27.2±4.83	31.3±6.75	32.7±4.92	0.026 ^a
Gravida	2 (1-3)	2 (2-3)	3 (2-4)	0.148
Parity	1 (0-1)	1 (1-2)	2 (1-2)	0.044 ^b
Number of living children	1 (0-1)	1 (0-2)	2 (1-2)	0.047 ^c
Abortion	0 (0-1)	0 (0-1)	0 (0-1)	0.939
BMI (kg/m ²)	26 (23-27)	26 (25-27)	26 (22-31)	0.372
Gestational age at abortion (week)	23 (22-25)	23 (22-29)	26(25-28)	0.059
Duration of hospitalization (hour)	36 (24-48)	48 (48-72)	48(48-48)	0.005 ^d
Duration of abortion(hour)	15 (11-22)	24 (9-33)	0.162 ϕ	
Pre-abortion hemoglobin (g/l)	12.2±0.99	11.5±1.07	11.6±1.33	0.162
Pre-abortion hematocrit (%)	37 (35-40)	35 (33-38)	37 (32-39)	0.237
Post-abortion hemoglobin (g/l)	11.7±1.13	10.8±1.32	10.5±1.14	0.024 ^c
Post-abortion hematocrit (%)	36±3.6	32±3.4	32±2.8	0.019 ^b
Difference between hemoglobins (%)	2 (1-6)	6 (0-12)	9 (8-10)	0.057
Difference between hemoglobins (g/l)	0.25 (0.13-0.68)	0.8 (0-1.4)	1 (0.9-1.2)	0.066

BMI: Body mass index. Data are expressed as mean±SD, median and quartiles (Q1-Q3), or number (percentage) where appropriate. A p value of <0.05 indicates a significant difference. Statistically significant p-values are in bold.

ϕ Caesarean Section group was not included in the statistical analysis.

^aStatistical significance is between groups I-II and I-III. There is no statistical significance between groups II-III. Post-hoc analysis: LSD

^bNo statistically significant difference was found in the post-hoc analysis when comparing the groups with each other. Post-hoc analysis: Dunn adjusted with Bonferroni correction.

^cStatistical significance is between groups I-III. There is no statistical significance between groups II-III and I-II. Post-hoc analysis: Dunn adjusted with Bonferroni correction.

^dStatistical significance is between groups I-II. There is no statistical significance between groups II-III and I-III. Post-hoc analysis: Dunn adjusted with Bonferroni correction.

Table 2. Perinatal and Genetic Outcome of the Pregnant Womans Included in the Study.

	Group I (Misoprostol) (n=48)	Group II (Foley Catheter) (n=30)	Group III (Caesarean Section) (n=14)	p
Birth weight (gr)	670 (495-880)	955 (850-1004)	760 (595-933)	0.052
Indications for termination				
Multiple anomalies	12 (25)	10 (33.3)	6 (42.9)	0.206
CNS anomaly	10 (20.8)	12 (40)	8 (57.1)	
Cardiac anomaly	14 (29.2)	2 (6.7)	0 (0)	
Others	12 (25.0)	6 (20)	0 (0)	
Genetic diagnosis				
Amniocentesis	28 (58.3)	16 (53.3)	8 (57.1)	0.164
Chorionous villus sampling	0 (0)	2 (6.7)	0 (0)	
Cordocentesis	0 (0)	2 (6.7)	2 (14.3)	
Fetal skin biopsy	2 (4.3)	2 (6.7)	0 (0)	
Patients without genetic diagnosis	18 (37.5)	8 (26.7)	4 (28.6)	
Prenatal genetic diagnosis indications				
Prenatal high risk screening test	2 (4.2)	6 (20)	0 (0)	0.546
Patients with ultrasound findings	28 (58.3)	16 (53.8)	10 (71.4)	
Fatal congenital anomaly (genetic evidence without effect on prognosis)	18 (37.5)	8 (26.7)	4 (28.6)	

CNS: Central nervous system. . Data are expressed as median and quartiles (Q1-Q3), or number (percentage) where appropriate. A p value of <0.05 indicates a significant difference. Statistically significant p-values are in bold.

of hospital stay was considerably reduced in the misoprostol group compared to the other groups ($p = 0.013$). The percentage difference in the variations of HB and HTC values in these patients did not show statistical significance.

When we compared the termination methods in our study based on the demographic characteristics of the patients, we found that the group receiving misoprostol was the youngest group of patients. The difference between the groups was statistically significant, especially between misoprostol and the other 2 groups ($p = 0.026$). In the group that received misoprostol, there was a significantly lower number of living children and pregnancies compared to the other groups ($p = 0.044$ and $p = 0.047$, Table 1). We assume that this situation is due to doctors and patients avoiding the use of misoprostol, considering that the number of cesarean sections increases with the age of the patients and the number of gravidities. Out of the patients who asked for a cesarean section, 8 of them (57.1%) also sought a bilateral tubal ligation. Patients with uterine scars during abortions have become a significant category as a result of the rising rates of cesarean section during the past two decades (14). The existing literature lacks sufficient data regarding the safety of misoprostol usage, particularly in individuals who have undergone three or more cesarean sections (14,15). In a meta-analysis published by Andrikopoulou et al., they found that the rate of uterine rupture in patients with a cesarean section was similar to that

in patients without a uterine scar, but that the risk of uterine rupture increased 17-fold in patients with 2 or more previous cesarean sections with the use of misoprostol. This meta-analysis revealed a greater incidence of placental retention and the requirement for blood transfusions in patients with uterine scars (16). Ho et al. discovered that the use of misoprostol in abortions should be decreased starting from the 22nd week (17). This situation, which is consistent with our study, explains the increasing use of gravida and methods such as Foley catheters and cesarean section with increasing age.

There are studies on the safety of misoprostol. The use of misoprostol, especially in patients with previous uterine surgery, is still a medical problem for doctors in our country. In a study conducted by Dickinson et al. it was discovered that administering 400 mcg of misoprostol every 6 hours to patients with a prior uterine scar did not impact the length of abortion and did not lead to additional difficulties when compared to pregnant women without a uterine scar (18). In a study conducted by Berghella et al., it found that patients with a lower segment uterine incision had a uterine rupture rate of 0.4%, a hysterectomy rate of 0%, and a transfusion requirement of 0.2% (19). Fawzy and AbdelHady administered a low dosage of misoprostol on the first day to women with uterine scarring. For those who did not respond, the dosage was increased twofold on the second day. This application had a success rate of 90% without any issues (14). Nevertheless, there are

still research papers that advocate for the use of misoprostol in low doses and advise avoiding increasing the dosage in patients who have a prior cesarean scar on the uterus due to safety concerns (20). In our study, however, we had one patient with a complication in the misoprostol group. She underwent surgery for a uterine rupture. We did not have a patient who had to undergo a hysterectomy. Our results indicate that the use of misoprostol is safe.

Severe fetal deformities are the primary reason for using intracardiac potassium chloride (KCL) to terminate most pregnancies, as stated in the literature (9,21). The rates of medical termination in the 2nd and 3rd trimesters have shown a substantial increase in recent years. The cause of this predicament is the escalating efficacy of 2nd Trimester fetal anatomical screening ultrasounds (22). The diagnosis of 70% of terminated pregnancies occurs during the second or third trimester (23). All termination indications in our study were exclusively related to fetal or chromosomal abnormalities. We categorized individuals based on syndromes, central nervous system anomalies, cardiac anomalies, and other factors. No statistically significant difference was seen between the kind of fetal abnormality and the technique of termination, as indicated in Table 2. Cayrac et al. did a study where they reported that the average gestational age of patients who underwent fetocide was 23 weeks and 2 days (22). In our study, the average gestational age at termination was 23 (22-25) in the misoprostol group, 23 (22-29) in the Foley catheter group and 26 (25-28) in the cesarean section group. Although the average gestational week in the cesarean group was 26, there was no statistically significant difference seen between the termination method and the gestational week.

Multiple studies have demonstrated that Misoprostol effectively speeds up the process of expelling a fetus during the middle trimester by 40-50% and decreases the necessity for dilation and curettage. Additionally, it has been proven to be a safe method (9,24,25). Our investigation revealed no discernible distinction in the duration of abortion between the group administered misoprostol and the group administered a Foley catheter. Nevertheless, our findings indicate that the duration of hospitalization was shorter among the participants who utilized misoprotol compared to those who employed alternative treatments.

There exist scholarly investigations in the body of literature about maternal hemorrhage problems during abortion. In their investigation, Chapman et al. showed a link between prior uterine surgery and the need for blood transfusions (26). In their study, Ruano et al. found that using fetocide during terminations can effectively decrease hemorrhage in individuals with complete placenta previa (27). However, to our knowledge, there is no study in the current literature examining the effect of the termination procedure on the change of hb and htc levels. Our current study on this subject shows that there is no statistically significant change in the percentage and value of hb and htc values ($p = 0.162$ and $p = 0.237$). Indeed, the patient asserts that the likelihood of experiencing a reduction in hemoglobin levels that would

lead to an increase in morbidity is minimal, even if the patient undergoes a cesarean section. Nevertheless, further research is required on this topic.

The main limitations of our study are that it is a retrospective study and the number of patients is relatively small. Our research findings confirm that the administration of misoprostol is safe for patients with uterine scarring, consistent with existing literature. In addition, hb and htc values were evaluated within 3 termination methods, and the change was not statistically significant. Even when the caesarean section method is used for termination, it does not appear to be an important factor in increasing morbidity.

Our recommendation to clinicians: The duration of hospitalization was significantly shorter in the group receiving misoprostol, misoprostol was cost-effective; simultaneously, both groups can utilize this shared approach without any disparity in terms of problems or a reduction in HB levels. However, we maintain the belief that utilizing procedures such as cesarean section or Foley catheter on the patient, regardless of the reason, does not result in any rise in problems, reduction in HB-HTC levels, or heightened requirement for blood transfusion. This can provide doctors with a sense of security.

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