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RESEARCH ARTICLE

Clinical Outcomes of Intravaginal Misoprostol Use in Cases with Therapeutic Abortion Indications

Behram Barlas,[1] Yavuz Tahsin Ayanoğlu[1]
[1]Department of Gynecology and Obstetrics Clinic, Taksim Hospital, Istanbul, Türkiye

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ORCIDs of the authors:
BB :0009-0006-0473-4193
YTA : 0000-0002-1605-3620

Abstract

Introductıon: This study aimed to evaluate the clinical outcomes of intravaginal misoprostol for therapeutic abortion indications and to determine whether this regimen represents a safe and effective option in routine practice.

Methods: This prospective observational study included 36 patients (mean age 27.5 ± 6.8 years; mean gestational age 16.3 ± 8.5 weeks) admitted with therapeutic abortion indications. Following baseline ultrasound and pelvic examination with modified Bishop scoring, intravaginal misoprostol was administered every 6 hours: 200 µg for pregnancies ≤20 weeks and 100 µg for >20 weeks, until expulsion. Patients were monitored with 2-hourly vital signs and post-expulsion uterine revision when indicated. Outcomes analyzed included success rates, adverse events, and induction-to-delivery intervals.

Results: The mean age of patients was 27.5 ± 6.8 years, with gestational ages ranging from 7–40 weeks. Most cases (80.6%) occurred at ≤20 weeks. The overall successful abortion rate was 97.2%. Mean induction-to-delivery intervals was significantly shorter at ≤20 weeks (583 ± 437 min) compared to >20 weeks (1183 ± 933 min; $p < 0.001$). Dose escalation beyond the initial dose occurred in over half of patients in both gestational groups (51.7% at ≤20 weeks and 57.2% at >20 weeks). Only one patient experienced transient diarrhea; no severe complications occurred.

Conclusion: Intravaginal misoprostol demonstrates high efficacy and safety for therapeutic abortion across all gestational ages, with appropriate adjustments in dosing. Initial higher doses at ≤20 weeks and cautious dosing escalation beyond 20 weeks appear effective and safe.

Correspondence Address: Cumhuriyet Mah Gürpınar Yolu Cad, Şafak Sokak, E Blok No: 1 34500 İstanbul - Türkiye
Phone: +90 532 275 17 21 / **e-mail:** behram.barlas@yahoo.com

Introduction

Although abortions are increasingly being performed earlier in gestation worldwide, about 10–15% still occur at relatively later stages.[1] Second-trimester terminations often arise from serious fetal anomalies or intrauterine fetal demise and pose greater clinical challenges compared to first-trimester procedures. Second-trimester terminations can be done surgically (e.g., dilation and evacuation) or via medical induction, the latter being more common in settings without surgical expertise.[2] However, there remains no universal consensus on the optimal method for terminating second-trimester pregnancies indicated by fetal anomalies or fetal death,[3] underscoring the need for evidence-based approaches in this context.

One pharmacologic agent central to mid-trimester abortion care is misoprostol, a prostaglandin E_1 analog. It is widely used for second-trimester termination because of its high effectiveness, low cost, ease of use (multiple routes of administration), and generally mild adverse effects.[4] International guidelines support misoprostol as a safe and effective option: for example, the World Health Organization recommends a misoprostol-only regimen (approximately 400 µg administered vaginally or sublingually every 3–6 hours) for induced abortions beyond the first trimester, including in cases of fetal demise between 14–28 weeks.[5] A meta-analysis of second and third trimester pregnancy losses reported that both vaginal and oral misoprostol regimens resulted in 100% expulsion of the fetus within 48 hours in those trials.[6] Importantly, misoprostol also has a generally favorable safety profile when used for second-trimester induction. Serious complications, such as uterine rupture, are rare.[7] However, caution and close monitoring are recommended, particularly in patients with multiple uterine scars.[8,9] Ongoing research continues to refine the optimal misoprostol protocol for mid-trimester termination, examining the ideal dose, route, and dosing interval for various gestational ages and indications.[10,11]

Despite the widespread use of misoprostol for second-trimester pregnancy termination, the literature is relatively limited and heterogeneous regarding its use as a single agent in therapeutic abortion cases. Many studies focus on specific regimens or subpopulations, and further data are needed to establish the most effective and safe protocol for varying indications. Therefore, this study aimed to evaluate the clinical efficacy and outcomes of intravaginal misoprostol for terminating pregnancies indicated for therapeutic abortion.

Material and Methods

This was a single-center prospective study conducted in an Obstetrics and Gynecology Clinic during the period from March 1995 to November 1995. The study adhered to internationally recognized ethical standards, including those outlined in the Declaration of Helsinki.

During the study period, 36 patients admitted to the hospital with indications for therapeutic abortion were included in the study. Patients who had a Bishop score >3, ultrasound-detected dilation of the cervical internal os, or cervical canal length <30 mm were excluded from the study. Based on ultrasonographically determined gestational age, patients were grouped into ≤20 weeks and >20 weeks categories.

Pre-procedure assessment

All patients underwent ultrasonography (US) using a Hitachi EUB-310 system (Hitachi, Tokyo, Japan) equipped with 3.5- and 5-MHz convex transducers. The US examination assessed fetal biometry, fetal structural anomalies, placental location, internal cervical os patency, cervical canal length, and fetal cardiac activity (FCA). A pelvic examination was then performed and cervical favorability was graded with a modified Bishop score, incorporating station, cervical consistency, position, effacement, and dilatation.[12] Following US and pelvic examination, baseline laboratory tests were obtained, including a complete blood count and bleeding/clotting times; serum fibrinogen was measured when clinically indicated. Patients were subsequently admitted for induction. Laminare and balloon methods were not used.

Indications for therapeutic abortion were classified into two groups: those related to maternal health (cardiovascular diseases, cases where heart surgery is not possible, causes leading to heart disease, lung diseases, kidney diseases, severe skeletal deformities and diseases, dermatological diseases, endocrine diseases, malignant tumors, birth-related diseases, psychiatric diseases) and those related to child health (severe hereditary diseases, viral diseases, ionizing radiation, maternal teratogenic drug use).

Intravaginal misoprostol protocol

To facilitate dissolution of the tablets, a vaginal lavage with 10 mL of normal saline was performed prior to placement. Misoprostol tablets were moistened with normal saline and placed into the posterior vaginal fornix at 6-hour intervals until abortion or delivery occurred. Dosing was based on ultrasound-estimated gestational age: patients ≤20 weeks received 200 µg (1 tablet) per dose, and patients >20 weeks received 100 µg (½ tablet) per dose. No further doses were given to patients who developed effective uterine contractions. Patients remained on bedrest for 2 hours after each dose.

Monitoring and outcome measurements

Patients were monitored every 2 hours until abortion or delivery. At 2-hour intervals the following were recorded: arterial blood pressure, pulse rate (beats per minute), and axillary temperature. The time from the administration of the first misoprostol dose to the onset of abortion (incomplete abortion) or to delivery was recorded for each patient. Any adverse events potentially related to the medication were recorded.

Post-Expulsion Management

For all patients ≤20 weeks' gestation, uterine evacuation was accompanied by an infusion of 20 IU oxytocin (Syntocinon) added to 1000 mL 0.9% saline; uterine evacuation was performed concomitantly. For patients >20 weeks, uterine evacuation was performed selectively based on ultrasound assessment of the uterine cavity following expulsion. After evacuation, a control complete blood count was obtained and patients were evaluated for any drug-related side effects; findings were recorded.

Statistical analysis

All data were analyzed using SPSS version 6.0 for Windows software (SPSS Inc., Chicago, IL, ABD). Numerical data are given as mean ±standard deviation (SD) values, while categorical variables are given as numbers and percentages.

Results

The patients comprised 36 patients with a mean age of 27.5 ± 6.8 years (range, 17–42 years) and a mean gestational age of 16.3 ± 8.5 weeks (range, 7–40 weeks). Terminations predominantly occurred at ≤20 weeks (80.6%), with the remainder beyond 20 weeks (19.4%). The predominant indication was in utero fetal demise (IUFD) (72.2%), followed by premature rupture of membranes (PROM) (8.3%) and inadequate fetal visualization on ultrasound (8.3%). Less frequent indications included fetal anomaly (2/36; 5.6%), hydrops fetalis (1/36; 2.8%), and anembryonic pregnancy (1/36; 2.8%). Patient demographic data are detailed in Table 1.

Table 1. Demographic and clinical findings.

Variable	All population n = 36
Age, years	27.5 ± 6.8
Gestational age, weeks	16.3 ± 8.5
≤20 weeks, n (%)	29 (80.6)
>20 weeks, n (%)	7 (19.4)
Indication, n (%)	
Maximum dose of misoprostol, n (%)	26 (72.2)
Premature rupture of membranes	3 (8.3)
Fetus not clearly visualized	3 (8.3)
Fetal anomaly	2 (5.6)
Hydrops fetalis	1 (2.8)
Anembryonic pregnancy	1 (2.8)
Maximum dose of misoprostol, n (%)	
100 µg	3 (8.3)
200 µg	16 (44.4)
400 µg	10 (27.8)
>400 µg	7 (19.4)
Successful evacuation, n (%)	35 (97.2)
Adverse event, n (%)	
Diarrhea	1 (2.8)
Serious complication, n (%)	0
Revision curettage, n (%)	30 (83.3)
≤20 weeks (n=29)	29 (100)
>20 weeks (n=7)	1 (14.3)

Data were were shown as number (percentages) or mean ± SD.

Misoprostol resulted in successful uterine evacuation in 35 patients (97.2%), with one case of failure (Table 1). In this unsuccessful case, abortion was not achieved approximately 36 hours after administration of 1200 µg misoprostol. However, cervical ripening occurred, with the Bishop score rising from an initial 0 to 5. Vaginal mycosis was detected, and repeated attempts revealed insufficient tablet dissolution. The decision to use alternative methods was made with consideration of the patient's request. Extra-amniotic rivanol instillation (150 cc) was performed first, followed by administration of 1000 cc of serum containing 40 units of Syntophin after 6 hours. As abortion did not occur within 24 hours, serum with a higher concentration (50 units of Syntophin in 500 cc) was infused, ultimately achieving abortion. The case was classified as a failure, resulting in a 97.2% overall success rate.

Only one patient experienced transient watery diarrhea (5–6 times per day); no other adverse effects or complications were observed. Revision curettage was performed after abortion in all cases at ≤20 weeks gestation, and in 14.3% of cases beyond 20 weeks due to suspected retained intrauterine tissue (Table 1). For pregnancies ≤20 weeks gestation, the mean induction-to-delivery intervals was 583 ± 437 min (range: 120–2040 min), compared to 1183 ± 933 min (range: 210–2400 min) in those >20 weeks (Table 2).

Multiparity was more frequently observed in pregnancies ≤20 weeks, whereas nulliparity was more common in pregnancies >20 weeks (Table 2). Mean induction-to-delivery intervals was longer in the >20-week group than in the ≤20-week group (1183 ± 933 vs. 583 ± 437 min; $p < 0.001$). Within parity strata, nulliparous patients showed the same pattern. For primiparous and multiparous patients at >20 weeks, only one case was available in each category (times 1770 and 210 min, respectively), precluding meaningful intergroup comparisons (Table 2).

Table 2. Parity distribution and time to expulsion according to gestational age group.

Variables	≤20 weeks n = 29	>20 weeks n = 7	p
Maximum dose of misoprostol, n (%)			
100 µg	-	3 (42.8)	<0.001*
200 µg	14 (48.3)	2 (28.6)	
400 µg	10 (34.5)	-	
>400 µg	5 (17.2)	2 (28.6)	
Parity, n (%)			
Nulliparous	9 (31.0)	5 (71.4)	<0.001*
Primiparous	8 (27.6)	1 (14.3)	
Multiparous	12 (41.4)	1 (14.3)	
Induction-to-delivery intervals, min	583 ± 437	1183 ± 933	<0.001*
Nulliparous	443 ± 150	1260 ± 988	0.027*
Primiparous†	565 ± 377	1770	-
Multiparous†	698 ± 588	210	-

Data were were shown as number (percentages) or mean ± SD. * P-value <0.05 shows statistical significance. † Due to having only one patient each in primiparous and multiparous categories for pregnancies over 20 weeks, intergroup comparisons could not be performed.

Discussion

Our findings indicate that both misoprostol regimens were highly effective for inducing uterine evacuation, with no significant difference in the overall success rates or induction-to-delivery intervals between the lower-dose and higher-dose protocols. Nearly all patients in both groups achieved complete expulsion within 24 hours, which is consistent with the high efficacy of misoprostol reported in the literature for first-, second-, and third-trimester pregnancy termination and stillbirth management.[6,13-16] The average induction time observed in our study is comparable to that in prior studies using misoprostol regimens, underscoring that misoprostol can reliably induce delivery within a day in the majority of case.[17]

The choice of initial misoprostol dose, the total dose administered, and the interval between doses are all key factors influencing the success and speed of abortion. Numerous studies suggest that gestational age plays a crucial role in determining optimal dosing, with higher doses generally required as pregnancy progresses. A trial in very early gestation (≤8 weeks) observed a 91% overall success rate (96% efficacy in <6-week pregnancies) using repeated 800-µg vaginal misoprostol doses.[18] In one study, women were administered 800 µg of vaginal misoprostol every 24 hours, with a maximum of three doses. The study reported a complete abortion rate of 87%. Notably, 73% achieved complete abortion after a single dose, while an additional 9% required two doses and 5% needed all three doses to complete the process.[19]

However, increased uterine sensitivity with advancing gestational age underscores the importance of cautious dose adjustment. In a randomized trial of second-trimester abortion, an initial 200 µg misoprostol dose achieved a significantly higher success rate than a 100 µg dose (92% vs. 74% complete abortion within 36 hours).[20] This aligns with existing evidence that misoprostol is a safe option in the second trimester even in patients with a prior cesarean (under carefully controlled doses), as studies have reported no increase in adverse outcomes when using moderate dosages in women with uterine scars.[21,22] Overall, our results confirm that misoprostol is an efficient and safe agent for midtrimester labor induction, achieving high success rates within 24–48 hours as noted in international studies.[23,24] Nevertheless, starting with too low of a dose may lead to protracted inductions or the need for multiple dosing rounds. Likewise, a recent cohort study of late second-trimester intrauterine fetal demise found that low-dose protocols (≤200 µg in 6 hours) were associated with a substantially prolonged induction, whereas higher-dose regimens accelerated the time to expulsion; women in the low-dose group were almost twice as likely to still be undelivered after 12 hours compared to those receiving higher cumulative doses.[25] Using only 100–200 µg as an initial vaginal dose in mid-pregnancy often yields slower uterine activation; one comparative study noted significantly lower efficacy with a 200 µg regimen than with 400 µg.[14]

While a dose-response plateau at approximately 400 µg is considered optimal,5 exceeding this dose does not significantly enhance effectiveness and could increase the likelihood of side effects. In our cohort, we opted for a lower starting dose in more advanced pregnancies to mitigate the risk of uterine hyperstimulation or rupture. Approximately half of the patients in each gestational age group required some dose escalation beyond the initial dose (with about 17% of ≤20 week cases and 29% of >20 week cases needing a cumulative dose above 400 µg), yet only one patient experienced any notable side effect. A comprehensive review has suggested that 400 µg vaginal misoprostol every 3–6 hours is an optimal regimen for second-trimester abortion, whereas exceeding about 800 µg in total dosage may lead to increased side effects (particularly diarrhea).[26] A pivotal dose-optimization study by Dickinson and Evans compared vaginal misoprostol administered as 200 µg every 6 hours, 400 µg every 6 hours, or a 600 µg loading dose followed by 200 µg every 6 hours. The 400 µg and the 600/200 µg regimens significantly shortened the median time to delivery compared to the 200 µg regimen, though the 600/200 µg regimen was associated with higher side effects.[27] Reported side effects of misoprostol include maternal fever, chills, nausea, vomiting, diarrhea, and gastrointestinal symptoms such as abdominal pain.[21] Although no serious complications were observed in our study, the occurrence of diarrhea in one patient was consistent with the existing literature.

This study is limited by its small sample size (36 cases) and single-center design. Second, we did not have a comparison group using an alternative method or a different misoprostol regimen (such as a mifepristone–misoprostol group or a different dosing schedule). Third, the number of patients beyond 20 weeks' gestation was low, which limits the strength of conclusions regarding outcomes in later second trimester or in nulliparous vs. multiparous subgroups. Finally, the study focused on intravaginal administration exclusively – while this route is well-supported by evidence, we cannot comment on outcomes with oral or sublingual use of misoprostol from our data. Future studies with larger samples, randomized designs, and broader inclusion criteria would be valuable to confirm and expand upon our findings.

Conclusion

Our study provides meaningful insights into the design of clinically translatable 3D cartilage grafts. The regimen achieved high success rates in first- and second-trimester abortions and proved capable of inducing third-trimester labor in cases of fetal anomaly or demise. Using a higher initial dose in earlier gestations (200 µg ≤20 weeks) appeared to facilitate faster expulsion, while a lower starting dose beyond 20 weeks balanced efficacy with safety considerations for the more sensitive, late-pregnancy uterus. Importantly, most failures responded to repeated or escalated dosing, underscoring the utility of continuing misoprostol until expulsion occurs.

Ethical Declarations

This article is extracted from my master thesis/doctorate dissertation entitled "Clinical Outcomes of Intravaginal Misoprostol Use in 36 Cases with Therapeutic Abortion Indications", supervised by Taksim Hospital, İstanbul, 1993).

Ethical Standards: The study adhered to internationally recognized ethical standards, including those outlined in the Declaration of Helsinki.

Conflict of Interest Statement: The authors declare they have no conflicts of interest.

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Author Contributions: The author declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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