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Spontaneous abortion – Factors Determining Effectiveness of Pharmacotherapy with Misoprostol

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SUMMARY

Objectives: To evaluate clinical and demographic factors influencing the effectiveness of misoprostol pharmacotherapy in women diagnosed with spontaneous abortion.

Materials and Methods: This retrospective study included 120 women aged 23–41 years diagnosed with spontaneous abortion and treated at the University Hospital in Krakow from January 2023 to February 2025. Exclusion criteria were contraindications to misoprostol, preference for surgical treatment, and ectopic or unknown-location pregnancies. Diagnosis was confirmed by transvaginal ultrasound or by declining serum beta-human chorionic gonadotropin (β-hCG) levels without fetal cardiac activity. Misoprostol was administered following a standardized protocol, with ultrasound monitoring before each dose. The number of doses and treatment-related symptoms were recorded. Statistical analysis included the Mann–Whitney U, chi-square or Fisher's exact tests, and logistic regression to identify predictors of treatment failure. A p-value ≤ 0.05 was considered statistically significant.

Results: Of 120 women, 58 (48%) were successfully treated with misoprostol alone, while 62 (52%) required surgical curettage. No significant differences in age, body mass index (BMI), or obstetric history were observed between groups. Successful treatment was associated with lower gestational age (–10.6%). Adverse events such as diarrhea and mild abdominal pain occurred similarly in both groups; no hemorrhages were reported in the misoprostol-only group.

Conclusions: Gestational age is the primary predictor of successful pharmacological management of miscarriage with misoprostol. The treatment is safe and effective, supporting its use as first-line therapy in selected patients.

Keywords: β-hCG, Misoprostol; Missed miscarriage; Surgical curettage; Gestational age

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INTRODUCTION

Miscarriage, also defined as spontaneous abortion, is diagnosed as a nonviable intrauterine pregnancy up to 20 (22) weeks and affects approximately 20% of all pregnancies [1]. The most common causes include genetic abnormalities, maternal health conditions such as cardiovascular diseases and lifestyle factors like poor diet, smoking, alcohol consumption, and obesity. Advanced maternal age (35 years or older) is also a significant risk factor, along with a history of previous miscarriage or ectopic pregnancy [2].

There are three main approaches to miscarriage management: expectant, medical, and surgical, selected based on clinical context and patient preferences [3]. In the absence of spontaneous abortion or in cases of incomplete miscarriage, pharmacotherapy is a method of choice. Misoprostol is frequently administered for the medical treatment of miscarriage, promoting uterine contractions and, consequently, the expulsion of pregnancy tissue [3]. The effectiveness of therapy with misoprostol is approximately 86% [4]. Lack of effectiveness of the treatment requires the implementation of a surgical approach, which is related to increased complications such as uterine damage, hemorrhage, or intrauterine infection. The use of an appropriate therapy allows the procedure to be shortened, limits the risk of complications, and reduce the time to the next pregnancy. Therefore, the aim of this study was to evaluate the factors influencing effectiveness of pharmacotherapy in women diagnosed with spontaneous abortion.

METHODOLOGY

In this retrospective study, we enrolled women aged 23–41 years with diagnosed miscarriage, admitted to the Department of Gynecological Endocrinology, University Hospital in Krakow, between January 2023 and February 2025. Exclusion criteria were: contraindications to misoprostol therapy; preference for surgical management without pharmacotherapy; pregnancies of unknown location or ectopic pregnancies.

The Diagnosis

The diagnosis of spontaneous abortion was made based on Transvaginal Ultrasonography (TVU) where a non-viable pregnancy was confirmed, or decreasing β-hCG levels measured at least twice after 48 hours, with no fetal cardiac activity observed.

The Treatment with Misoprostol

Treatment was administered with misoprostol according to a standardized protocol developed based on published guidelines and previous research. Before each course of misoprostol, TVU was performed to assess the progress of pharmacotherapy. We recorded the number of misoprostol doses administered, along with symptoms reported by the patients, including abdominal pain, vaginal bleeding, and diarrhea. The study was approved by the Ethics Committee at Jagiellonian University Medical College (reference number KBET 1072.6120.220.2022).

Statistical analysis

Data were analyzed using appropriate statistical methods. Continuous variables are presented as medians with interquartile ranges and were compared using the Mann–Whitney U test. Categorical variables are expressed as percentages and were analyzed using the chi-square test or Fisher's exact test, as appropriate. Additionally, logistic regression analysis with backward elimination was conducted to identify factors - including gestational age, maternal age, BMI, gravidity, and a history of cesarean sections or vaginal deliveries - that might influence failure of pharmacological induction of miscarriage. The results are presented as adjusted odds ratios (OR) with 95% confidence intervals, with a p-value $\leq$ 0.05 considered statistically significant.

RESULTS

Baseline characteristics

The analysis included 120 women. Fifty-eight women (48%) were successfully treated with misoprostol, whereas 62 women (52%) needed curettage due to insufficient response to pharmacotherapy. There were no differences in baseline characteristics regarding age, BMI and number of previous vaginal deliveries or cesarean deliveries (Table 1). Women with successful treatment outcomes after misoprostol alone had lower gestational age (-10.6%) compared with women who required combined pharmacotherapy and curettage.

Treatment

Intergroup analysis revealed no differences in the number of doses given to women with pharmacotherapy and women with combined pharmacotherapy with curettage. There were no differences in treatment-related adverse events in two studied groups (Tab.1).

DISCUSSION

Our study showed that the effectiveness of pharmacological management with misoprostol in women with miscarriage depends mainly on the gestational age. Other factors, including maternal age, BMI, number of previous vaginal and/or cesarean deliveries did not influence the effectiveness of the treatment. These findings highlight the importance of early diagnosis of miscarriage to enable nonsurgical treatment. The earlier the treatment is initiated, the greater the likelihood of its success without the need for surgical intervention, which carries a higher risk of complications such as uterine injury, intrauterine infection, bleeding and prolonged recovery [4-6].

Based on current literature, several clinical and demographic factors influence the efficacy of misoprostol in the medical management of missed miscarriage. Higher success rates have been reported among women with a gestational age below nine weeks, absence of uterine scarring, and nulliparity [7,8]. Our findings support the association between earlier pregnancy and treatment success, as women who did not require curettage had significantly lower gestational age. Additional positive predictors described in previous studies include prior vaginal delivery and lower β-hCG levels at the start of treatment [1]. While our data did not reveal differences related to obstetric history or β-hCG levels, this may reflect the characteristics of our study group, where maternal age, BMI, and obstetric history did not differ significantly between the compared groups. Conversely, treatment failure has been associated in the literature with increased BMI, absence of pre-treatment symptoms, presence of a viable fetus, and sublingual misoprostol administration [2]. Moreover, although combined pre-treatment with mifepristone has been shown to improve outcomes, this was not part of our treatment protocol.

Tab. 1. Data are shown as median (IQR) or number (percentage).

	Pharmacotherapy (n=58)	Pharmacotherapy with curettage (n=62)	p
	Baseline characteristics		
Age, yrs	34.8±3.7	36.3±4.0	0.77
BMI, kg/m²	24.7±4.8	24.3±4.2	0.69
CD, n (%) **1** **≥2**	 11 (19.0) 7 (12.1)	 9 (14.5) 8 (12.9)	
VD, n (%) **1** **≥2**	 12 (20.7) 3 (5.2)	 10 (16.1) 5 (8.1)	
Age of the pregnancy, days	63.0 [52.8-70.3]	70.5 [63.0-82]	<0.001
	Treatment		
Doses of misoprostol used, n	5.5 [4.0-9.0]	6.0 [4.0-8.0]	
Adverse events, n (%) **Severe abdominal pain** **Diarrhea** **Hemorrhage**	 1 (1.7) 5 (8.6) 0 (0)	 6 (9.7) 4 (6.5) 9 (14.5)	

Its role in enhancing efficacy, especially in more advanced gestations, remains an important consideration for future research and clinical application [2].

Misoprostol is a widely used drug that rarely causes side effects. The most common ones are related to the digestive tract (e.g., diarrhea, nausea and abdominal pain) [9].

In our study, reported adverse events included severe abdominal pain, diarrhea and hemorrhage. Side effects were three times more common in patients who, in addition to pharmacotherapy, required curettage. Diarrhea was a frequent adverse reaction in both groups (6.5% in the pharmacotherapy and curettage group and 8.6% in the pharmacotherapy group), however, in other studies, gastrointestinal symptoms (e.g., diarrhea, nausea, vomiting) were even more common [10]. Among patients treated with misoprostol alone, severe abdominal pain was reported by 1.7% of them, and no cases of hemorrhage were observed. The overall incidence of serious side effects was low, consistent with findings from other studies [9]. Other side effects reported in literature included nausea, vomiting, chills and fever, yet none were observed in our research [11,12].

The non-randomized, observational nature and short follow-up are limitations of our study. We did not analyze long-term safety of the treatment; however, other studies have shown that misoprostol has no impact on future fertility [10,13]. Moreover, due to the limited sample size, the study may be underpowered to detect smaller differences between groups or to identify less common side effects. Therefore, further research is needed to validate our findings.

CONCLUSION

The present study demonstrated that gestational age was the primary factor associated with the effectiveness of pharmacological management of missed miscarriage using misoprostol. Patients with successful treatment outcomes had significantly lower gestational age compared with women requiring surgical intervention. Maternal age, body mass index, and obstetric history did not significantly influence treatment efficacy. Misoprostol showed a favorable safety profile, with the incidence of adverse effects, such as diarrhea and abdominal pain, was low and comparable between groups. These findings support the use of misoprostol as a first-line treatment option in women with missed miscarriage, particularly in earlier gestational weeks. Further prospective studies with larger sample sizes are warranted to identify additional prognostic factors, including the potential role of β-hCG levels and combined regimens incorporating mifepristone. Such research may contribute to the development of more precise clinical algorithms for selecting patients for pharmacological management.

DATA AVAILABILITY

Data are available from the authors upon reasonable request.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Concept and study design: MP, OKJ, RJ

Methodology: MMZ, MB, KB

Statistical analysis: MP, OKJ

Data collection and processing: MMZ, MB, KB

Drafting of the manuscript: MMZ, MB, KB

Manuscript review and editing: MP, OKJ, RJ

Supervision: MP

All authors have read and approved the final version of the manuscript and agreed to its publication.

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The authors declare no conflicts of interest.

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