# Assessment of patient acceptability of medical treatment in case of non-viable first trimester pregnancy

## Ocena akceptacji leczenia zachowawczego w przypadkach ciąży obumarłej w I trymestrze

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## Abstract

***Objectives:*** *The aim of the present study was to assess patient acceptability and satisfaction with medical treatment (vaginal misoprostol) of non-viable first trimester pregnancy.*

***Material and methods:*** *A total of 64 women, treated with vaginal misoprostol for non-viable first trimester pregnancy between October 2012 and December 2012 at the First Department of Obstetrics and Gynecology, Medical University of Warsaw, were included in this questionnaire-based study. Questions pertaining to advantages and disadvantages of misoprostol treatment as compared to potential surgical intervention were used. The respondents also determined whether they would choose medical treatment if they were to decide again. The Visual Analogue Scale (VAS) was used to assess pain and bleeding intensity.*

***Results:*** *Medical treatment was successful in 57 and surgical treatment was needed in 7 women. Average pain and bleeding intensity were 5.8 and 5.3, respectively. The most common side effects included diarrhea (27%), dizziness (22.2%), nausea (15.9%), and chills (15.6%). The most important advantages of misoprostol therapy were avoidance of the risk of uterine perforation (96.4%) and formation of intrauterine adhesions (74.6%), whereas the most significant disadvantages were prolonged bleeding (21.4%), pain (21.4%), and longer treatment duration (42.9%). Overall, 95.6% of the patients with successful treatment outcome declared they would choose this procedure if they were to decide again, as compared to 85.6% of women with treatment failure (p>0.05).*

***Conclusions:*** *Medical treatment with vaginal misoprostol is acceptable and well-tolerated by the vast majority of women with non-viable first trimester pregnancy. Satisfaction is expressed by both, respondents with successful as well as unsuccessful treatment outcome.*

Key words: **missed abortion** / **misoprostol** / **dilatation and curettage** /

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Otrzymano: **15.10.2014**
Zaakceptowano do druku: **17.11.2014**

## Streszczenie

***Cel:*** *Celem pracy była ocena akceptacji i stopnia satysfakcji pacjentek z farmakologicznej indukcji poronienia mizoprostolem w przypadkach ciąży obumarłej w I trymestrze.*

***Materiał i metody:*** *Wśród 64 pacjentek z ciążą obumarłą w I trymestrze hospitalizowanych od października 2012 roku do grudnia 2013 roku w I Klinice Położnictwa i Ginekologii Warszawskiego Uniwersytetu Medycznego leczonych mizoprostolem, przeprowadzono ankietę zawierającą pytania dotyczące akceptacji i satysfakcji z zastosowanej metody. W kwestionariuszu znalazły się również pytania o zalety i wady leczenia mizoprostolem w porównaniu do potencjalnego leczenia zabiegowego. Pacjentki ponadto wskazywały, czy w razie konieczności ponownie zdecydowałyby się na farmakoterapię.*

***Wyniki:*** *U 57 pacjentek leczenie farmakologiczne było skuteczne, natomiast 7 wymagało zabiegu wyłyżeczkowania jamy macicy. Stopień nasilenia bólu oraz krwawienia podczas leczenia pacjentki oceniały w wizualnej skali analogowej (VAS). Wynosił on odpowiednio 5,8 pkt i 5,3 pkt.*

*Najczęściej zgłaszanymi działaniami niepożądanymi były: biegunka (27%), zawroty głowy (22.2%), nudności (15.9%) i dreszcze (15.6%). Za największe korzyści terapii mizoprostolem uznano uniknięcie ryzyka uszkodzenia macicy podczas zabiegu (96.4%) oraz powstania zrostów wewnątrzmacicznych (74.6%).*

*Wśród wad wymieniano: przedłużone krwawienie (21,4%), ból (21,4%) i dłuższy czas terapii w porównaniu do postępowania zabiegowego (42.9%). Wyniki leczenia nie wpłynęły na ewentualny ponowny wybór tej metody przez pacjentki. Przy skutecznym leczeniu mizoprostolem 95,6% kobiet ponownie zdecydowałoby się na zaproponowane postępowanie, natomiast przy nieefektywnym leczeniu 85,6% (p>0,05).*

***Wnioski:*** *W przypadku ciąży obumarłej w I trymestrze, indukcja poronienia przy zastosowaniu mizoprostolu dopochwowo jest metodą akceptowalną i dobrze tolerowaną przez zdecydowaną większość pacjentek. Zadowolenie z leczenia mizoprostolem wyrażają zarówno pacjentki z efektywną, jak i nieskuteczną terapią.*

Słowa kluczowe: **poronienie zatrzymane** / **mizoprostol** / / **wyłyżeczkowanie jamy macicy** /

## Introduction

Non-viable first trimester pregnancy is a common complication, diagnosed in 10-20% of women with clinically confirmed pregnancy [1]. The diagnosis is made on the basis of transvaginal ultrasound examination revealing a gestational sac without the embryo and yolk sac (anembryonic pregnancy) or containing an embryo without visible heart rate (missed abortion). Naturally, the products of conception are expulsed from the uterus after a variably long period of time. Expectant management is one of the options. According to the results of a meta-analysis performed by Graziosi et al., the persistence of trophoblast in the uterine cavity is not associated with an increased risk of complications, but expectant management implicates the necessity of a long observation and its effectiveness is significantly lower when compared to other treatment methods [2].

The diagnosis of miscarriage, apart from the medical aspect, significantly influences the emotional sphere of the affected woman. Pregnancy loss is commonly related to the feeling of loss and sadness and these emotions may have a negative impact on the woman even many years later. Therefore, patients often expect an active form of management as well as help in coping with the negative emotions. Taking into account the expectations and procreative plans of the affected women, management must be characterized by high effectiveness and patient acceptability, as well as enable rapid resolution of procreative functions.

In many gynecology centers, dilatation and curettage (D&C) remains the method of choice for missed abortion or anembryonic pregnancy. However, the procedure is associated with various risks, i.e. injury to the uterine cervix, perforation of the uterine wall, infection, as well as damage to internal organs and formation of intrauterine adhesions. Moreover, surgical evacuation requires anesthesia which is also associated with specific risks. Recently, a number of reports confirming the effectiveness and safety of misoprostol used as a sole agent to treat non-viable first trimester pregnancy have been published [3-7]. These results were consistent with the findings of the present study [8].

## Objectives

The present study is a continuation of research conducted at the First Department of Obstetrics and Gynecology, Medical University of Warsaw, concerning medical treatment with misoprostol as a sole management option (without subsequent D&C) for non-viable first trimester pregnancy. The aim of the study was to assess patient acceptability of the procedure in relation to its effectiveness and the course of treatment.

## Material and methods

A total of 67 patients with non-viable first trimester pregnancy confirmed by ultrasound examination, treated at the First Department of Obstetrics and Gynecology, Medical University of Warsaw between October 2012 and December 2013, were enrolled. All women underwent medical treatment with 800 mcg of misoprostol administered vaginally. If substantial bleeding occurred, transvaginal ultrasound was performed after 6 hours in order to determine whether the gestational sac had been expulsed. If not, another dose of vaginal misoprostol was administered. If necessary, the same regimen was repeated the next day. A patient was only discharged when expulsion of the sac was confirmed by an ultrasound examination. The treatment was considered unsuccessful if the gestational sac remained in the uterine cavity

after 48 hours. In these cases, D&C was performed (Figure 1). In all patients an ultrasound examination was performed following their first period post-miscarriage, in order to confirm that the uterus was empty. The questionnaire was filled out 6 weeks post-treatment, during a control visit (36 cases) or via e-mail (31 cases). The questionnaire is shown in Figure 2.

## Results

The questionnaire was filled out by 64 women who gave their consent to the medical treatment of non-viable first trimester pregnancy. The consent form was signed by the patient after discussing all the advantages and risks of the procedure. Approximately 23.8% of the patients were not aware of the possibility of medical treatment after missed abortion, believing surgical treatment was always necessary. The treatment was successful in 57 (89%) of the patients, whereas D&C had to be performed in 7 (11%) women. Mean patient age was 32.6 years and mean gestational age was 9 weeks 6 days (SD 1.51). Nulliparas comprised 66.1% of the study group.

According to the respondents, the most important advantages of the medical treatment were avoidance of both, the risk of uterine perforation (96.4%), and formation of intrauterine adhesions (74.6%), whereas the most significant drawbacks included prolonged bleeding (21.4%), pain (21.%), and longer duration of the therapy as compared to curettage (42.9%) (Table I).

The most common symptoms accompanying medical treatment of non-viable first-trimester pregnancy were also analyzed. Pain and bleeding intensity was assessed with the use of the Visual Analogue Scale (VAS). Mean intensity of pain was 5.8 points, irrespective of parity. In 84.1% of the cases, standard doses of non-opioid analgesics (paracetamol, ibuprofen, ketoprofen) sufficed to relieve the pain. Mean intensity of bleeding was 5.3 points (Table II).

The most common side effects of vaginal misoprostol were diarrhea (27%), dizziness (22.2%), nausea (15.9%), and chills (15.6%) (Table III).

Overall, 95.6% of the women with successful treatment would choose the same method if they were to decide again. The rate was lower (85.6%) among women with unsuccessful treatment in whom D&C had to be performed. The difference was not statistically significant ($p>0.05$).

## Discussion

Medical treatment of non-viable first-trimester pregnancy has recently become more popular. Nevertheless, about 25% of the women from the present study were not aware of the possibility of avoiding D&C. According to the recommendations of the Royal College of Obstetricians and Gynecologists (RCOG), surgical uterine evacuation should be performed in case of persistent excessive bleeding, hemodynamic instability, infection of the retained products of conception, and suspected gestational trophoblastic disease [9].

Misoprostol has been proven to be an effective and safe alternative to D&C in early pregnancy failure [3-7]. The choice of the therapeutic option depends not only on its effectiveness, but also on patient acceptability of the management. The latter is influenced by the duration of hospitalization, side effects, administration, as well as time that passes until the completion of miscarriage.

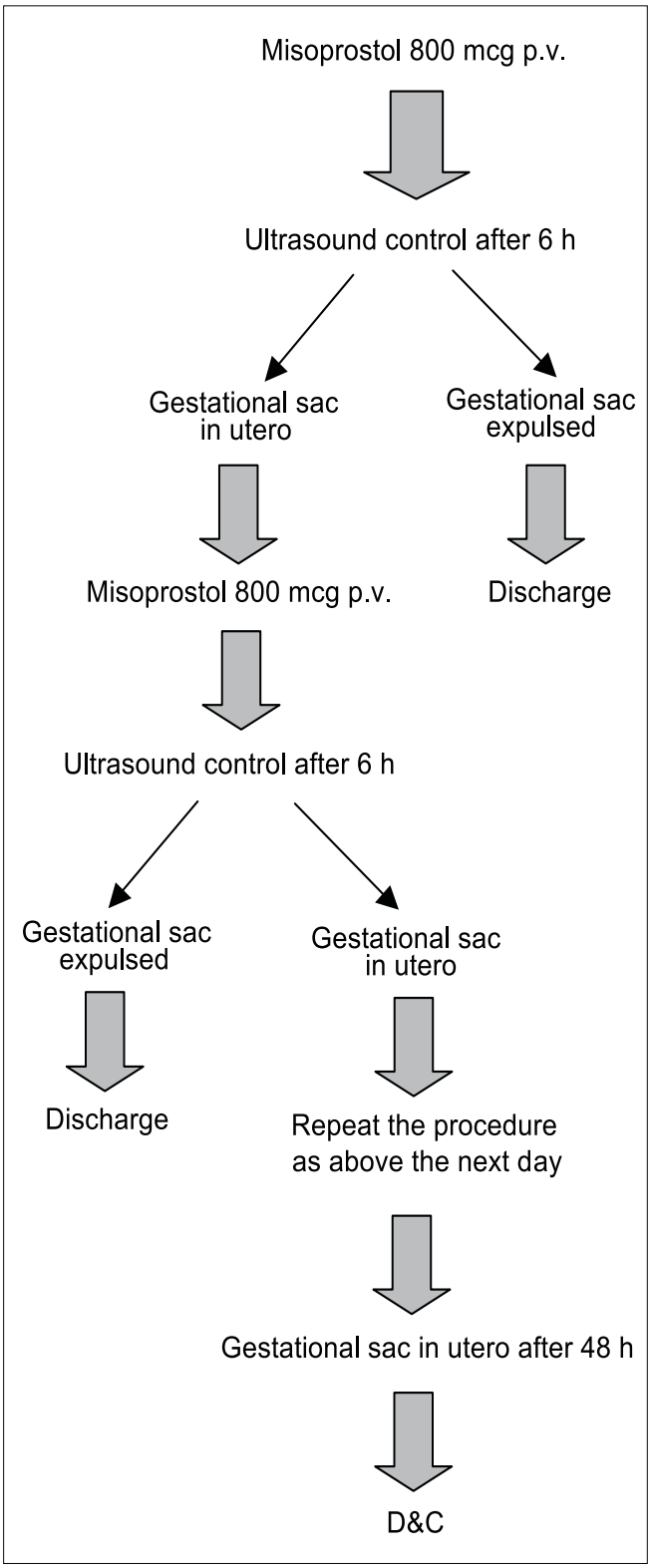


**Figure 1.** Management of non-viable first trimester pregnancy.

In a study performed by Tang et al., patient acceptability of medical treatment with misoprostol was assessed in two groups of patients: after oral and vaginal administration. The intensity of side effects was similar in both groups [10]. In the present study, the above mentioned results cannot be confirmed, since all women received misoprostol vaginally.

**Table I.** Advantages and disadvantages of medical treatment- patients' opinions.

| Advantages | | | |
|---|---|---|---|
| | **All patients** | **Nulliparas** | **Multiparas** |
| Avoidance of the risk for uterine perforation | 60 (95.2%) | 34 (94.4%) | 18 (94.7%) |
| Avoidance of anesthesia | 36 (57.1%) | 18 (50%) | 14 (73.7%) |
| Avoidance of the risk for formation of intrauterine adhesions | 47 (74.6%) | 27 (75%) | 13 (68.4%) |
| Imitation of natural miscarriage | 33 (52.4%) | 17 (47.2%) | 11 (57.9%) |
| **Disadvantages** | | | |
| Pain | 14 (22.2%) | 9 (24.3%) | 2 (10.5%) |
| Longer duration of the procedure | 12 (19%) | 4 (11.1%) | 4 (26.3%) |
| Vaginal bleeding | 13 (20.6%) | 6 (16.7%) | 2 (10.5%) |

**Table II.** Pain and bleeding intensity assessed with VAS.

| | **All patients** | **Min.** | **Max.** | **nulliparas** | **multiparas** | **P** |
|---|---|---|---|---|---|---|
| **Pain** | 5.8 (2.54) | 1 | 10 | 6.11 (2.3) | 5.63 (2.63) | >0.05 |
| **Bleeding** | 5.3 (2.34) | 0 | 10 | 5.67 (2.12) | 4.94 (2.42) | >0.05 |

Data are given as mean (SD)

In another study, a multicenter randomized clinical trial (over 650 patients), medical treatment with vaginal misoprostol was compared to vacuum aspiration. Misoprostol was shown to be both, effective and highly acceptable. The majority of women would choose this treatment option if they were to decide again. However, it should be stressed that failure of this treatment significantly reduces patient acceptability [11]. Likewise, Graziosi et al., reported that patient acceptability of misoprostol treatment for early pregnancy failure depends mainly on the effectiveness of the therapy. Approximately 76% of the patients in whom misoprostol caused complete miscarriage would choose the method again, compared to 38% of women with unsuccessful medical treatment of early pregnancy failure ($p<0.01$) [12, 13].

In the present study, the vast majority of women would opt for medical treatment with misoprostol if they were to choose again: 95.6% of the patients in whom misoprostol caused complete evacuation and 85.6% of women who had to undergo surgical evacuation ($p>0.05$).

The acceptability levels of various side effects of medical and surgical treatment were similar in the majority of reports. Differences were seen only in terms of pain and bleeding intensity. In an analysis performed by Harwood et al., patients who were treated with vaginal misoprostol reported greater pain, higher intensity of vaginal bleeding, and longer symptom duration than those who underwent vacuum aspiration ($p<0.001$) [11]. In the present study, the patients also evaluated the intensity of lower abdominal pain and vaginal bleeding as rather high. However, the results were not compared to other treatment modalities. Other studies on the use of misoprostol confirm these findings [10, 14].

According to another study, a randomized trial performed by Kong et al., lower abdominal pain and vaginal bleeding were also the most common side effects of misoprostol. However, these authors emphasized high incidence of gastrointestinal symptoms in women who received this medication. The study group, which consisted of 180 patients with non-viable first trimester pregnancy, was divided into three groups, depending on the chosen treatment method: surgical evacuation, medical treatment with misoprostol, or expectant management. The outcomes were assessed during the follow-up visit 14 days later, with ultrasound examination. If medical treatment or expectant management proved ineffective, surgical evacuation was recommended. Complete miscarriage rates were as follows: 98% (surgical treatment), 79% (misoprostol) and 79.3% (expectant management). Women who underwent surgical evacuation reported shorter bleeding but had an increased risk of infection. Women treated with misoprostol complained about gastrointestinal symptoms significantly more often than women from the other two groups ($p<0.05$). Despite inter-group differences, the assessment of quality of life in relation to physical symptoms was similar [15].

**Table III.** Side effects of vaginal misoprostol.

| | **All patients** |
|---|---|
| **Diarrhea** | 17 (27%) |
| **Dizziness** | 14 (22.2%) |
| **Chills** | 10 (15.6%) |
| **Nausea** | 10 (15.9%) |
| **Fever** | 8 (12.5%) |
| **Headache** | 7 (11.1%) |
| **Vomiting** | 5 (7.9%) |
| **Fainting** | 3 (4.8%) |

Data are given as n (%).

1. Were you aware of the possibility of avoiding curettage when you were admitted to the hospital?
   YES NO

2. Evaluate the intensity of bleeding you experienced during the procedure:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| very light | | | | | | | | very heavy | |

3. Evaluate the intensity of pain you experienced during the procedure:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| no pain | | | | | | | | | unbearable pain |

4. Did you notice any of the following symptoms during the treatment (mark all the symptoms you noticed):
   a. fever
   b. chills
   c. nausea
   d. vomiting
   e. diarrhea
   f. headache
   g. fainting
   h. dizziness
   i. other……

5. If pain occurred, did you use any painkillers?
   YES NO
   If YES, did they resolve the pain adequately?
   YES NO

6. Which of the aspects of the medical treatment do you consider most favorable:
   a. avoidance of the risk for damage to the uterus
   b. avoidance of anesthesia
   c. avoidance of the risk for formation of intrauterine adhesions
   d. the method imitates natural miscarriage

7. Which of the aspects of the medical treatment do you consider least favorable:
   a. longer duration compared to surgical treatment
   b. vaginal bleeding
   c. pain
   d. other……

8. If you were to decide once again, would you opt for:
   a. medical treatment or
   b. dilatation and curettage?

**Figure 2.** The questionnaire.
A paired t-test and Fisher's exact test were used for statistical analysis.

Gastrointestinal symptoms, such as vomiting and diarrhea, were also the most common symptoms reported by women included in the present study.

In the majority of the above mentioned studies, medical treatment with misoprostol was undertaken on an outpatient basis. This fact may influence the differences in the level of acceptability of side effects. In the present study, all patients stayed at the hospital until the miscarriage was completed. The necessity of hospitalization may additionally negatively influence the acceptability of medical treatment. The incidence and intensity of side effects is well-tolerated by patients and the procedure can be safely performed on an outpatient basis. Limiting the number of surgical procedures reduces the risk of complications, whereas performing medical treatment on an outpatient basis diminishes stress and reduces the costs.

## Conclusions

Medical treatment with vaginal misoprostol is a safe, highly effective and well-tolerated procedure. Satisfaction is expressed both, patients with successful and failed therapy. Uniform schemes of qualification, dosage and follow-up would enable a wide use of misoprostol as the basic management of early pregnancy failure.

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**Źródło finansowania:**
Praca nie była finansowana przez żadną instytucję naukowo-badawczą, stowarzyszenie ani inny podmiot, autorzy nie otrzymali żadnego grantu.

**Konflikt interesów:**
Autorzy nie zgłaszają konfliktu interesów oraz nie otrzymali żadnego wynagrodzenia związanego z powstawaniem pracy.

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