Journal of Medical & Pharmaceutical Sciences
Volume (6), Issue (2): 30 Jun 2022
P: 91 - 98
ISSN: 2522- 333X
مجلة العلوم الطبية والصيدلانية
المجلد (6)، العدد (2): 30 يونيو 2022 م
ص: 91 - 98

# Comparison of misoprostol doses in termination of pregnancy in the first trimester

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**Abstract:** Objective: The aim of this study is to compare the efficacy of vaginal misoprostol with different doses for abortion in the first trimester.

Patients and Methods: Descriptive Comparative Study conducted for the period one year (July 2020 –July 2021) at Tishreen University Hospital in Lattakia- Syria. The study included 80 pregnant women in the first trimester who had a therapeutic indication for termination of pregnancy after taken consent from it and her fathers, and were divided into group A was (40 women): were administrated 400 µg of vaginal misoprostol and repeated every 6 h for 48 h, and group B was (40 women): were administrated 800 µg of vaginal misoprostol repeated after 24 h.

Results: Abortion rate after the first dose in group B was higher than group A (67.5% vs.10%). The rate of complete abortion was significantly higher in group B (72.5%) vs. (17.5%) in group A, p= 0.0001, and mean induction- abortion interval in group B was significantly shorter than group A (13.8±3.3 vs. 29.4±5.9, p: 0.004). There weren't significant associations between both indications and results of abortion with the number of pregnancies in the two groups (p>0.05). Nausea was the most frequent side effect in the two groups without significant difference (p>0.05).

Conclusion: Misoprostol represents a safe and effective alternative to invasive methods for termination early intrauterine pregnancy.

**Keywords**: Misoprostol, first trimester, abortion.

# مقارنة بين جرعات الميزوبروستول في إنهاء الحمل في الثلث الأول من الحمل

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**المستخلص**: هدفت الدراسة إلى مقارنة فعالية الميزوبروستول المعطى عن طريق المهبل بجرعات مختلفة في إنهاء الحمل في الثلث الأول منه.

طريقة البحث: كانت هذه دراسة مقارنة وصفية أجريت في مشفى تشرين الجامعي في اللاذقية- سوريا خلال الفترة الممتدة ما بين تموز 2020- تموز 2021. شملت الدراسة 80 حاملاً في الثلث الأول من الحمل مع وجود أحد استطبابات إنهاء الحمل لديهن وتم تقسيمهن إلى مجموعتين: مجموعة (A) شملت 40 حاملاً تم إعطاؤهن الميزوبروستول مهبلياً بجرعة 400 ميكروجرام مع تكرارها كل 6 ساعات لمدة 48 ساعة، ومجموعة (B) شملت 40 حاملاً تم إعطاؤهن الميزوبروستول مهبلياً بجرعة 800 ميكروجرام مع تكرارها بعد 24 ساعة.

النتائج: إن معدل حدوث الإسقاط بعد الجرعة الأولى كان مرتفعاً في المجموعة B مقارنة مع المجموعة A (67.5% مقابل 10%). كان معدل حدوث الإسقاط التام مرتفعاً بشكل هام في المجموعة B (72.5%) مقابل (17.5%) في المجموعة A، P: 0.0001، ومتوسط المدة الزمنية التحريض- الإسقاط كان أقل في المجموعة B مقارنة مع المجموعة A (13.8±3.3 مقابل 29.4± 5.9، P: 0.004). لم يلاحظ وجود علاقة ذات دلالة إحصائية بين كل من استطبابات الإسقاط ونتائجه في كلا المجموعتين مع عدد الحمول (P>0.05). إن أكثر الآثار الجانبية تواتراً هي الغثيان في كلا المجموعتين من دون أهمية إحصائية (P>0.05).

الاستنتاج: يمثل الميزوبروستول طريقة بديلة عن الطرق الغازية آمنة وفعالة لإنهاء الحمل بشكل باكر.

**الكلمات المفتاحية**: ميزوبروستول، الثلث الأول، الإسقاط.

## Introduction.

Induced abortion, the intentional termination of pregnancy by artificial means before the stage of viability, is among the most common of gynecological procedures [1]. Worldwide, the estimated rate for abortion was 35 per 1000 women ages 15 to 44 year, and abortion mortality accounts for at least 13% of all maternal mortality [2, 3].

There are medical factors both maternal and fetal that contribute to the decision of therapeutic abortion. Maternal indications include: hypertensive disorders with organ dysfunction, sepsis, severe exacerbation of autoimmune disorder, severely deteriorating cardiac function, and rapidly progressing malignancies. Fetal indications include risk of abnormality from either genetic or environmental factors [4]. The two main options for termination are medical and surgical treatment with a complete abortion rate of around 95% and 97% respectively [5]. The choice of treatment depends on the period of gestation, availabilities of drugs, women's own preference and presence of medical contraindications [6].

First trimester termination of pregnancy is considered a safe and effective procedure (WHO 2012). Medical methods refer to the termination of pregnancy by using medications to induce process similar to a miscarriage [7]. They are feasible alternatives to surgery and avoid patients the risk of anesthesia [8]. The first drug used was mifepristone in 1988, and methotrexate was also used in early 1990 [9]. Misoprostol is a prostaglandin E- 1 analogue which induces uterine contractions, cervical dilatation and ripening. It is the sole prostaglandin approved by FDA for use for medication abortion [10]. Several studies have explored utilization of misoprostol alone with different doses and intervals of administration with variable efficacy.

The objectives of this review were: to compare the effectiveness of different doses of medical abortion containing misoprostol with different intervals and compare the side effects of the two methods.

## Patients and Methods:

This is Descriptive Comparative Study of a group of pregnant women attending department of Obstetrics and Gynecology at Tishreen University Hospital in Lattakia- Syria during one-year period (July 2020- July 2021) who requested medical termination of pregnancy in the first trimester. The inclusion criteria were: presence of missed abortion, blighted ovum, nonviable pregnancy and fetal exposure to

known teratogen. The exclusion criteria were:- history of cardiac, respiratory, and renal diseases, prior uterine surgery, known allergy to prostaglandins or misoprostol, prior use of misoprostol before attending hospital and presence of active bleeding.

Ethical consideration: All patients were provided a complete and clear informed written consent from it and her husband after discussion about the study and hazards of induction in the 1st trimester. This study was performed in accordance with the Declaration of Helsinki.

The following workup included: Demographic characteristics as ages, gestational age, obstetric history, history of medical diseases (present, family and past) and physical examination were written. Gestational age was measured from the first day of the last menstrual period according to menstrual history and pelvic ultrasonography examination. Women assigned to Group A were given 400 µg of vaginal misoprostol and repeated every 6 hours for 48 hours, and Group B were administrated 800 µg of vaginal misoprostol repeated after 24 hours. Baseline vital signs were taken before initiation the first dose, reevaluated after administration with 4 hour intervals, and side effects were recorded.

**Statistical Analysis**

Statistical analysis was performed by using IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations (SD), Frequency and percentages. To examine the relationships and comparisons between the two group, chi- square test was used or Fisher exact test if it need. Independent t student test was used to compare two independent groups. All the tests were considered significant at a 5% type I error rate ($p<0.05$), $\beta$: 20%, and power of the study: 80%.

## Results.

As shown in Table (1), the mean age was 29.7±7.4 in group A and 28.1±7.6 in group B, p: 0.3. The mean gestational age was 10.1±1.2 in group A vs. 9.6±1.5 in group B, p: 0.2. Missed abortion was the most frequent indication for termination of pregnancy followed by blighted ovum in the two groups without significant differences ($p> 0.05$). There were no significant differences between the two groups regarding to obstetric history and presence of previous abortions ($p>0.05$).

**Table (1) Demographic characteristics of the study population by comparison of the two**

| Variables | Group A (n=40) | Group B (n=40) | P value |
|---|---|---|---|
| Age (years) | 29.7±7.4 | 28.1±7.6 | 0.3 |
| Gestational age (weeks) | 10.1±1.2 | 9.6±1.5 | 0.2 |
| Obstetric history | | | |
| Nulliparous | 8 (20%) | 8 (20%) | 1 |
| Multiparous | 32 (80%) | 32 (80%) | |
| Previous abortions | 12 (30%) | 15 (37.5%) | 0.4 |

| Variables | Group A (n=40) | Group B (n=40) | P value |
|---|---|---|---|
| Indications of termination of pregnancy | | | |
| Missed abortion | 22 (55%) | 21 (52.5%) | 0.3 |
| Blighted ovum | 18 (45%) | 18 (45%) | 1 |
| Maternal medical disorders | 0 (0%) | 1 (2.5%) | 0.3 |

Abortion rate after 1st dose in the group B was higher than group A (67.5% vs.10%), and most cases of abortion of group A were after 4th dose (40%), Table (2).

**Table (2) Abortion rates after each dose of misoprostol in the two groups**

| Variable | Group A (n=40) | Group B (n=40) |
|---|---|---|
| After 1st dose | 4 (10%) | 27 (67.5%) |
| After 2nd dose | 6 (15%) | 13 (32.5%) |
| After 3rd dose | 6 (15%) | ----- |
| After 4th dose | 16 (40%) | ----- |
| After 5th dose | 4 (10%) | ----- |
| After 6th dose | 2 (5%) | ----- |
| After 7th dose | 1 (2.5%) | ----- |
| After 8th dose | 1 (2.5%) | ----- |

Mean induction- abortion interval in Group B was significantly shorter than group A (13.8±3.3 vs. 29.4±5.9, p: 0.004). The rate of complete abortion was higher in group B (72.5% vs.17.5% in group A, p: 0.0001). Curettage was applied mainly due to incomplete abortion in the two groups (65% in group A vs.25% in group B, p: 0.005), followed by failure medical induction (17.5% vs.2.5%, p: 0.02).

**Table (3) Result of abortion by comparison of the two group**

| | Group A (n=40) | Group B (n=40) | P value |
|---|---|---|---|
| Induction- abortion interval (h) | 29.4±5.9 | 13.8±3.3 | 0.004 |
| Complete abortion | 7 (17.5%) | 29 (72.5%) | 0.0001 |
| Curettage (n, %) | 33 (82.5%) | 11 (27.5%) | 0.0001 |
| Incomplete abortion | 26 (65%) | 10 (25%) | 0.005 |
| Failure medical induction | 7 (17.5%) | 1 (2.5%) | 0.02 |

As shown below in Table (4), there weren't significant associations between both indications and results of abortion with the number of pregnancies in group A (p>0.05).

**Table (4) Distribution of the study population according to the obstetric history and results of abortion in group A**

| Variable | Group A (n=40) | | P value |
|---|---|---|---|
| | Nulliparous | Multiparous | |
| Indications of abortion | | | |
| Missed abortion | 3 (37.5%) | 19 (59.4%) | 0.09 |
| Blighted ovum | 5 (62.5%) | 13 (40.6%) | 0.08 |
| Results of termination | | | |
| Complete abortion | 2 (25%) | 5 (15.6%) | 0.2 |
| Incomplete abortion | 5 (62.5%) | 21 (65.6%) | 0.1 |
| Failure medical induction | 1 (12.5%) | 6 (18.8%) | 0.8 |

As shown below in Table (5), there weren't significant associations between both indications and results of abortion with the number of pregnancies in group B ($p>0.05$).

**Table (5) Distribution of the study population according to the obstetric history and results of abortion in group B**

| Variable | Group B (n=40) | | P value |
|---|---|---|---|
| | Nulliparous | Multiparous | |
| Indication of abortion | | | |
| Missed abortion | 5 (62.5%) | 16 (50%) | 0.2 |
| Blighted ovum | 3 (37.5%) | 15 (46.9%) | 0.9 |
| Maternal medical disorders | 0 (0%) | 1 (3.1%) | 0.1 |
| Results of termination | | | |
| Complete abortion | 6 (75%) | 23 (71.9%) | 0.9 |
| Incomplete abortion | 2 (25%) | 8 (25%) | 0.5 |
| Failure medical induction | 0 (0%) | 1 (3.1%) | 0.1 |

There weren't significant differences between indications and the results of abortion in the group A ($p>0.05$).

**Table (6) Results of termination according to the indications of abortion in the group A**

| Results of termination | Group A (n=40) | | P value |
|---|---|---|---|
| | Missed abortion | Blighted ovum | |
| Complete abortion | 2 (9.1%) | 5 (27.8%) | 0.07 |
| Incomplete abortion | 16 (72.7%) | 10 (55.5%) | 0.8 |
| Failure medical induction | 4 (18.2%) | 3 (16.7%) | 0.1 |

There weren't significant differences between indications and the results of abortion in the group B ($p>0.05$).

**Table (7) Results of termination according to the indications of abortion in group B**

| Results of termination | Group B (n=40) | | | P value |
|---|---|---|---|---|
| | Missed abortion | Blighted ovum | Maternal medical disorders | |
| Complete abortion | 16 (76.2%) | 13 (72.2%) | 0 (0%) | 0.7 |
| Incomplete abortion | 5 (23.8%) | 4 (22.2%) | 1 (100%) | 0.9 |
| Failure medical induction | 0 (0%) | 1 (5.6%) | 0 (0%) | 0.5 |

The incidence of all reported side effects are in table (8). The two groups didn't differ significantly with respect to side effects. Nausea was more frequently in the two group without significant differences (p: 0.09).

**Table (8) Incidence of side effects after misoprostol administration**

| Side effects | Group A (n=40) | Group B (n=40) | P value |
|---|---|---|---|
| Nausea | 5 (12.5%) | 11 (27.5%) | 0.09 |
| Vomiting | 0 (0%) | 1 (2.5%) | 0.6 |
| Headache | 1 (2.5%) | 1 (2.5%) | 1 |
| Fever | 1 (2.5%) | 1 (2.5%) | 1 |
| Tachycardia | 1 (2.5%) | 1 (2.5%) | 1 |

## Discussion.

The current study describes the efficacy of the use different methods of misoprostol for the medical termination of early pregnancy. Our study demonstrated the superiority of vaginal use of misoprostol with a dose of 800 µg repeated after 24 h in efficacy compared to using a dose of 400 µg repeated every 6 h for 48 h, in which abortion rate after one dose was higher, mean induction- abortion interval was significantly shorter, and rate of complete abortion was higher. Curettage was applied more frequently in the group A, mainly due to incomplete abortion. The most frequent adverse effect was nausea, and major side effects such as bronchospasm and uterine rupture didn't occur. There weren't significant associations between both indications and results of abortion with the number of pregnancies in the two groups. The results of this study are comparable to the findings reported by previous studies.

These findings might be explained by the effects of misoprostol which include: inducing cervical softening, dilation and uterine contractions at all gestational ages, thereby facilitating uterine evacuation, but these effects varies with gestational age, route of administration, the dose, and dosing interval [11].

Zaikopoulos *et al.*, (2002) found that vaginal misoprostol- alone regimen is effective highly for women seeking medical abortion with better efficacy was achieved at a gestational age of <42 days (96.3%) vs.86.3% in gestation: 42- 56 days [12].

Ayati *et al.*, (2008) demonstrated that termination of pregnancy in the first trimester with vaginal misoprostol (800µg repeated every 24 h for a maximum of three doses) is effective and safe, in which 83% of women had successful complete abortion, without important side effects [13].

In contrast to our results, Farzaneh *et al.*, (2018) found that lower and multiple doses of vaginal misoprostol (400 µg every 6 h) was more effective than 800µg daily in termination of pregnancy in the first trimester (60% vs.37%, p: 0.04), and most frequent side effects were diarrhea and fever without serious complications [14].

In summary, abortion by 800µg of vaginal misoprostol with a 24- h interval was more effective than 400 µg with 6- h interval and can safely be offered to women seeking care in the first trimester.

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