

Oral versus Vaginal Misoprostol in Management of Blighted Ovum

Mostafa Gamal Abdelhaleem Mohammed

Obstetrics & Gynecology Department, Al-Galaa Teaching Hospital, Cairo, Egypt

Corresponding author: Mostafa Gamal Abdelhaleem, Mobile: (+20) 01014494022, E-Mail: drmostafagamal2011@gmail.com

ABSTRACT

Background: Vaginal misoprostol is preferable than oral misoprostol in the first trimester of pregnancy, according to clinical research.

Objective: Comparing the success rate, tolerability and side effects between oral and vaginal 600µg misoprostol in the management of blighted ovum.

Subjects and Methods: Our study was carried out on 100 pregnant women diagnosed as blighted ovum, admitted to the Obstetric Unit in Al-Galaa Teaching Hospital and after careful U/S examination and after second opinion examination all of the participants were informed about the procedures and the possible failure of our study. Two groups were created (50 in each group), (A) took misoprostol orally and (B) group took misoprostol virginally.

Results: The gestational ages did not differ significantly between the two groups of participants ($P>0.05$). Patients who successfully completed medicinal abortions and those who needed surgical evacuation were not statistically different. Also, according to side effects, there was no statistically significant difference in the two groups ($P>0.05$) except for diarrhea and vomiting, which were significantly increased in oral group.

Conclusion: Using oral and vaginal misoprostol 600µg as medical managing for a blighted ovum, their effectiveness is practically identical.

Keywords: Misoprostol, Blighted Ovum, Termination of Pregnancy.

INTRODUCTION

Premature termination of a pregnancy, known as miscarriage or spontaneous abortion, occurs when the fetus or embryo does not have the ability to survive into the 20th week of pregnancy. In early pregnancy, miscarriage is by far the most prevalent issue that might arise⁽¹⁾.

Early pregnancy loss or chemical pregnancy is the medical term for miscarriages that occur before the sixth week of a woman's last menstrual period. An abortion that occurs after six weeks of pregnancy is known as a clinical spontaneous abortion by medical professionals. Fifteen to 20 percent of all pregnancies are complicated by early pregnancy failure, often known as a blighted ovum, an early fetal demise, or a missed abortion⁽²⁾.

Blighted ova are fertilized eggs that implant but do not develop. The gestational sac continues to expand, but the fetus does not expand with it. The yolk and fetal pole will be absent if the ovum is indeed blighted. Fifteen percent of all clinically diagnosed pregnancies result in a miscarriage, according to some estimates. Only about 45 to 55 percent of all pregnancies end in miscarriage as a result of a blighted ovum, according to current estimates⁽³⁾.

Just how much we don't understand about the blighted ovum is astounding. Even though it is commonly referenced in medical literature, the blighted ovum is not the subject of a large number of research publications. An anomaly in chromosomes 16 or 22 may be responsible for a blighted ovary, according to the general consensus⁽⁴⁾.

It is more common in older women and the egg, rather than the sperm, that is the source of the problem with a blight. When it happens only once, it's thought to be a freak accident. However, a miscarriage is a possibility in any pregnancy. As long as you are healthy

and have experienced one blighted ovum, your chance of miscarriage is not increased because of this ovum⁽⁵⁾.

Recently, medical management of miscarriage has been investigated as an alternative. The efficacy of prostaglandins with or without mifepristone has been studied in several investigations. Developing an alternative to mifepristone, which is expensive and unavailable in many countries, is important because of the disparities in selection criteria, choice, and criteria for diagnosing complete miscarriage⁽⁶⁾.

In comparison to prostaglandin E2 analogues, misoprostol is a prostaglandin E1 analogue with lower costs, longer shelf lives at room temperature, and less side effects. It is recommended that women use the prostaglandin misoprostol, which can be taken orally, vaginally, or sublingually. Pregnancy termination in the first trimester has been examined with misoprostol. Vaginal misoprostol is preferable than oral misoprostol in the first trimester of pregnancy, according to clinical research⁽⁷⁾.

Surgical evacuation of the uterus is another option, but it has drawbacks, such as infection, uterine perforation, or Asherman's syndrome, and was once the standard of care⁽⁸⁾.

When it comes to dealing with miscarriage, expectant management is a viable choice. It eliminates iatrogenic complications and is cost-effective, however the complete abortion rate varies depending on the monitoring period⁽⁹⁾.

The objectives of this study are to compare the success rate, tolerability and side effects between oral and vaginal 600 microgram misoprostol in the management of blighted ovum.

SUBJECTS AND METHODS

One hundred women were included in this randomized controlled clinical trial; those were attending

the Obstetrics and Gynecology Departments at Al-Galaa Teaching Hospital, Cairo city.

Ethical consent:

Research Ethics Council at Zagazig University approved the study (ZU-IRB #5630) as long as all participants provided informed consent forms. Ethics guidelines for human experimentation were adhered to by the World Medical Association's Helsinki Declaration.

Pregnant females previously diagnosed as blighted ovum and referred to our hospital for pregnancy termination.

All patients fulfilled the inclusion criteria which were:

- Gestational age > 6 weeks gestation as proved by ultrasound examination and first day of last menstrual period (LMP).
- An intrauterine empty gestational sac > 2cm in diameter without fetal pole.

The patients were divided randomly in two groups:

- **Groupe A** (oral misoprostol group): consisted of 50 patients, they received misoprostol tablets (prostaglandin E1 analogue) 600µg misotac tablets (each tablet contains misoprostol 200µg) every 3 hrs for a maximum 3 doses.
- **Group B** (vaginal misoprostol group): consisted of 50 patients, they received misoprostol tablets (prostaglandin E1 analogue) 600µg mistotac tablets, (each tablet contains misoprostol 200 µg) vaginally every 3 hrs for a maximum 3 doses.

The exclusion criteria:

- 1- Medical disease (Diabetes mellitus, hypertension heart disease, branchial asthma and thyroid disease).
- 2- Coagulation defect.
- 3- Known sensitivity to misoprostol.
- 4- Indication for surgical interference: Severe vaginal bleeding, severe uncontrolled abdominal pain, and patient request.

If the transvaginal ultrasound on day 7 following misoprostol revealed the presence of a gestational sac or a considerable amount of foetal products in the uterus, the treatment's success was determined.

The inclusion criteria:

- Women with blighted ovum confirmed.
- Gestational age: > 6 weeks from the first day of LMP and confirmed by U/S.
- An empty gestational sac > 2cm in diameter without fetal pole.

The following was done to each patient on admission:

1- Full history was taken:

- Personal history: name, age, occupation, marital status special habits and address.
- Complaint and present history.
- Obstetric history: parity, gravidity and mode of previous deliveries or abortions.
- Menstrual history: first day of the period (LMP).
- Past history: of diabetes mellitus (DM), Hypertension, cardiac problems, renal troubles, bleeding tendency, blood disease, Bronchial asthma, Glucoma, allergy or previous operations (especially previous uterine scare).
- Family history: of DM or hypertension.

2- General examination included:

- Measurement of blood pressure, pulse, temperature.
- Presence of pallor or jaundice.
- Presence of petichae or ecchymosis.
- Cardiac and chest examination.
- Presence of edema.

3- Abdominal examination:

- Presence of scars of previous operations.
- Organomegaly (liver, spleen, and kidney).

4- Vaginal examination:

- Bimanual and speculum examination.

5- Investigation:

- Ultrasound was done for confirmation of the diagnosis.
- Laboratory tests (most of them done routinely at admission): Full blood count and hemoglobin for all patients before and after treatment. Blood group and Rh typing. Coagulation profile (prothrombin time, activated partial thromboplastin time, INR). Fasting and 2hrs post prandial blood glucose level.
- Liver enzymes (SGOT, SGPT) and bilirubin.
- Blood urea and serum creatinine.
- Urine analysis.

The following was conducted to each patient after admission:

There were three dosages of misoprostol given every three hours for a total of three doses.

The patients were followed for side effects as: Pain in the lower abdomen, headache, chills, and fever (> 38°C) are all symptoms of a serious illness. Every hour, blood pressure, pulse rate, side effects such as

nausea, vomiting, diarrhea, and weariness, as well as the body temperature were measured, and if the women complained of severe pain, oral or parenteral analgesics were administered.

Women were allowed to go home after finishing their misoprostol treatment as long as they weren't experiencing any heavy vaginal bleeding or discomfort. On their way out, the women were told to come back and pick up their things. The offspring of domestic conception.

Histological testing was performed on the product of conception.

Additional surgical intervention is required: At 7-10 days after treatment with misoprostol, patients with endometrial thickness of less than 11 mm will be regarded to have had a complete abortion, whereas those with endometrial thickness greater than 15 mm would require surgical evacuation⁽¹⁰⁾.

Statistical analysis

In order to analyze the data acquired, Statistical Package of Social Sciences (SPSS), version 20 was used. In order to convey the findings, tables and graphs were employed. The quantitative data was presented in the form of the mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t-test was used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X²) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

RESULTS

Maternal age and gestational age did not differ significantly between the two research groups (Table 1).

Table (1): Comparison between the two groups as regard maternal age and gestational age (GA) at time of admission

Variables	Group				t	P	Sig
	Oral		Vaginal				
	Mean	±SD	Mean	±SD			
Maternal age (year)	24.7	6.2	25.6	6.0	-0.707	0.481	NS
GA at time of admission (week)	9.9	2.0	9.9	1.3	0.121	0.904	NS

For parity, the two study groups did not differ significantly (Table 2).

Table (2): Comparison between the two groups as regard parity

Variable		Group				X ²	P	Sig
		Oral		Vaginal				
		N	%	N	%			
Parity	P0	11	22.0%	21	42.0%	5.208	0.074	NS
	P1	10	20.0%	10	20.0%			
	P≥2	29	58.0%	19	38.0%			

There was no significant difference between two study groups as regard patients aborted (completed abortion) and patients needed surgical evacuation (Table 3).

Table (3): Comparison between the two groups as regard patients aborted (completed abortion) and patients needed surgical evacuation

Variables		Oral		Vaginal		X ²	P	Sig
		N	%	N	%			
Completed abortion after treatment	Yes	28	56.0%	33	66.0%	1.05	0.305	NS
	No	22	44.0%	17	34.0%			
Need surgical evacuation	Yes	19	38.0%	12	24.0%	2.29	0.130	NS
	No	31	62.0%	38	76.0%			

Some side effects, such as vomiting, diarrhoea, and headache, were found to be more common in the oral group than in the intravenous group. In terms of other side effects, however, there was no statistically significant difference between the two groups (Table 4).

Table (4): Comparison between oral and vaginal groups as regard side effects

Variables		Oral		Vaginal		X ² / Fisher	P	Sig
		N	%	N	%			
Nausea	Yes	28	56.0%	22	44.0%	1.440	0.230	NS
	No	22	44.0%	28	56.0%			
Vomiting	Yes	26	52.0%	12	24.0%	8.319	0.004	HS
	No	24	48.0%	38	76.0%			
Diarrhea	Yes	30	60.0%	8	16.0%	20.543	0.0001	HS
	No	20	40.0%	42	84.0%			
Lower abdominal pain	Yes	47	94.0%	49	98.0%	Fisher	0.617	NS
	No	3	6.0%	1	2.0%			
Headache	Yes	25	50.0%	9	18.0%	11.408	0.0001	HS
	No	25	50.0%	41	82.0%			
Fatigue	Yes	26	52.0%	17	34.0%	3.305	0.069	NS
	No	24	48.0%	33	66.0%			
Fever temperature	Yes	24	48.0%	16	32.0%	2.667	0.102	NS
	No	26	52.0%	34	68.0%			
Chills	Yes	6	12.0%	4	8.0%	0.444	0.505	NS
	No	44	88.0%	46	92.0%			

Before and after therapy, there was no statistically significant change in Hb levels between the two study groups (Table 5).

Table (5): Comparison between the two groups as regard Hb before and after treatment

Variable	Group				t	P	Sig
	Oral		Vaginal				
	Mean	±SD	Mean	±SD			
Hb before	10.35	1.23	10.25	1.26	-0.402	0.688	NS
Hb after	10.08	1.25	9.98	1.25	-0.384	0.702	NS

DISCUSSION

One in every four women may experience an early miscarriage at some point in their lives, with spontaneous abortion, embryonic gestation, and embryonic or foetal death among the most prevalent causes⁽¹¹⁾.

In many places of the world, miscarriage is treated surgically, and this procedure is widely accepted. With a success rate of up to 98%, it is a successful procedure⁽¹²⁾.

Post-abortion pelvic infection, uterine perforation, cervical damage and Asherman's syndrome are all possible consequences. These problems can have long-term effects on a woman's ability to become pregnant in the future. The use of expectant and medical management as treatment options for silent miscarriage is a relatively new development⁽¹³⁾.

The possibility of miscarriage control throughout pregnancy is an appealing one. As a result, it is more likely to be safe and less likely to cause side effects than other treatment options⁽¹⁴⁾. According to this study, the rate of complete abortions is influenced by the length of time the study is conducted.

Vaginal misoprostol is more effective than oral misoprostol in the termination of first-trimester pregnancies, according to clinical studies. Misoprostol doses and intervals have been compared in a few

randomized trials in the context of medical abortion, and the results were mixed. Using repeated dosages of oral and vaginal misoprostol in the medical therapy of blighted ovum was the goal of this investigation⁽¹⁵⁾.

In this study; oral group: the mean age was 24.7 ± 6.2years (range from 17-31yrs) gravidity ranging from (1-3), mean gestational age was 9.9±2.2 (range from 7-12 wks).

In the current study; vaginal group: the mean age was 25.6 ± 6.0 ranging from (18-31yrs) gravidity ranging from (1-3). The mean of gestational age 9.9 ± 1.3 (range from 8-12wks). By comparison of characteristics of women of both groups we found that both groups were nearly similarly un-characteristics.

In this study, oral group results were 28 patients (56.0%) had complete abortion, 19 patients (38%) had incomplete abortion and 3 patients (6.6%) had no abortion. Vaginal group results were 33 patients (66.0%) had complete abortion, 12 patients (24.0%) had incomplete abortion and 5 patients (10%) had no abortion.

In prospective randomized study, **Tang et al.**⁽¹⁶⁾ used sublingual misoprostol in the treatment of first trimester silent miscarriages as a comparison to repeated vaginal misoprostol dosages. Women received 600µg of misoprostol sublingually or vaginally every 3 hours for a total of three doses. Both groups had the

same success rates of medical management (complete abortion).

In an earlier study by **Tang et al.**⁽¹⁷⁾, for a total of five doses, the ladies received 600µg of misoprostol sublingually every three hours. The overall abortion rate was found to be 86% (95% confidence interval: 74-93).

The oral group had a larger percentage of patients experiencing adverse effects such vomiting and diarrhoea than the other group, and this difference was significant between the two studies.

However, no significant difference was present between both groups regarding other side effects. Side effects of oral group consisted of 60% suffered from diarrhea, 52% suffered from vomiting and 94% suffered from lower abdominal pain. Side effects of vaginal group consisted of 16% suffered from diarrhea, 24% suffered from vomiting and 98% suffered from lower abdominal pain, no other complications of vaginal group.

In similar study, **Parveen et al.**⁽⁷⁾ found that first-trimester abortions were studied using three distinct methods of delivery of misoprostol before surgical evacuation. For the sublingual, vaginal, and oral studies, a total of 150 randomly selected married women were placed into three groups: A single dose of 400 g of misoprostol. Pain in the abdomen was reported in all three groups, with the vaginal route having the most cases, while the oral group had more cases of diarrhea, and both the oral and sublingual misoprostol groups had cases of nausea, vomiting, and gastrointestinal ill effects. The vaginal route of bleeding was more common.

The difference between our results of vaginal group and **Parveen et al.**⁽⁷⁾ study regarding vaginal bleeding may be due to the type of pregnancy (missed abortion and blighted ovum) in **Parveen et al.**⁽⁷⁾ study may be due to lower mean gestational age in in **Parveen et al.**⁽⁷⁾ study, which was 8.5 ± 2.3 weeks or lower misoprostol dose (400 µg).

The observed side effects like loose motions (diarrhea) was similar to the results from the earlier study by **Tang et al.**⁽¹⁶⁾. Sublingual (70%) and vaginal (27.5%) routes of administration were shown to have a greater rate of diarrhoea ($P < 0.005$). There were no significant differences in any of the other adverse effects between the two groups. Like our study, diarrhea was the most common side effect found by **Tang et al.**⁽¹⁷⁾.

In a randomized study performed by **Saxena et al.**⁽¹⁸⁾, they compared between sublingual, oral and vaginal route of misoprostol for first-trimester pregnancy termination. In the study, 200 women had randomized to 4 groups to receive 400µg every 6hrs misoprostol either vaginally (n=50), orally (n=50) or sublingually (n=50) and admitted to hospital for follow up and care. Patients in control group (n=50) did not receive any medication. The groups differed in terms of complications like vomiting (0%, 2%, 2% and 0%),

nausea (4%, 10%, 16% and 2%) in vaginal, oral, sublingual and control groups, respectively.

The difference between **Saxena et al.**⁽¹⁸⁾ study and our study may be explained due to type of pregnancy in both studies and may be due to different route of administrations of misoprostol, which is oral, sublingual and vaginal in **Saxena et al.**⁽¹⁸⁾ study and oral and vaginal in our study. They also use lower misoprostol dose (400µg) than ours (600µg).

In our study, the success rate in oral group was (56%) and in vaginal group was 66%, the incidence of diarrhea was in oral group (60%) than in vaginal group (16%), vomiting in oral group (59%) and in vaginal group (24%).

In a study conducted by **Shuaib and Alharazi**⁽¹⁹⁾, patients were randomly divided into two groups: group A (55 patients) underwent surgery, while group B (52 patients) received 400µg of Misoprostol vaginally as an initial dose, followed by 200µg every four hours. The study compared the two methods for ending a first-trimester missed miscarriage, The surgical group performed dilatation and curettage, and patients were requested to return one week later for a follow-up visit.

Vaginal misoprostol (Medical group) had an 80.7% success rate in this research. It turned out that only one of the medical group's patients needed to be readmitted for a blood transfusion. Hemorrhage was reported in 7.7 percent of the Alia study's vaginal group⁽¹⁹⁾.

The difference between results of vaginal group in our study and **Shuaib and Alharazi**⁽¹⁹⁾ study may be due to type of pregnancy by comparison of side effects of misoprostol in our study and previous studies we found that in our study that nausea (56%), vomiting (52%). Diarrhea were higher in oral group than vaginal group witch (44%) for nausea: diarrhea (16%) and vomiting (24%).

In **Shuaib and Alharazi**⁽¹⁹⁾ study the side effects of vaginal misoprostol were infection (3.8%) and hemorrhage (7.7%).

CONCLUSION

Using oral and vaginal misoprostol 600 µg as medical managing for a blighted ovum, their effectiveness is practically identical. The use of oral misoprostol is effective for management of blighted ovum as vaginal misoprostol with slight increasing in side effects like diarrhea, vomiting and nausea in oral group than vaginal group.

Conflict of interest: The authors declare no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

REFERENCES

1. **Tulandi T, Al-Fozan H (2011):** Spontaneous abortion: Risk factors, etiology, clinical manifestations, and diagnostic evaluation. UpToDate. <https://www.uptodate.com/contents/recurrent-pregnancy-loss-definition-and-etiology>
2. **Li L, Leung P, Chung T et al. (2014):** Systematic review of Chinese Medicine for miscarriage during early pregnancy. *Evid Base Complement Altern Med.*, 2(5): 2014-9.
3. **Farquharson R, Stephenson M (2010):** Early pregnancy. In: Immunotherapy and early pregnancy. Farquharson R, Stephenson M (Eds.): Cambridge University Press, Pp. 7-9. <https://www.cambridge.org/core/books/abs/early-pregnancy/immunotherapy-and-early-pregnancy/97B43E961851B3970B90C2371B0E443E>
4. **Shekoohi S, Mojarrad M, Raoofian R et al. (2013):** Chromosomal Study of Couples with the History of Recurrent Spontaneous Abortions with Diagnosed Blighted Ovum. *Int J Mol Cell Med.*, 2(4):164-9.
5. **Larsen E, Christiansen O, Kolte A et al. (2013):** New insights into mechanisms behind miscarriage. *BMC Med.*, 11(1):154-9.
6. **Rizzuto M, Oliver R, Odejinmi F (2008):** Laparoscopic management of ectopic pregnancy in the presence of a significant haemoperitoneum. *Arch Gynecol Obstet.*, 5:433-6.
7. **Parveen S, Khateeb Z, Mufti S et al. (2011):** Comparison of sublingual, vaginal, and oral misoprostol in cervical ripening for first trimester abortion. *India J Pharmacol.*, 43(2):172-8.
8. **Babigumira J, Vlassoff M, Ahimbisibwe A et al. (2015):** Surgery for Family Planning, Abortion, and Post-Abortion Care. In: Debas H, Donkor P, Gawande A, Jamison D, Kruk M, Mock C (Eds.): *Essential Surgery: Disease Control Priorities*, 3rd Ed. Washington (DC): The International Bank for Reconstruction and Development / The World Bank, Pp. 109-28. <http://dcp-3.org/chapter/1766/surgery-family-planning-abortion-and-postabortion-care>
9. **Tang O (2004):** The clinical applications of sublingual misoprostol in Gynaecology. (Doctoral dissertation, Faculty of Medicine, University of Hong Kong): <https://www.amazon.ae> > Clinical-Applications-Sublingual-Misoprostol...
10. **Moodliar S, Bagratee J, Moodley J (2005):** Medical vs. surgical evacuation of first-trimester spontaneous abortion. *Int J Gynaecol Obstet.*, 91: 21-6.
11. **Cunningham F, Leveno K, Bloom S et al. (2014):** Early Pregnancy Complications: Abortion. *Williams Obstetrics*, 24th ed. McGraw-Hill. Pp. 350-75. <https://accessmedicine.mhmedical.com/content.aspx?bookid=1057§ionid=59789157>
12. **Ash A, Smith A, Maxwell D (2007):** Caesarean scar pregnancy. *BJOG: An Int J Obstet Gynaecol.*, 114(3): 253-63.
13. **Shochet T, Diop A, Gaye A et al. (2012):** Sublingual misoprostol versus standard surgical care for treatment of incomplete abortion in five sub-Saharan African countries. *BMC Pregnancy and Childbirth*, 12(1): 127-31.
14. **Yu D, Wong Y, Cheong Y et al. (2008):** Asherman syndrome—one century later. *Fertil Steril.*, 89(4): 759-79.
15. **Chetty M (2012):** Novel biochemical markers in the diagnosis and management of early pregnancy problem. *Int J Gynaecol Obstet.*, 13: 127-31.
16. **Fiala C, Gemzell-Danielsson K, Tang O et al. (2007):** Cervical priming with misoprostol prior to transcervical procedures. *Int J Gynecol Obstet.*, 99(2): 142-8.
17. **Tang O, Lau W, Ng E et al. (2003):** A prospective randomized study to compare the use of repeated doses of vaginal with sublingual misoprostol in the management of first trimester silent miscarriages. *Human Reproduction*, 18(1): 176-81.
18. **Tang O, Miao B, Lee S et al. (2002):** Pilot study on the use of repeated doses of sublingual misoprostol in termination of pregnancy up to 12 weeks gestation: efficacy and acceptability. *Human Reproduction*, 17(3): 654-8.
19. **Saxena P, Sarda N, Salhan S et al. (2008):** A randomised comparison between sublingual, oral and vaginal route of misoprostol for pre-abortion cervical ripening in first-trimester pregnancy termination under local anaesthesia. *Australian New Zealand J Obstet Gynaecol.*, 48(1): 101-6.
20. **Shuaib A, Alharazi A (2013):** Medical versus surgical termination of the first trimester missed miscarriage. *Alexandria J Med.*, 49(1): 13-16.