

## The Effectiveness of Misoprostol in Causing a Complete Miscarriage in a Blighted Ovum Pregnancy

Amira Zaidan, MD\* Zainab A. Al-Juffairi, MHPE, FRCOG\*\*

**Objective:** To assess the effectiveness of Misoprostol in causing a complete evacuation of the uterus, in a blighted ovum as an alternative to surgical intervention.

**Design:** A Retrospective Cross-Sectional Study.

**Setting:** Salmaniya Medical Complex, Kingdom of Bahrain.

**Method:** Two hundred ninety-five females with a Blighted Ovum of gestational age up to 12 weeks between 1 January 2008 and 31 August 2013 were included in the study. The patients were treated with Misoprostol according to the International Federation of Gynecology and Obstetrics (FIGO) regimen and later assessed sonographically for the need of surgical evacuation.

**Result:** Two hundred thirty-six (80%) patients had complete miscarriage with Misoprostol in a blighted ovum pregnancy. The surgical evacuation was required in 59 (20%) patients. Advanced maternal age and the increase in gravidity of the patient decreased the response to Misoprostol. Gestational weeks had no effect on the medication.

**Conclusion:** Misoprostol is a safe and effective way to cause a complete abortion in a pregnancy with blighted ovum during the first trimester; it showed a higher response in younger or primigravida patients.

*Bahrain Med Bull 2019; 41(2): 71 - 74*

Spontaneous miscarriage is the most common complication of early pregnancy. It occurs in 11-20% of spontaneous and induced first trimester pregnancies<sup>1</sup>. Previously, the surgical uterine evacuation was the mainstay for treating miscarriages. However, surgical management is associated with many complications such as infection, uterine perforation, bowel injuries, Asherman's syndrome and anesthetic morbidities<sup>2</sup>. Expectant management was introduced later as an option in dealing with miscarriage but it is accompanied with increased anxiety<sup>3,4</sup>. Expectant and medical management of miscarriages with Misoprostol has been suggested by systematic reviews with evidence to be acceptable alternatives to surgical evacuation of the uterus<sup>5</sup>.

Medical management of abortion was first approved by France in 1988 for the use of Mifepristone<sup>6</sup>. Early in the 1990s, Methotrexate was used for terminating pregnancies medically<sup>7</sup>.

Misoprostol is a thermo-stable prostaglandin E1 analog which has been initially used for the treatment and prevention of gastric ulcer disease<sup>8</sup>; it was found to accidentally induce abortion<sup>9,10,11</sup>. Since then, Misoprostol has been investigated as an agent to induce abortion<sup>12,13,14</sup>.

Misoprostol has been used in termination of pregnancy in women with missed abortion or blighted ovum for the past 10 years at Salmaniya Medical Complex and has almost replaced suction evacuation. However, there are no studies from our

center to evaluate the efficacy and safety of misoprostol use in termination of anembryonic pregnancy or blighted ovum. Though misoprostol has also been tested for the management of incomplete miscarriage in different regimens and settings, very few studies concentrated on its effectiveness in blighted ovum<sup>15,16,17,18</sup>.

The aim of this study is to assess the effectiveness of Misoprostol in causing a complete evacuation of the uterus in a blighted ovum as an alternative to surgical intervention.

### METHOD

The study was performed from 1 January 2008 to 31 August 2013. "Blighted Ovum" was diagnosed based on the mean of three measurements of a gestational sac more than or equal to 25 mm with no yolk sac and no fetal pole<sup>19</sup>. The scan has to be repeated after two weeks to avoid diagnostic error.

Three hundred fourteen patients were diagnosed with blighted ovum with gestational age up to 12 weeks. Patients who were hemodynamically unstable, or with hypersensitivity to Misoprostol were excluded. Patients who chose to get a second opinion were also excluded. The remaining 295 patients were included in this study.

The patients received one or two doses of Misoprostol either 800 mcg per vagina 3 hours apart, or 600mcg sublingual 3

---

\* Senior Resident  
\*\* Consultant Obstetrician and Gynecologist  
Obstetrics & Gynecology Department  
Salmaniya Medical Complex  
Kingdom of Bahrain  
E-mail: amirazaidan@yahoo.com

hours apart<sup>20</sup>. If the patient bleeds, they are assessed by a transvaginal ultrasound scan to determine whether the abortion is complete or incomplete. The ultrasound should be within 24 hours to 36 hours after receiving the Misoprostol. If the endometrial thickness was less than 17 mm and no intrauterine gestational sac was seen, no surgical intervention was required. If the patients were hemodynamically unstable, they were immediately transferred for emergency surgical evacuation without the assessment of the endometrial thickness.

The collected data were analyzed using SPSS software version 22. P-value for significance, mean and percentage were used for descriptive statistics.

**RESULT**

A total of 295 women were enrolled in this study. The average age was 29.9 years (Std. Deviation: 7.45 years) with a minimum of 16 and a maximum of 54 years old. The gestational age ranged from 7 to 12 weeks' gestation. The majority were less than 8 weeks of gestation 160 (54.2%). The remaining was between 8 to 12 weeks of gestation, see table 1. The patients were divided into primigravidas and multigravidas. One hundred and twenty-one (41%) patients were primigravidas and 174 (59%) were multigravida.

**Table 1: The Response Rate to Misoprostol According to Gestational Age**

	Gestational Weeks	Abortion Type		Total
		Complete Abortion	Needed Evacuation	
	less than 8 weeks	135 (84.4%)	25 (15.6%)	160 (100%)
	8 to 10 weeks	52 (76.5%)	16 (23.5%)	68 (100%)
	11 to 12 weeks	49 (73.1%)	18 (26.9%)	67 (100%)
	<b>Total</b>	<b>236 (80%)</b>	<b>59 (20%)</b>	<b>295 (100%)</b>

P-value = 0.110

The total number of patients that had aborted successfully with Misoprostol was 239 (81%) and 56 (19%) needed surgical evacuation.

The response rate to misoprostol was high in the age group of 20-30 years, 135 (90%). Nineteen patients were less than 20-year-old; 17 (89.4%) of them had a complete medical abortion. In the age group of 31-40 years, 67 (69%) had a complete abortion. Similarly, 17 (58.6%) patients aged over 41 responded to Misoprostol and 12 (41.4%) required surgical evacuation. There was a significant statistical difference in the response rate according to the patients' ages (P-value<0.0001), see table 2.

The response rate to misoprostol was 84% in the patients less than 8 weeks of gestation compared to 76% in the group between 8-10 weeks. On the other hand, 73% had a complete abortion in the group 10-12 weeks. No statistically significant difference was seen between different gestational age groups and successful response to misoprostol (P = 0.110).

**Table 2: The Response Rate to Misoprostol According to Maternal Age**

	Age	Abortion Type		Total
		Complete Abortion	Needed Evacuation	
	Less than 20	17 (89.5%)	2 (10.5%)	19 (100.0%)
	20 to 30	135 (90.0%)	15 (10.0%)	150 (100.0%)
	31 to 40	67 (69.1%)	30 (30.9%)	97 (100.0%)
	More than 41	17 (58.6%)	12 (41.4%)	29 (100.0%)
	<b>Total</b>	<b>236 (80.0%)</b>	<b>59 (20.0%)</b>	<b>295 (100.0%)</b>

P-value<0.0001

One hundred nineteen (98.3%) primigravidas responded to Misoprostol. While only 117 (67.2%) of the multigravidas had complete abortion. Surgical evacuation was required in only 2 (1.6%) primigravidas as compared to 57 (32.8%) multigravidas. The difference between both groups was significant. (P-value<0.001), see table 3.

**Table 3: The Response Rate to Misoprostol According to Gravidity**

	Gravida	Abortion Type		Total
		Complete Abortion	Needed Evacuation	
	Multigravidas	117 (67.2%)	57 (32.8%)	174 (100%)
	Primigravidas	119 (98.3%)	2 (1.7%)	121 (100%)
	<b>Total</b>	<b>236 (80%)</b>	<b>59 (20%)</b>	<b>295 (100%)</b>

P-value<0.001

**DISCUSSION**

Our study revealed that Misoprostol was successful in completing the miscarriage in a blighted ovum in the majority of the patients (81%). Gurung et al found that the success rate of misoprostol was 87.5% in all types of miscarriages and 79.5% for blighted ovum<sup>21</sup>. Other studies revealed that the success rate of Misoprostol in patients who were diagnosed with incomplete abortions ranged between 70% to 96%<sup>22,23,24,25,26</sup>.

This study revealed that the success rate of misoprostol was significantly better in young patients and decreased as maternal age advances, see table 2. Similarly, this study showed that the primigravidas had a significantly higher response rate to the medication than multigravidas. Studies revealed that medical abortion success rates decreased if the parity is more than three<sup>27,28,29</sup>. Other studies revealed that patients with parity of less than two have a higher response rate than the multigravidas<sup>30,31,32</sup>. Similarly, those that have previously given birth are more likely to require surgery compared to nulliparous women<sup>33</sup>. Nevertheless, no significant difference has been noted in other studies of Misoprostol efficacy and gravidity<sup>21,30</sup>. The age and the gravidity could be related to each other as younger patients will have fewer pregnancies but this would need further study.

The majority of our patients were less than 8 weeks of gestation. The success rate of misoprostol was lower with increased gestational age but it did not reach a significant statistical difference.

There are several limitations to this study. A retrospective study has inherent drawbacks. The cut-off point of the ultrasound was 17mm while in other studies it was up to 30mm. Different routes' effects also could be studied to maximize the benefit of misoprostol use. Lastly, the number of parity, previous cesareans, and previous abortions could be further investigated to save time and implement the most beneficial treatment of choice.

## CONCLUSION

**The overall success of medical treatment with Misoprostol is high and has proved to be effective in completing miscarriage in blighted ovum in first trimester. Advance in maternal age and multiparity have a significant effect on Misoprostol success rate but the gestational age does not alter the effectivity of the drug.**

**Misoprostol should be investigated for its potential use in outpatient settings rather than inpatient in accordance with its availability and safety. Higher response might be noted if we assess patients after two weeks rather than one to two days.**

---

**Author Contribution:** All authors share equal effort contribution towards (1) substantial contribution to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version should be published. Yes.

**Potential Conflicts of Interest:** None.

**Competing Interest:** None.

**Sponsorship:** None.

**Acceptance Date:** 4 April 2019.

**Ethical Approval:** Approved by the Secondary Care Medical Research Subcommittee, Salmaniya Medical Complex, Bahrain.

## REFERENCES

- Steer C, Campbell S, Davies M, et al. Spontaneous Abortion Rates after Natural and Assisted Conception. *BMJ* 1989; 299:1317–1318.
- Grossman D, Blanchard K, Blumenthal P. Complications after Second Trimester Surgical and Medical Abortion. *Reprod Health Matters* 2008; 16 (31 Suppl): 173–182.
- Pauleta JR, Clode N, Graça LM. Expectant Management of Incomplete Abortion in the First Trimester. *Int J Gynaecol Obstet* 2009; 106: 35–38.
- Deutchman M, Tubay AT, Turok D. First Trimester Bleeding. *Am Fam Physician* 2009; 79: 985–994.
- Neilson JP, Gyte GM, Hickey M, et al. Medical Treatments for Incomplete Miscarriage (Less Than 24 Weeks). *Cochrane Database Syst Rev* 2010; (1):CD007223.
- Couzinet B, Le Strat N, Ulmann A, et al. Termination of Early Pregnancy by the Progesterone Antagonist RU 486 (Mifepristone). *N Engl J Med* 1986; 315, 1565-1570.
- Creinin MD, Darney PD. Methotrexate and Misoprostol for Early Abortion. *Contraception* 1993; 48:339–48.
- Norman JE, Thong KJ, Baird DT. Uterine Contractility and Induction of Abortion in Early Pregnancy by Misoprostol and Mifepristone. *Lancet* 1991; 338, 1233-1236.
- Barbosa RM, Arilha M. (1993) The Brazilian experience with Cytotec. *Stud. Fam. Plann* 1993; 24, 236-240.
- Coelho HL, Teixeira AC, Santos AP, et al. Misoprostol and Illegal Abortion in Fortaleza, Brazil. *Lancet* 1993; 341, 1261-1263.
- Costa SH, Vessey MP. (1993) Misoprostol and Illegal Abortion in Rio de Janeiro, Brazil. *Lancet* 1993; 341, 1258-1261.
- Anderson AMN, Wohlfahrt J, Christens P, et al. Maternal Age and Fetal Loss: Population-Based Register Linkage Study. *BMJ* 2000; 320: 1708–1712.
- Chung TK, Lee DT, Cheung LP, et al. Spontaneous Abortion: A Randomised Controlled Trial Comparing Surgical Evacuation with Conservative Management Using Misoprostol. *Fertil Steril* 1999; 71: 1054–1059.
- Trinder J, Brocklehurst P, Porter R, et al. Management of Miscarriage: Expectant, Medical, or Surgical? Results of Randomized Controlled Trial (Miscarriage Treatment (MIST) Trial) *BMJ* 2006; 332: 1235–1238.
- Kushwah B, Singh A. Sublingual versus Oral Misoprostol for Uterine Evacuation following Early Pregnancy Failure. *Int J Gynaecol Obstet* 2009; 106: 43–45.
- Paritakul P, Phupong V. Comparative Study between Oral and Sublingual 600 µg Misoprostol for the Treatment of Incomplete Abortion. *J Obstet Gynaecol Res* 2010; 36: 978–983.
- Taylor J, Diop A, Blum J, et al. Oral Misoprostol as an Alternative to Surgical Management for Incomplete Abortion in Ghana. *Int J Gynaecol Obstet*, 112 (1) (2011): 40–44.
- Montesinos R, Durocher J, León W, et al. Oral Misoprostol for the Management of Incomplete Abortion in Ecuador *Int J Gynaecol Obstet* 2011;115 :135–139.
- Ricki Lweis. First Do No Harm: Guidelines Define a Nonviable Pregnancy. *N Engl J Med* 2013; 369:1443-1451.
- FIGO. Misoprostol-Only Recommended Regimens 2017. [https://www.figo.org/sites/default/files/uploads/project-publications/Miso/FIGO\\_Dosage\\_Chart%20EN\\_0.pdf](https://www.figo.org/sites/default/files/uploads/project-publications/Miso/FIGO_Dosage_Chart%20EN_0.pdf) Accessed January 2018.
- Gurung G, Rana A, Baral J: Use of Misoprostol in the Management of Early Pregnancy Loss. *NJOG* 2012; 7 (2): 9-13.
- Zhang J, Gilles JM, Barnhart K, et al. A Comparison of Medical Management with Misoprostol and Surgical Management for Early Pregnancy Failure. *N Engl J Med*. 2005;353(8):761-9.
- Zikopoulos KA, Papanikolaou EG, Kalantaridou SN, et al. Early Pregnancy Termination with Vaginal Misoprostol before and after 42 Days' Gestation; *NCBI* 2002; 17(12):3079-83.
- Verschuur MAC, Lemmers M, Bossuyt PM, et al. Surgical versus Expectant Management in Women with an

- Incomplete Evacuation of the Uterus after Treatment with Misoprostol for Miscarriage: The Misorest Trial. *BMC Pregnancy and Childbirth* 2013; 13:102.
25. Mahmoud S, Mohamed F, Mostafa H, et al. Vaginal Misoprostol versus Vaginal Evacuation of First Trimester Incomplete Abortion: Comparative Study. *Middle East Fertility Society Journal* 2014; 19 (2); 96–101.
  26. Shochet T, Diop A, Gaye A, et al. Sublingual Misoprostol versus Standard Surgical Care for Treatment of Incomplete Abortion in Five Sub-Saharan African Countries. *BMC Pregnancy and Childbirth* 2012; 12:127.
  27. Creinin MD, Vittinghoff E, Keder L, et al. Methotrexate and Misoprostol for Early Abortion: A Multi-Center Trial. Safety and Efficacy. *Contraception* 1996; 53, 321-327.
  28. Wiebe ER. Abortion Induced with Methotrexate and Misoprostol: A Comparison of Various Protocols. *Contraception* 1997; 55, 159-163.
  29. Borgatta L, Burnhill MS, Tyson J, et al. Early Medical Abortion with Methotrexate and Misoprostol. *Obstet Gynecol* 2001; 97, 11-16.
  30. Francisco B, Catalina DP, Jose JLE, et al. The Management of Missed Miscarriage in an Outpatient Setting: 800 versus 600 mcg of Vaginal Misoprostol. *Aust N Z J Obstet Gynaecol* 2012; 52(1):39-43.
  31. Creinin MD, Huang X, Westhoff C, et al. Factors Related to Successful Misoprostol Treatment for Early Pregnancy Failure. *Obstet Gynecol* 2006; 107: 901-907.
  32. Odeh M, Tendler R, Kais M, et al. Early Pregnancy Failure: Factors Affecting Successful Medical Treatment. *IsrMed Assoc J* 2010;12: 325-328.
  33. Bartley J, Tong S, Everington D, et al. Parity is a Major Determinant of Success Rate in Medical Abortion: A Retrospective Analysis of 3161 Consecutive Cases of Early Medical Abortion Treated with Reduced Doses of Mifepristone and Vaginal Gemeprost. *Contraception* 2000; 62: 297-303.