https://doi.org/10.29309/TPMJ/2022.29.08.6892

The Professional Medical Journal
www.theprofesional.com
2022, Volume, 29 Issue, 08

ORIGINAL ARTICLE

Effectiveness, safety and acceptability of outpatient medical treatment of first trimester miscarriage.

Fauzia Ali[1], Rubina Izhar[2], Zubaida Masood[3], Tazeen Fatima[4], Sarwat Mumtaz[5], Fareeda Sumbul[6]

Article Citation: Ali F, Izhar R, Masood Z, Fatima T, Mumtaz S, Sumbul F. Effectiveness, safety and acceptability of outpatient medical treatment of first trimester miscarriage. Professional Med J 2022; 29(8):1250-1260.https://doi.org/10.29309/TPMJ/2022.29.08.6892

ABSTRACT… Objective: To evaluate the effectiveness, safety and acceptability of outpatient medical treatment of first trimester miscarriage with misoprostol. **Study Design:** Descriptive Longitudinal study. **Setting:** Outpatient Department, Gynae Unit 1 of Abbasi Shaheed Hospital. **Period:** September 2020 to April 2021. **Material & Methods:** Patients of first trimester miscarriage up to 10 weeks gestation were included in the study through non probability consecutive sampling technique. Written consent were taken from all the patients fulfilling inclusion criteria and advised patients to start tab. Misoprostol 400 microgram 4 hrly 3 doses in 24hours orally at home. Patients were advised to follow in outpatient department after 72 hours with report of ultrasound if no active complain. Those who came with heavy bleeding per vaginum or with severe pain, we abandoned the medical treatment and surgical evacuation was done. After completion of treatment either by medical or surgical we took opinion from patients regarding their satisfaction with the chosen method. **Results:** In this study 60 patients of first trimester miscarriage, medically managed with misoprostol were included. Overall assessment was done for effectiveness, safety and acceptability of medical management by Misoprostol. 23.3% patients needed further surgical evacuation and 76.7% patients were managed successfully by medical treatment, overall satisfaction was reported in 73.3% patients, and treatment acceptance showed by 76.7%. According to 78.3% they will prefer the treatment again. **Conclusion:** Misoprostol is safe and effective drug for the termination of first trimester miscarriage up to 10 weeks, orally, as outpatient treatment, with high success rates, patient acceptability and tolerable side effects.

Key words: Acceptance, Evacuation, Effectiveness, Miscarriage, Safety.

INTRODUCTION

First trimester bleeding problems occur in around a quarter of all pregnant women. Non-obstetric etiology, early miscarriage, and ectopic pregnancy are among the potential causes. Clinical assessment, observations, laboratory investigations, and ultrasound can all be utilized to investigate the first trimester bleeding.[1] Approximately 15-20% of all pregnancies end in miscarriage.[2] Surgical, pharmacological, or expectant methods can be used to treat a spontaneous or accidental miscarriage. Suction evacuation and dilatation and evacuation (D&E), are surgical intervention used to evacuate the uterus. There is a possibility of complications associated with the surgical procedure which includes anesthesia complications, bleeding, and infections. Other risks include cervical damage, uterine perforations, uterine adhesions, and infections, which can affect fertility. Surgical evacuation is associated with a 4-10% risk of complications. The surgical procedure also necessitates hospitalization, which can last up to 24 hours, having a detrimental effect on the patient.[3]

Misoprostol is a synthetic prostaglandin used to treat early pregnancy termination, such as anembryonic gestation, missed miscarriage, incomplete miscarriage and also termination of pregnancy in the midtrimester.[4] Use of misoprostol is a safe and effective way to terminate early miscarriages. There have been several studies that suggest termination by using misoprostol

1. MCPS, FCPS, Assistant Professor Gynae & Obs, Karachi Medical & Dental College (KMDC) Abbasi Shaheed Hospital (ASH).
2. FCPS, FRCOG, Professor & Head Gyne & Obs, Karachi Medical & Dental College (KMDC) Abbasi Shaheed Hospital (ASH).
3. FCPS, Associate Professor Gyne & Obs, Karachi Medical & Dental College (KMDC) Abbasi Shaheed Hospital (ASH).
4. FCPS, Assistant Professor Gyne & Obs, Karachi Medical & Dental College (KMDC) Abbasi Shaheed Hospital (ASH).
5. MCPS, Associate Consultant Gynae & Obs, Abbasi Shaheed Hospital (ASH).
6. MCPS, Senior Registrar Gynae & Obs, Abbasi Shaheed Hospital (ASH).

Correspondence Address:
Dr. Fauzia Ali
Department of Gynae & Obs,
Karachi Medical & Dental College (KMDC)
Abbasi Shaheed Hospital (ASH).
fauziaalisr@yahoo.com

Article received on: 09/11/2021
Accepted for publication: 08/04/2022

is preferable than expectant management of miscarriages.[5] Synthetic prostaglandin analogues are not metabolised as efficiently as natural prostaglandins and have a longer period of effect compared to natural prostaglandin. Misoprostol, a prostaglandin E1 analogue, is inexpensive, orally efficient, and viable at room environment. Misoprostol is also used for cervical ripening and to control post-partum hemorrhage.[6,7] It can be used vaginally or orally but the side effects are less in the vaginal route. Side effects of misoprostol are nausea, vomiting, diarrhea, pyrexia, infection and heavy vaginal bleeding. The surgical evacuation has an efficacy rate of about 95%.[5,8] Surgical evacuation is the standard treatment for miscarriages, and it has been routinely used over the past 50 years all over the world.[2] Unfortunately, the expenses of procedure and hospitalizations, and also the risks of operation and anesthesia, remain a major unsolved issue. In addition to infections and hemorrhage, reduced fertility induced by intrauterine adhesions may be generally unsatisfactory for women. As a result, several investigations have shown that expectant or pharmacological treatment may be preferable to operative evacuation.[5] Several researches on the effectiveness of medical treatment have been performed, and it has been proven to be successful in 53-99 percent of patients who experience miscarriages, based on the dosage and route of administration of the drug. Peterson et al[9] obtained 78% efficacy by using misoprostol on OPD basis while study in 2014 showing success rate of 68.6%.[10,11] Misoprostol is an efficient, effective, and noninvasive method for termination of early miscarriages.[5]

Medical treatment with misoprostol reduces the stress of patient related to anesthesia, fear of surgical procedure and complications related to instrumentation. Medical treatment with misoprostol is used for first trimester miscarriage as inpatient treatment but it takes time and because of long hospital stay patient request for surgical evacuation to discharge earlier from hospital. Outpatient misoprostol treatment for first trimester miscarriage is an established treatment modality but is not utilized frequently in Pakistan. So by this study we can assess the safety and efficacy of outpatient therapy of miscarriage with misoprostol and also assess the patient acceptability with the outpatient treatment. Despite the fact that several investigations have been undertaken on this out-patient procedure, most of the clinicians remain unconvinced due to concerns of heavy bleeding at home. Therefore this study aims to build confidence in our local doctors to adopt out-patient medical methods in first trimester miscarriage to prevent complications from surgical procedures, lower the patient's financial burden, and decrease the hospital's burden.

MATERIAL & METHODS

This descriptive longitudinal study was conducted at outpatient Department, Gynae Unit 1, of Abbasi Shaheed Hospital, Karachi during September 2020 to April 2021. Study was done according to Helsinki Declaration and after departmental permission. All patients came to outpatients department of the hospital with first trimester miscarriage and ultrasound showing either non viable fetus or blighted ovum on two scans and those with incomplete miscarriage but with mild bleeding were included. Sample was calculated 60, by using WHO sample size calculator. Taking the proportion of successful medical management in patients with 1st trimester miscarriage 81%[12] with margin of error 10% with confidence interval 95%. 60 cases were included in this study through Non probability consecutive sampling technique. Those women came with early pregnancy up to 10 week gestation with two ultrasound reports showing missed miscarriage or blighted ovum or incomplete miscarriage with no heavy bleeding were included in the study. Patients with and without scar were included. All those who were agreed for outpatient treatment were included. Those who were allergic to misoprostol, with known cardiac disease, known bleeding disorder, concurrent anticoagulation therapy, inflammatory bowel disease or Irritable bowel syndrome were excluded from the study. All those with incomplete miscarriage and heavy bleeding, molar pregnancy and ectopic pregnancy were also excluded. Anaemic patients were also excluded.

We have advised all baseline investigation including PT/APTT and if all normal with no contraindication of the drug we filled the proforma with written consent and advised patients to start treatment in morning at home (tab. misoprostol 400 microgram 4 hrly 3 doses in 24 hours orally).[13] NSAIDS were advised for pain and fever. Patients were advised to report in ER in case of severe hemorrhage or acute abdominal pain or excessive vomiting. If no active complain patient were followed in outpatient department after 72 hours with report of ultrasound. If no retained products found patients were reassured and if products found or endometrial thickness >1.5 repeat dose was advise (400microgram 4hourly 2 doses) to the patient. Repeat ultrasound was advised after 5days and sent her home. In those, where second course was unsuccessful or any patient who refused further treatment were advised for MVA or surgical evacuation. Those who came with heavy bleeding per vaginum or with severe pain we abandoned the medical treatment protocol and surgical evacuation done. We kept record of those who required hospital admission due to any reason (bleeding, pain, fever and vomiting) surgical evacuation, blood transfusion or refuse for further medical treatment for any reason. After completion of treatment either by medical or surgical we took opinion from patients regarding their satisfaction with the chosen method.

Operative Definitions

Treatment effectiveness
Comprehensive pregnancy termination without the requirement for further medical procedure

Treatment Safety
Significant adverse outcomes were used to evaluate safety, like requirement for hospitalization, transfusion of blood or mortality.

Acceptability
Measured as women's overall satisfaction with treatment.

Overall satisfaction with treatment and side effects like nausea, vomiting, diarrhea, chills and fever were also reported. The patient's experience of pain during the treatment and pain was classified as none, mild, moderate or severe and about bleeding after starting treatment and classified it as mild, moderate or heavy. We also asked about their satisfaction with the duration of treatment, their choice of treatment in future if required and overall satisfaction with the treatment. All the details related to the treatment were noted down in the pre-designed proforma.

Data was evaluated by SPSS.20. Continuous variables age, gestational age was reported by applying mean, standard deviation and categorical variables were reported by occurrence and percentages. Chi-square test will be applied to observe the association among effect modifiers and outcomes of the study. Significant difference is defined as a P-value≤0.05.

RESULTS
In this study, there were 60 outpatients of first trimester miscarriage who were medically managed by misoprostol. Mean age of patients was 29.15+/-6.2 years and mean gestational age of the patients was 8.15+/-2.02 weeks. In parity status most of the women 48.3% were multiparous (para 2-4) while 26.7% were nulliparous. Most of the women were 41.7% were graduate and 36.7% done their secondary level education. More than half 53.3% study subjects were belonged from middle income, 30% were from high income and only 16.7% were from lower income. 55% women had no history of miscarriages while 28.3% had previously 1 miscarriage and 16.7% subjects had 2 or more miscarriages. 35% women had uterine scar. (Table-I)

Overall assessment was done for efficiency, safety and tolerability of medical treatment by Misoprostol. Early complications were identified as followed; out of total 25% had complaint of nausea, 21.7% had vomiting, fever was found in 10%, chills and diarrhea was noted in 18.3% and 23.3% women. Most common early complication was nausea followed by diarrhea. All the patients suffer from post treatment bleeding and abdominal pain. Majority of patients 53.3% had moderate amount of bleeding, 43.3% patients

had mild bleeding and only 3.3% women had severe bleeding. Abdominal pain was noted in the most of the patients but 76.7% had mild severity of pain, 18.3% had moderate severity of pain and 5% had severe pain. 18.3% patients admitted post management. 23.3% patients needed further surgical evacuation and 76.7% patients were managed medically successfully. No one required blood transfusion and ICU admission. Almost half of the patients were visited to hospital for more than 2 times. Satisfaction was assessed; 83.3% patients were satisfied with the hospital visits, 83.3% patient's husband were satisfied with the treatment, 86.7% patients were satisfied with the expenses, 80% patients were satisfied with the duration of treatment and 83.3% satisfied with outpatient treatment. Among 31.7% patients compliant about treatment related stress. According to 78.3% will prefer the same treatment management. Most of them 63.3% found the outpatient treatment really helpful while 38.3% and 35% of the patients were very satisfied and mostly satisfied. Only 1.7% patients said that they will not go for this treatment in future. (Table-II)

Association between management success of medical approach and other study variables were showed. Following variables; abdominal pain, need of admission, outpatient treatment acceptability, future preference for the treatment and number of visits found to have significant connection to the treatment success (p value<0.05). (Table-III)

Relation between patient's overall satisfaction and other study variables were showed that parity, early complications like nausea, abdominal pain, need of admission, outpatient treatment acceptability, future preference for the treatment and number of visit found to have significant association with the patients satisfaction with the treatment (p value less than 0.05). (Table-IV)

Association among patient acceptance and other study variables were showed that socioeconomic status, early complications like diarrhea, abdominal pain, need of admission, outpatients treatment acceptability, future preference for the treatment and number of visit found to have significant association with the patients acceptance with the treatment (P<0.05). (Table-V)

Study Variables		Frequency (%)
Age group (in years)	25 or less	17 (28.3%)
	26-30	24 (40%)
	More than 30	19 (31.7%)
Parity	Nulliparous	16 (26.7%)
	Single para	7 (11.7%)
	Multiparous	29 (48.3%)
	Grand Multiparous	8 (13.3%)
Educational status	Illiterate	6 (10%)
	Primary	7 (11.7%)
	Secondary	22 (36.7%)
	Graduate	25 (41.7%)
Socioeconomic status	Less than 15000	10 (16.7%)
	15000 – 40000	32 (53.3%)
	More than 40000	18 (30%)
No of previous miscarriages	No	33 (55%)
	1	17 (28.3%)
	2 or more	10 (16.7%)
Previous scar	No	39 (65%)
	Yes	21 (35%)
Total		60 (100%)

Table-I. Descriptive statistics of demographic and clinical characteristics

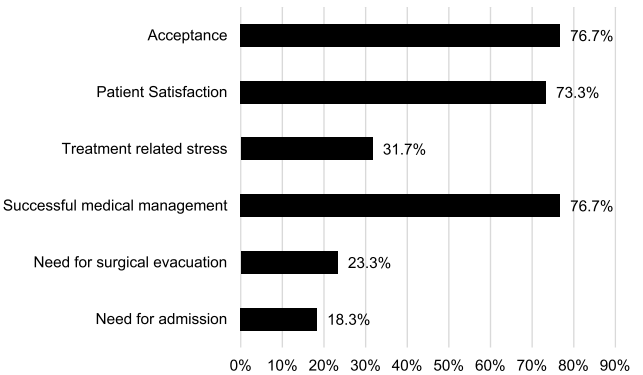

Figure-1. Treatment outcomes

DISCUSSION

This study was conducted to evaluate effectiveness, safety and acceptability of outpatient medical treatment of first trimester miscarriage up to 10 weeks gestation with misoprostol. This current study explored the effectiveness of treatment, pain and bleeding following miscarriage, adverse effect experiences, patient compliance and therapeutic acceptability. Most of the patients were of more than 25 years of age-group and

multiparous. Majority of the participants were literate. The average gestational age was 8.15+/-2.02 weeks. Missed miscarriage was the most common initial ultrasound finding followed by blighted ovum.

Many studies have indicated the effectiveness and safety of misoprostol alone for missed abortion. Nevertheless, the trials differed in terms of misoprostol administration and chances of success. The dosages varied from 100-800 micrograms and may be administered orally, sublingually, or vaginally. The best misoprostol method and dosage for a failed abortion are yet unknown. The National Institute for Health and Care Excellence (NICE) recommended a single dosage of 800 micrograms of misoprostol given vaginally or orally for missed abortions. Some investigations, on the other hand, have found that a lesser dose or alternative forms of misoprostol can be also beneficial.[5,11,14] In current study all the patients were administrated through oral route.

In our study, successful medical management which was described as no need of surgical evacuation achieved in 76.7% patients which was similar to the another study conducted in India[15] where final success rate was reported 74%. This increased our success rates when without increasing the burden on health facilities. Medical intervention was shown to be effective in 82 % in a Spanish study, with decreased rates of minor side effects. This study also advised a waiting period of 7 to 10 days to improve the success rate of medical therapy.[16] In another study, Egyptian women had a 78 percent success rate, with a median interval span of 18 hours between pill to expulsion in the successful medical therapy group.[17] The success rate was more than half in a study conducted in Lahore in-patient trial of 1st trimester miscarriage with misoprostol, and similar findings obtained in another research performed in Karachi both studies were in-patient studies, and the lower rate of success was attributed to early evacuation after failure of complete miscarriage during the initial 24 hours, the overall efficacy of misoprotol for first trimester miscarriage was decreased.[13,18]

Study Outcomes		N (%)
Early complications	Nausea	15(25%)
	Vomiting	13(21.7%)
	Fever	6(10%)
	Chills	11(18.3%)
	Diarrhea	14(23.3%)
Bleeding	Mild	26(43.3%)
	Moderate	32(53.3%)
	Severe	2(3.3%)
Abdominal pain	Mild	46(76.7%)
	Moderate	11(18.3%)
	Severe	3(5%)
Need for admission	No	49(81.7%)
	Yes	11(18.3%)
Need for surgical evacuation	No	46(76.7%)
	Yes	14(23.3%)
Successful medical management	No	14(23.3%)
	Yes	46(76.7%)
Number of visits to hospital	1-2	31(41.7%)
	3-5	29(48.3%)
Satisfaction	With Visits	50(83.3%)
	Of Husband	50(83.3%)
	With Expenses	50(86.7%)
	With treatment duration	48(80%)
	With outpatient treatment	50(83.3%)
Treatment related stress	No	41(68.3%)
	Yes	19(31.7%)
Future preference of the treatment	No	13(21.7%)
	Yes	47(78.3%)
Has the outpatient treatment you received, helped you to deal with your problem more effectively?	Indifferent or mildly dissatisfied	13(21.7%)
	No, it seemed to make things worst	1(1.7%)
	No, they really didn't help	8(13.3%)
	Yes, It helped a great deal	38(63.3%)
How Satisfied are you?	Indifferent or mildly dissatisfied	10(16.7%)
	Mostly satisfied	21(35%)
	Quite dissatisfied	6(10%)
	Very satisfied	23(38.3%)
Would you prefer the method again in case of future miscarriage?	Yes (definitely)	21(35%)
	Yes(I think so)	25(41.7%)
	No (definitely not))	1(1.7%)
	No (I do not think so)	13(21.7%)
Total		60(100%)

Table-II. Efficacy, safety and tolerability of Misoprostol.

Study Variables		Successful Medical Management		Total	P-Values
		Yes	No		
Age group	25 or less	16(94.1%)	1(5.9%)	17(100%)	0.115*
	26-30	16(66.7%)	8(33.3%)	24(100%)	
	More than 30	14(73.7%)	5(26.3%)	19(100%)	
Parity	Nulliparous	10(62.5%)	6(37.5%)	16(100%)	0.435*
	Single pera	6(85.7%)	1(14.3%)	7(100%)	
	Multiparous	24(82.8%)	5(17.2%)	29(100%)	
	Grand Multiparous	6(75%)	2(25%)	8(100%)	
Educational Status	Illiterate	5(83.3%)	1(16.7%)	6(100%)	0.881
	Primary	6(85.7%)	1(14.3%)	7(100%)	
	Secondary	16(72.7%)	6(27.3%)	22(100%)	
	Graduate	19(76%)	6(24%)	25(100%)	
Socioeconomic Status	Less than 15000	9(90%)	1(10%)	10(100%)	0.149
	15000 – 40000	26(81.3%)	6(18.8%)	32(100%)	
	More than 40000	11(61.1%)	7(38.9%)	18(100%)	
No of previous miscarriages	No	24(72.7%)	9(27.3%)	33(100%)	0.824
	1	14(82.4%)	3(17.6%)	17(100%)	
	2	7(77.8%)	2(22.2%)	9(100%)	
	3	1(100%)	0(0%)	1(100%)	
Previous scar	Yes	16(76.2%)	5(23.8%)	21(100%)	0.949*
	No	30(76.9%)	9(23.1%)	39(100%)	
Ultrasound findings; (before treatment)	Anembrynoic Sac/ Blighted ovum	16(94.1%)	1(5,8%)	17(100%)	0.331
	Incomplete abortion/ RPOCS	6(66.6%)	3(33.3%)	9(100%)	
	Missed abortion	24(70.6%)	10(29.4%)	34(100%)	
Nausea	Yes	10(66.7%)	5(33.3%)	15(100%)	0.290*
	No	36(80%)	9(20%)	45(100%)	
Vomiting	Yes	9(69.2%)	4(30.8%)	13(100%)	0.474*
	No	37(78.7%)	10(21.3%)	47(100%)	
Fever	Yes	3(50%)	3(50%)	6(100%)	0.104*
	No	43(79.6%)	11(20.4%)	54(100%)	
Chills	Yes	6(54.5%)	5(45.5%)	11(100%)	0.107*
	No	40(81.6%)	9(18.4%)	49(100%)	
Diarrhea	Yes	9(64.3%)	5(35.7%)	14(100%)	0.211*
	No	37(80.4%)	9(19.6%)	46(100%)	
Severity of Bleeding	Mild	18(69.2%)	8(30.8%)	26(100%)	0.264
	Moderate	27(84.4%)	5(15.6%)	32(100%)	
	Severe	1(50%)	1(50%)	2(100%)	
Abdominal pain	Mild	37(80.4%)	9(19.6%)	46(100%)	0.006
	Moderate	9(81.8%)	2(18.2%)	11(100%)	
	Severe	0(0%)	3(100%)	3(100%)	
Need for admission	Yes	2(18.2%)	9(81.8%)	11(100%)	0.001*
	No	44(89.8%)	5(10.2%)	49(100%)	
Any mental stress during the treatment	Yes	6(31.6%)	13(68.4%)	19(100%)	0.001*
	No	40(97.6%)	1(2.4%)	41(100%)	
Acceptability / satisfaction with the outpatient treatment	Yes	44(88%)	6(12%)	50(100%)	0.001*
	No	2(20%)	8(80%)	10(100%)	
Future preference of the treatment	Yes	43(91.5%)	4(8.5%)	47(100%)	0.001*
	No	3(23.1%)	10(76.9%)	13(100%)	
No. of visits	1-2	29(93.5%)	2(6.5%)	31(100%)	0.001*
	3-5	17(58.6%)	12(41.4%)	29(100%)	
Total		46(76.7%)	14(23.3%)	60(100%)	

Chi-Square/Fisher Exact test* applied. Significance degree: p value<0.05.

Table-III. Association of successful medical management with study variables

Study Variables		Patients Satisfaction		Total	P-Values
		Dissatisfied	Satisfied		
Age group	25 or less	5(29.4%)	12(70.6%)	17(100%)	0.951
	26-30	6(25%)	18(75%)	24(100%)	
	More than 30	5(26.3%)	14(73.7%)	19(100%)	
Parity	Nulliparous	7(43.8%)	9(56.3%)	16(100%)	0.022
	Single pera	4(57.1%)	3(42.9%)	7(100%)	
	Multiparous	3(10.3%)	26(89.7%)	29(100%)	
	Grand Multiparous	2(25%)	6(75%)	8(100%)	
Educational Status	Illiterate	1(16.7%)	5(83.3%)	6(100%)	0.319
	Primary	0(0%)	7(100%)	7(100%)	
	Secondary	7(31.8%)	15(68.2%)	22(100%)	
	Graduate	8(32%)	17(68%)	25(100%)	
Socioeconomic Status	Less than 15000	1(10%)	9(90%)	10(100%)	0.095
	15000 - 40000	7(21.9%)	25(78.1%)	32(100%)	
	More than 40000	8(44.4%)	10(55.6%)	18(100%)	
No of previous miscarriages	No	11(33.3%)	22(66.7%)	33(100%)	0.510
	1	4(23.5%)	13(76.5%)	17(100%)	
	2	1(11.1%)	8(88.9%)	9(100%)	
	3	0(0%)	1(100%)	1(100%)	
Previous scar	Yes	6(28.6%)	15(71.4%)	21(100%)	0.807*
	No	10(25.6%)	29(74.4%)	39(100%)	
Ultrasound findings; (before treatment)	Anembrynic sac/ blighted ovum	3(17.6%)	14(82.3%)	17(100%)	0.641
	Incomplete miscarriage/RPOCS	2(22,2%)	7(7%)	9(100%)	
	Missed Miscarriage	11(32.4%)	23(67.6%)	34(100%)	
Nausea	Yes	7(46.7%)	8(53.3%)	15(100%)	0.043*
	No	9(20%)	36(80%)	45(100%)	
Vomiting	Yes	6(46.2%)	7(53.8%)	13(100%)	0.073*
	No	10(21.3%)	37(78.7%)	47(100%)	
Fever	Yes	3(50%)	3(50%)	6(100%)	0.173*
	No	13(24.1%)	41(75.9%)	54(100%)	
Chills	Yes	5(45.5%)	6(54.5%)	11(100%)	0.119*
	No	11(22.4%)	38(77.6%)	49(100%)	
Diarrhea	Yes	6(42.9%)	8(57.1%)	14(100%)	0.118*
	No	10(21.7%)	36(78.3%)	46(100%)	
Severity of Bleeding	Mild	10(38.5%)	16(61.5%)	26(100%)	0.111
	Moderate	5(15.6%)	27(84.4%)	32(100%)	
	Severity	1(50%)	1(50%)	2(100%)	
Abdominal pain	Mild	11(23.9%)	35(76.1%)	46(100%)	0.012
	Moderate	2(18.2%)	9(81.8%)	11(100%)	
	Severity	3(100%)	0(0%)	3(100%)	
Need for admission	Yes	8(72.7%)	3(27.3%)	11(100%)	0.001*
	No	8(16.3%)	41(83.7%)	49(100%)	
Need for surgical evacuation	Yes	12(85.7%)	2(14.3%)	14(100%)	0.001*
	No	4(8.7%)	42(91.3%)	46(100%)	
Any mental stress during the treatment	Yes	14(73.7%)	5(26.3%)	19(100%)	0.001*
	No	2(4.9%)	39(95.1%)	41(100%)	
Acceptability /satisfaction with the outpatient treatment	Yes	8(16%)	42(84%)	50(100%)	0.001*
	No	8(80%)	2(20%)	10(100%)	
Future preference of the treatment	Yes	5(10.6%)	42(89.4%)	47(100%)	0.000*
	No	11(84.6%)	2(15.4%)	13(100%)	
No. of visits	1.00	1(3.2%)	30(96.8%)	31(100%)	0.000*
	2.00	15(51.7%)	14(48.3%)	29(100%)	
Total		16(26.7%)	44(73.3%)	60(100%)	

Chi-Square/Fisher Exact test* applied. Significance: p value<0.05.

Table-IV. Association of patient's satisfaction with study variables

Study Variables		Acceptance		Total	P-Values
		No	Yes		
Age group	25 or less	3(17.6%)	14(82.4%)	17(100%)	0.664
	26-30	7(29.2%)	17(70.8%)	24(100%)	
	More than 30	4(21.1%)	15(78.9%)	19(100%)	
Parity	Nulliparous	6(37.5%)	10(62.5%)	166(100%)	0.387
	Single pera	2(28.6%)	5(71.4%)	76(100%)	
	Multiparous	5(17.2%)	24(82.8%)	296(100%)	
	Grand Multiparous	1(12.5%)	7(87.5%)	86(100%)	
Educational Status	Illiterate	0(0%)	66(100%)	6(100%)	0.450
	Primary	1(14.3%)	6(85.7%)	7(100%)	
	Secondary	6(27.3%)	16(72.7%)	22(100%)	
	Graduate	7(28%)	18(72%)	25(100%)	
Socioeconomic Status	Less than 15000	0(0%)	10(100%)	10(100%)	0.004
	15000 - 40000	5(15.6%)	27(84.4%)	32(100%)	
	More than 40000	9(50%)	9(50%)	18(100%)	
No of previous miscarriages	No	10(30.3%)	23(69.7%)	33(100%)	0.520
	1	3(17.6%)	14(82.4%)	17(100%)	
	2	1(11.1%)	8(88.9%)	9(100%)	
	3	0(0%)	1(100%)	1(100%)	
Previous scar	Yes	5(23.8%)	16(76.2%)	21(100%)	0.949*
	No	9(23.1%)	30(76.9%)	39(100%)	
Ultrasound finding	Blighted ovum/Anembryonic sac	1(5.8%)	16(94.1%)	17(100%)	0.262
	Incomplete Miscarriage/ RPOCS	2(22.2%)	7(77.7%)	9(100%)	
	Missed Miscarriage	11(32.4%)	23(67.6%)	34(100%)	
Nausea	Yes	5(33.3%)	10(66.7%)	15(100%)	0.290*
	No	9(20%)	36(80%)	45(100%)	
Vomiting	Yes	5(38.5%)	8(61.5%)	13(100%)	0.145*
	No	9(19.1%)	38(80.9%)	47(100%)	
Fever	Yes	3(50%)	3(50%)	6(100%)	0.104*
	No	11(20.4%)	43(79.6%)	54(100%)	
Chills	Yes	5(45.5%)	6(54.5%)	11(100%)	0.055*
	No	9(18.4%)	40(81.6%)	49(100%)	
Diarrhea	Yes	6(42.9%)	8(57.1%)	14(100%)	0.049*
	No	8(17.4%)	38(82.6%)	46(100%)	
Severity of Bleeding	Mild	8(30.8%)	18(69.2%)	26(100%)	0.264
	Moderate	5(15.6%)	27(84.4%)	32(100%)	
	Severity	1(50%)	1(50%)	2(100%)	
Abdominal pain	Mild	10(21.7%)	36(78.3%)	46(100%)	0.004
	Moderate	1(9.1%)	10(90.9%)	11(100%)	
	Severity	3(100%)	0(0%)	3(100%)	
Need for admission	Yes	8(72.7%)	3(27.3%)	11(100%)	0.001*
	No	6(12.2%)	43(87.8%)	49(100%)	
Need for surgical evacuation	Yes	12(85.7%)	2(14.3%)	14(100%)	0.000*
	No	2(4.3%)	44(95.7%)	46(100%)	
Future preference of the treatment	Yes	2(4.3%)	45(95.7%)	50(100%)	0.000*
	No	12(92.3%)	1(7.7%)	13(100%)	
Any mental stress during the treatment	Yes	13(68.4%)	6(31.6%)	19(100%)	0.001*
	No	1(2.4%)	40(97.6%)	41(100%)	
No. of visits	1-2	0(0%)	31(1000%)	31(100%)	0.000*
	3-5	14(48.3%)	15(51.7%)	29(100%)	
Total		14(23.3%)	46(76.7%)	60(100%)	

Chi-Square/Fisher Exact test* applied. Significance level: P-value<0.05.

Table-V. Association of patient's acceptance with study variables

According to the study conducted in the rural area of Sind where only the vaginal route was used and the average induction to expulsion time was approximately 16 hours and the success rate was 63%. This was included both in and out patients, whereas ours was simply an out-patient study, and here exclusively employed the oral method for medication delivery, resulting in a greater success rate.[19] Similar to our study majority women labeled the side effects as tolerable. Overall acceptance rate to treatment was as 70% while in our study it was relatively higher 76.7%. More than two-thirds of success rates and acceptability rates demonstrate that misoprostol is a safe and effective non-surgical approach for treating missed miscarriage, with the oral administration having a greater overall performance. Medical treatment of a first trimester failed miscarriage as well as a blighted ovum is extremely beneficial in another research, with an overarching success record of 83.3 percent and a very smaller proportion of curettage in the first 48 hours following the surgery (7.4 percent). Lack of evacuated products of conceptions at the time of hospitalization, was identified as risk variable for complication incidence in the research.[20]

In our study, most frequent side effects were nausea, diarrhea and vomiting. Apart from that, several patients had chills with fever, which were adequately treated with anti-emetic as well as anti-diarrheal medications. Diarrhea is a common side effect of misoprostol, however it is a normal reaction of intestinal smooth muscles to elevated levels of PGs. This is generally moderate and self-limiting, and it resolves after a few days with ongoing medication. To improve the efficacy of the oral administration, more research into novel medication formulations for misoprostol is needed in the foreseeable future. To reduce the medication's GI adverse effects, it should be consumed with food. Previous literature also reported dizziness, headache and discharge per vaginum. No female suffered uterine rupture or died as a result of the treatment in our research. In a small number of women, heavy bleeding and significant post-treatment discomfort were reported, boosting acceptance of medical therapy and establishing it as a viable choice to operative evacuation. However, more research with a bigger sample size is needed to confirm our conclusions. Overall treatment satisfaction rate was also high 73.3%. More than 83.3% of the patients were satisfied with the visits required, expenses, duration of treatment and 83.3% patient's husband showed satisfaction towards treatment. Treatment related stress was reported 31.7% in patients. Few participants were dissatisfied with their therapy due to failure, adverse effects, or the length of time it lasted. However, when questioned if they would select the technique again in the future, 78.3 percent of patients responded positively. The therapy can also be given at the residence which might improve their comfort and confidentiality while also lowering the expense of clinical management.[15]

Misoprostol solely can be safe and efficient for achieving miscarriage in the first trimester, according to a meta-analysis of 42 trials that involved over 13,000 quantified females. Throughout all trials, nearly 78 percent of females had successful abortion services without needing to resort with surgery. Significant issues demanding hospitalizations or blood transfusions were recorded in less than 0.2 %. The significant proportion of the ladies was pleased with their therapy. The majority of women were pleased or extremely pleased with the therapy in studies that reported satisfaction statistics with an approximation of 78% (95% CI) and 71% (85%).[21]

In study in Nigeria a total of 92 % of subjects were successfully evacuated. The average age, parity, and gestational age were all 27.6 ± 5.6 years, 3.6 ± 2.3 and 7.6 ± 2.0 weeks, correspondingly, which was similar to our findings. The average time between the first misoprostol dosage and abortion was 5.1 ± 2.2 hours and the average length of vaginal hemorrhage was 5.9 ± 1.6(3–14) days. The only adverse consequences were nausea and vomiting, and all of the individuals who had successful evacuation were satisfied with the procedure and preferring it to surgical evacuation.[22] In both resource-rich and resource-poor situations, there is information that it is extremely successful in first-trimester pregnancy termination (missed miscarriage and incomplete miscar-

riage). Misoprostol is successful in evacuation of uterus for first trimester miscarriage in 80-90 percent of instances, according to reports from under developed nations. Pantaet al.[23] in on the other hand, found a 95 percent efficacy rate.[22,24] In this study more surgical evacuation required in older age (more than 25 years) and nulliparous patients.

A further systematic review found that successful abortion rates ranged from 78.6 to 94.6 percent for all programs studied. Repeat misoprostol dosage, both in combined and separately resulted in greater completion rates.[25] Misoprostol has a number of distinct benefits above similar prostaglandins, including the fact that it is thermally sustainable and so does not demand freezing for preservation. In our context, when electricity is a privilege, this pharmacodynamic feature or quality of misoprostol is important. Misoprostol also has a variety of administering options (rectal, intra-vaginal, buccal, or oral), as well as a reasonable cost.

This experience of outpatient medical treatment of first trimester miscarriage is consistent with the available studies. The findings of this study support the use of misoprostol, administered orally as a credible alternative to operative evacuation in cases of first trimester miscarriage, with promising outcomes, patient acceptance, and manageable adverse effects. It should, however, only be conducted by well qualified physicians who are capable of providing surgical intervention in the case of an unsuccessful miscarriage. Even if the patient is unable to evacuate, misoprostol's cervical ripening ability enables surgical evacuation considerably easier. Nevertheless, further research using randomized approaches is required.

CONCLUSION

Misoprostol is indeed a non-invasive, efficient, and safe medical treatment for first trimester miscarriage especially for those who are low risk and wants outpatient treatment. This outpatient medical treatment can reduce the hospital burden as well as the financial burden on the patient and can increase the confidence of clinician on outpatient management of these patients.

REFERENCES

1. Hendriks E, MacNaughton H, MacKenzie MC. **First trimester bleeding: Evaluation and management.** American Family Physician. 2019;99(3):166-74.

2. Behrashi M, Mahdian M. **Comparison of medical (misoprostol) and surgical management for terminating of first trimester missed abortion.** Pakistan Journal Biological Sciences. 2006; 9(7):1399-401.

3. Awan AS, Bakhtiar U, Najeeb R, Akhtar S. **Management of first trimester missed miscarriage with minimal surgical intervention.** PAFMJ. 2008;58(4):437-40.

4. Allen R, O'Brien BM. **Uses of misoprostol in obstetrics and gynecology.** Reviews in obstetrics and gynecology. 2009; 2(3):159.

5. Wu H-l, Marwah S, Wang P, Wang Q-m, Chen X-w. **Misoprostol for medical treatment of missed abortion: A systematic review and network meta-analysis.** Scientific reports. 2017;7(1):1-9.

6. Mahmood A, Das CM, Nusrat RM. **Medical Treatment of Missed Miscarriage before 24 Week of Gestation at Liaquat University Hospital.** Journal of Liaquat University of Medical & Health Sciences. 2016; 15:46-50.

7. Ho P. **Development of medical termination of pregnancy: A review.** BJOG: An International Journal of Obstetrics & Gynaecology. 2017; 124(13):1942-7.

8. Lyra J, Cavaco-Gomes J, Moucho M, Montenegro N. **Medical termination of delayed miscarriage: four-year experience with an outpatient protocol.** Revista Brasileira de Ginecologia e Obstetrícia. 2017; 39:529-33.

9. Petersen SG, Perkins AR, Gibbons KS, Bertolone JI, Mahomed K. **The medical management of missed miscarriage: Outcomes from a prospective, single-centre, Australian cohort.** Medical Journal of Australia. 2013; 199(5):341-6.

10. Verschoor MA, Lemmers M, Wekker MZ, Huirne JA, Goddijn M, Mol BWJ, et al. **Practice variation in the management of first trimester miscarriage in the Netherlands: a nationwide survey.** Obstetrics and gynecology international. 2014; 2014.

11. Tasneem S, Gul MS, Navid S, Alam K. **Efficacy and safety of misoprostol in missed miscarriage.** Raw Med J. 2014; 39(3):314-9.

12. Cubo Nava A, Soto Pino ZM, Haro Pérez AM, Hernández Hernández ME, Doyague Sánchez MJ, Sayagués Manzano JM. **Medical versus surgical treatment of first trimester spontaneous abortion: A cost-minimization analysis.** PloS one. 2019; 14(1):e0210449.

13. Khan F, Amin A, Ahmad F, Naeem N. **Medical termination of first trimester miscarriages.** Annals of King Edward Medical University. 2007; 13(2).

14. Seervi N, Hooja N, Rajoria L, Verma A, Malviya K, Mehta N. **Comparison of different regimes of misoprostol for the termination of early pregnancy failure.** medical journal armed forces india. 2014; 70(4):360-3.

15. Marwah S, Gupta S, Batra NP, Bhasin V, Sarna V, Kaur N. **A comparative study to evaluate the efficacy of vaginal vs oral prostaglandin E1 analogue (Misoprostol) in management of first trimester missed abortion.** Journal of clinical and diagnostic research: JCDR. 2016; 10(5):QC14.

16. Pacheco ER, de la Puente Yague M, Mendez NI, de la Fuente EA, y Jose MAHM, Aragon A. **Medical treatment of spontaneous abortion in the first trimester.** Journal of Clinical Gynecology and Obstetrics. 2015; 4(3):265-70.

17. MSA E. **Safety and efficacy of vaginal misoprostol in treatment of first trimester miscarriage ASSRJ.** 2020; 7(3):138-44.

18. Shah N, Azam SI, Khan NH. **Sublingual versus vaginal misoprostol in the management of missed miscarriage.** JPMA The Journal of the Pakistan Medical Association. 2010; 60(2):113.

19. Rizwan N, Uddin SF. **Medical treatment of the complication of first trimester pregnancy loss with misoprostol.** International Journal of Medicine and Medical Sciences. 2014; 6(9):211-4.

20. Serdinšek T, Reljič M, Kovač V. **Medical management of first trimester missed miscarriage: The efficacy and complication rate.** Journal of Obstetrics and Gynaecology. 2019; 39(5):647-51.

21. Raymond EG, Harrison MS, Weaver MA. **Efficacy of misoprostol alone for first-trimester medical abortion: A systematic review.** Obstetrics and gynecology. 2019; 133(1):137.

22. Abdul M, Palmer H, Aminu B, Ismail H, Kadas A. **Experiences in the use of misoprostol in the management of first trimester missed abortion in a low resource setting.** Tropical Journal of Obstetrics and Gynaecology. 2016; 33(2):201-4.

23. Panta O, Bhattarai D, Parajuli N. **Medical abortion versus manual vacuum aspiration in a hilly district hospital of eastern Nepal: A comparative study.** Kathmandu University Medical Journal. 2013; 11(3):206-9.

24. Blandine T, Ouattara AZ, Coral A, Hassane C, Clotaire H, Dao B, et al. **Oral misoprostol as first-line care for incomplete abortion in Burkina Faso.** International Journal of Gynecology & Obstetrics. 2012; 119(2):166-9.

25. Kapp N, Eckersberger E, Lavelanet A, Rodriguez MI. **Medical abortion in the late first trimester: A systematic review.** Contraception. 2019; 99(2):77-86.

AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Fauzia Ali	Conception, Design, Data collection, Analysis, Interpretation drafting.	
2	Rubina Izhar	Conception, Design, Analysis, Interpretation, Final approval.	
3	Zubaida Masood	Design Conception, Data collection, Analysis, Interpretatiaon, Drafting.	
4	Tazeen Fatima	Data collection, Analysis, Interpretation, Drafting.	
5	Sarwat Mumtaz	Data collection, Analysis, Interpretation, Drafting.	
6	Fareeda Sumbul	Data collection, Analysis, Interpretation, Drafting.