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Original Research Paper

TREATMENT OF INCOMPLETE AND MISSED ABORTION WITH ORAL MISOPROSTOL

Authors:
Dr. Siham Salman Muhauder, Dr. Zaid Al-Attar
Arab board in gynecology and obstetrics CABOG, Diploma in gynecology and obstetrics
Working in Al Arabi private hospital
HLA-unit in Al-Kindy College of Medicine , University of Baghdad
Corresponding Author:
Dr. Zaid Al-Attar
HLA-unit in Al-Kindy College of Medicine , University of Baghdad

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ABSTRACT:
Medical termination of pregnancy is now an accepted method of termination of pregnancy. We present an uncontrolled case series of women given three oral doses of misoprostol for the treatment of incomplete and missed abortion. We conducted a randomized prospective study of 110 pregnant women between 6 and 13 weeks with incomplete abortion, and between 6 and 20 weeks with missed abortion. Post therapy clinical evaluation were conducted 103 of 110 women 93.6 % had complete uterine evacuation without the need for surgical evacuation. 7 of 110 women ended with surgical evacuation 6.3%. In incomplete abortion group, the success rate was 8.3 %, 45 %, 85%, 93 % after 1st, 2nd, 3rd, 4th dose respectively. In missed abortion group, the success rate was 8.0 %, 44 %, 86 %, 94 % after 1^{ST} , 2nd , 3rd , 4th , dose respectively . So, the difference in response rate between the two groups at the end of each dose interval was not significant statistically for all intervals. Misoprostol administered as 2-4 oral doses proved to be effective in terminating pregnancies especially in women with early gestation. Misoprostol is a safe, effective alternative to surgical evacuation of the uterus. It is highly preferable by patients and is inexpensive. analogue as an alternative to surgery is acceptable to women), Medical abortion as an alternative to surgical abortion has many advantages since it does not require anesthetics and there is risk of cervical laceration or uterine perforation)

Keywords: termination of pregnancy, misoprostol, abortion

INTRODUCTION:

Medical termination of pregnancy is now an accepted method of termination of pregnancy. We present an uncontrolled case series of women given three oral doses of misoprostol for the treatment of incomplete and missed abortion (1, 2).

Aim of study: To investigate the use of misoprostol in the treatment of incomplete and missed abortion.

Patients And Methods:

Once a diagnosis of early pregnancy failure has been gynecological practice to proceed to evacuation of any retained products of conception. In many cases, however, there may be little residual tissue within the uterus, and the patient may be exposed to an unnecessary operative procedure. Transvaginal sonographic examination the selection of these cases which can safely be managed conservatively. In addition, the prostaglandin analogues, such as misoprostol, have been shown to be effective in emptying the uterus for termination of pregnancy and in spontaneous abortion) Medical treatment of incomplete abortion with prostaglandin effective medical method of elective termination early pregnancy.

Misoprostol Oral tab - contain either 100 mcg or 200 mcg of Prostaglandin E_1, Analogue.
Misoprostol contains approximately equal amount of the 2 diastereomers presented with their enatiomers indicated by (±). Causes abortion by competitively blocking progesterone receptors. For maximal effectiveness, a prostaglandin should be given 48 hrs. after mifepristone. Well informed written consent was obtained from all patients included in the study. The enrolled patients were 110 patients randomized into two groups. group 60 patients, in which all of them with incomplete abortion, while the 2nd group 50 patients, in which all of them with missed abortion. The two groups were received 2-4 doses of oral misoprostol and follow up of them was done. The data were translated into codes and converted into a computerized data base structure. Statistical analysis were The statistical significance of difference between two proportions was assessed by Chi square (x^2) test. The difference in median number of doses required for

a successful response between age groups was assessed for statistical significance by Kruskal Walli test while between two groups Mann Whitney test was used P-value less than 0.05 level of significance was considered statistically significant.

RESULTS:

As shown in table 1,2 ; There were no important or statistically difference in age range, mean and frequency distribution between the 2 study groups. It ranged between 18 and 45 years, with a mean of 28.7 +/ 5.9 (SD) for the incomplete abortion group and ranged between 17- 42 years with a mean of 28.9 +/- 7.4 (SD) for the missed abortion group. Subjects under 20 years of age were the least frequent in both study groups (3.3 % and 14 % among incomplete and missed abortion groups respectively). All subjects in the incomplete abortion group were in the first trimester of pregnancy, while 24 out of 50 (48%) of the missed abortion group were in the second trimester of pregnancy. The diagnosis of missed abortion was documented by U.S. in all the study sample, while incomplete abortion was confirmed by U.S. in 45/60 (75 %) of cases only. No obvious or statistically significant difference were observed in mean parity 2.7 and 2.8 for incomplete and missed abortion groups respectively) and mean number of abortions (0.8 for both study groups) . It is obvious that both groups were comparable in age, parity and abortion histories, therefore it is unlikely for these factors to distort the effect of studied drug in a differential way between the 2 groups

Table 1: Frequency distribution of the two study groups by different variables

	Incomplete abortion group		Missed abortion group	
	N	%	N	%
Age in years				
<20	2	3.3	7	14
20-29	32	53.3	19	38
30-39	21	35	20	40
40+	5	8.3	4	8
Range	18-45		17-42	
Mean	28.7		28.9	
SD	5.9		7.4	
P (t test) =0.89 ns				
Gestational age of pregnancy				
First trimester	60	100	26	52
Second trimester	0	0	24	48
Diagnoses of abortion				
U.S	45	75	50	100
Clinical	15	25	0	0
Total	60	100	50	100

Table 2: The mean parity and abortion in each study group

	Incomplete abortion n=60	Missed abortion n=50	P value
Parity			0.86 NS
Range	0-7	0-7	
Mean	2.7	2.8	
SD	1.7	1.8	
Abortion			0.84 NS
Range	0-5	0-3	
Mean	0.8	0.8	
SD	I	0.8	

Notes: Respondents are those ending with complete uterine evacuation without the need for surgical intervention. P (x) for the difference in response rate between the two groups at the end of each dose interval was significant statistically for all intervals .

Table 3: A comparison of the cumulative response rate at the end of dose interval between incomplete and missed abortions				
Number of given doses	**Incomplete abortion n=60**		**Missed abortion n=50**	
	N	**%**	**N**	**%**
1	5	8.3	4	8
2	27	45	22	44
3	51	85	43	86
4	56	93.3	47	94

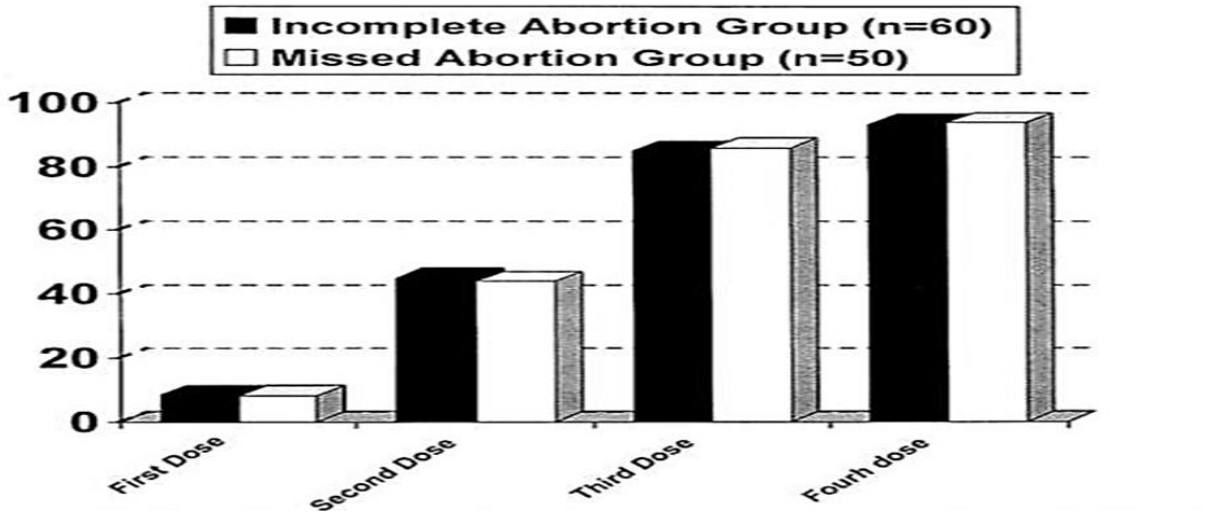

Figure 1: Bar chart comparing the response rate at the end of each dose interval between incomplete and missed abortion groups

Table 4: the response rate after each dose of the drug for subjects not responding to the previous dose among the incomplete abortion group

	Outcome of therapeutic trial			
	Total treated	**Surgical evacuation**	**Successful during the specific interval**	**Response rate for those taking a specific dose**
	N	**N**	**N**	**%**
First dose	60	0	5	8.3
Second dose	55	0	22	40
Third dose	33	4	24	72.7
Fourth dose	5	0	5	100

Note : successful outcome of therapeutic trial was the complete uterine evacuation without the need for surgical intervention

Table 5: the response rate after each dose of drug for subjects not responding to the previous dose among the missed abortion group

	Outcome of therapeutic trial			
	Total treated	**Surgical evacuation**	**Successful during the specific interval**	**Response rate for those taking a specific dose**
	N	**N**	**N**	**%**
First dose	50	0	4	8.3
Second dose	46	0	18	39.1
Third dose	28	2	21	75
Fourth dose	5	1	4	80

Note : successful outcome of therapeutic trial was the complete uterine evacuation without the need for surgical intervention

Reasons For Surgical Evacuation: As shown in table 6 , among the incomplete abortion group , subjects had surgical evacuation after 3 doses of misoprostol , 2 of them were performed on patients ' demand and the other 2 were done based on medical opinion (one case had criminal abortion and other one was blighted ovum) . Among the missed abortion group , 3 subjects ended in surgical uterine evacuation , one done on patients demand and another one because of incomplete evacuation after 3 doses of therapeutic trial . Only one case was a real failure since failed to respond after the 4th dose of misoprostol and surgical evacuation remaining choice. Complications of misoprostol Very little amount of blood loss occurred during uterine evacuation. No reported infections. Few patients (18 / 110- 16.4 %) reported mild nonspecific GIT complaints and 22/110 (20 %) had pain requiring analgesia.

Table 6: Reasons for surgical evacuation and number of doses received by each of 7 treatment failure

Reasons for surgical evacuation	Number of doses given
Incomplete abortion group	
Medical decision (criminal abortion)	3
Medical decision (blighted ovum)	3
Patients demand	3
Patients demand	3
Missed abortion group	
Patients demand	3
Failure after the fourth dose	4
Incomplete evacuation	3

Monitoring Progress: If one need to decide at each of the 4 steps of therapeutic trial when to stop the trial and shift to surgical intervention , knowledge about probability of successful response to each successive dose of oral misoprostol for those not responding dose together with the clinical condition of the subject at each step is required . As shown in table 4 and figure 2. A , among the incomplete abortion group the probability of responding successfully to the first dose of misoprostol was 8.3 % (5/60) . For those who failed respond after a single dose, taking a second dose will result in a success rate of 40 % (22/55). The response rate for the 33 subjects failing to respond after 2 doses is 24/33 (72.7 %) . Of the 9 subjects who failed to respond to 3 doses , 4 had surgical evacuation and the remaining 5 had another dose (4h) of misoprostol , all of which responded successfully (response rate for the 4th dose = 100 %) . As shown in table 5 and figure 2.B , among the missed abortion group the probability of responding successfully to the first dose of misoprostol was 8 % (4/50) . For those who failed to response after a single dose, taking a second dose will result in success rate of 39.1 % (18/46) . The response rate for the 28 subjects failing to respond after 2 doses is 12/28 (75 %) . Of the 7 subjects who failed to respond to 3 doses , 2 had surgical evacuation and the remaining 5 had another dose (4th) of misoprostol , among which 4 only responded successfully (response rate for the 4th dose = 80 %) .

Table 7: Frequency distribution of patients by complications of misoprostol

N=110	n	%
GIT symptoms	18	16.4
Pain requiring analgesia	22	20

Age , Gestational Age And Median Number of Doses Required For A Successful Outcome

As shown in table 8 , among the incomplete abortion group , the median number of doses required to achieve a successful outcome was slightly lower in youngest age group (2 doses for age < 20 years) . The difference however was not significant statistically. Among the missed abortion group the median number required to achieve a successful treatment was lowest (2 days) in the youngest age group (20 years) , it increased to a median of 3 days for the 20- 29 and 30-39 years age group to reach a maximum of 4 doses for the older age group (40 years and older) . This obvious positive trend with age failed to reach the level and statistical significance (possibly because of small sample size) . There were no obvious or statistical significance difference median number of doses required to achieve a successful outcome between subjects with first and second trimester missed abortion.

Table 8; the difference in median number of doses required for a successful outcome by age and gestational age among incomplete and missed abortion group

Age in years	Median number of doses given	
	incomplete abortion	Missed abortion
<20	2	2
20-29	3	3
30-39	3	3
40+	3	4
P (Kruskal -Wallis)	0.84 ns	0.07 ns
Gestational age of pregnancy in weeks		
First trimester		3
Second trimester		3
P (Mann Whitney)		0.92 ns

DISCUSSION:

Abortion occurs in at least one fourth of all recognized pregnancies (3, 4). Traditionally, the diagnosis and treatment of this condition has depended on the patient's symptoms because viability was difficult to determine before documentation of audible fetal heart tones in the 2nd trimester (5-7). Thus, the classic diagnostic categories and treatment approaches are based on clinical presentation. Threatened abortion cervix, but with cervix had dilated inevitable and incomplete spontaneous abortions were treated with uterine curettage because these conditions indicate non viability of the pregnancy (8, 9). Technologic developments, particularly vaginal ultrasound and sensitive assays for the beta submit of hCG (B- hCG) , have significantly enhanced our ability to determine accurately fetal viability as early as 6-7 weeks after the last menstrual period. Our study, was treatment of incomplete and missed abortion by using oral misoprostol (10, 11). The results of this study are encouraging suggesting that misoprostol is an effective method of evacuation of the uterus in women with incomplete and missed abortion. This confirms the results of this study with success rate of over 93 % with medical treatment. We used two or three doses reaching to four oral doses of misoprostol. The unique aspect of our study is that we administered three oral doses of 600, 400, 400, mcg of misoprostol at two hourly intervals and we repeated the regimen if necessary completely abortion of fetus and placenta and no any retained pieces, no bleeding and good uterine contraction . So the results were very encouraging, and by this way we can reduce the risk of extra uterine catheterization , infection , hysterectomy , perforation and bleeding Misoprostol is a synthetic prostaglandin E , analogue cheap, effective and dose not require special storage conditions . These features may be beneficial in regions with limited resources for health care. The procedure has been found well tolerated by most women. It reduces the cost of treating miscarriage, and will also reduce the risks of general anesthesia and surgical evacuation. Medical success of more than 93 %. The incomplete and missed abortion are unclear. Expectant management and surgical evacuation of the uterus are alternative treatments miscarriage rates. Alternatives of medical treatment of missed abortion in early trimester by surgical evacuation, and second trimester by using uterotonic agents such as the oxytocin drug in I.V. infusion with or without intrauterine catheterization (12, 13). Investigators have given misoprostol Vaginal application was found to be superior in some trails and is believed to lessen gastrointestinal side effects (7, 14, 15). Vaginal misoprostol has been studied as an abortifacient and as a means of predialation of the cervix before surgical abortions (16-19). Although misoprostol is being administered vaginally, there have been no reported studies of the pharmacokinetics of this mode of administration.

CONCLUSION:

This clinical trial demonstrated that for incomplete and missed abortion, medical treatment by using 2-4 doses of misoprostol orally is an effective, well tolerated and safe alternative to surgical the uterus.

Recommendations:

1. More studies are required for the acceptability of these treatments for
2. There needs randomized trial to compare expectant management, medical treatment and surgical evacuation of uterus missed abortion (spontaneous abortion).
3. We suggest that prostaglandin analogues may be practical alternative to surgical uterine evacuation in managing spontaneous, incomplete or missed abortion
4. Reproductive rights advocates, must always work towards securing safe, legal abortions for all women . However, in countries where the religious and / or political barriers are for the time being insurmountable, misoprostol is a much safer including abortion than other methods such as introducing sharp instruments

or caustic substances into the uterus.

5. For medical methods of abortion to work successfully, women must commit to completing the regimen, and both women and providers must wait while the therapy takes its course.

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