INTERNATIONAL JOURNAL OF MEDICAL AND APPLIED SCIENCES
E-ISSN:2320-3137

Research Article

SAFETY AND EFFICACY OF USING MIFEPRISTONE AND MISOPROSTOL COMBINATION IN TERMINATION OF FIRST TRIMESTER MISSED ABORTION-A PROSPECTIVE STUDY

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ABSTRACT

Objectives: The objective of the study was to find out the efficacy and safety of using Mifepristone and Misoprostol (PGE1) in the termination of first trimester missed abortion.Materials and Methods: This was a prospective study conducted in the department of Obstetrics and Gynecology at Sree Gokulam Medical College, Trivandrum during the time from February 2012 to January 2014.Results : A total of 92 cases of ultrasound confirmed missed abortion up to 13 weeks of amenorrhea were included in this study. Mifepristone 200 mg was given to all these patients. After 48 hours, PGE1, 800 microgram was given per vaginally to all these patients. Another dose of 400 microgram was given after 3 hours if there was no bleeding during this period. Outcome variables were doses of PGE1 required, need for surgical evacuation and side effects of PGE1. In the present study,49% (45 out of 92 cases) required single dose of PGE1,whereas 51% (47 out of 92 cases) required a repeat dose.10%(9 out of 92 cases) required surgical evacuation at 2 weeks, when ultrasound done at 2 weeks showed retained products of conception. The common complications were pain (4%), nausea and vomiting (2%) and fever (2%).Conclusion: Mifepristone and PGE1 combination can be safely used in first trimester missed abortion, thus reducing the need for surgical intervention.

Keywords*: missed abortion, Mifepristone, Misoprostol*

INTRODUCTION

Abortion or miscarriage is the spontaneous termination of pregnancy before the period of viability.15% of all clinically recognized pregnancy ends in miscarriage. Out of these, 80% are in the first trimester [1]. Missed abortion is the intrauterine death of the embryo or a nonviable fetus which is then passively retained inside the uterus. There is a history of amenorrhea followed by vaginal bleeding or spotting. Signs and symptoms of early pregnancy slowly disappear. Ultrasound will show a gestational sac smaller than expected with irregular and crenated margins. There may be a fetal node or fetus, but there will not be any cardiac activity [2]. Standard treatment of missed abortion is surgical viz., suction evacuation. Medical treatment is also resorted to nowadays. This includes oral Mifepristone, followed by varying doses of vaginal Misoprostol [PGE1].

With the increase in use of ultrasound early in pregnancy, large numbers of missed abortions are diagnosed earlier, before the onset of abdominal pain and bleeding. If medical methods, including a combination of Mifepristone and PGE1 proves to be safe and effective, a large number of patients will escape the need for surgical intervention and its complications. The

present study was carried out to find out the safety and efficacy of Mifepristone and Misoprostol combination for safe termination of first trimester missed abortion.

MATERIALS AND METHODS:

This is a prospective study conducted in the department of Obstetrics and Gynecology, Sree Gokulam Medical College and Research Foundation, Trivandrum, during the time from February 2012 to January 2014.during this period; all cases of missed abortion up to 13 weeks gestational age, 92 cases were included in this study. Only ultrasonographically confirmed cases of first trimester missed abortion were included in this study.

Women with a history of previous caesarian section, previous surgical evacuation and women with known hypersensitivity to prostaglandins were excluded from this study.

All patients with ultrasonographically confirmed cases of first trimester missed abortion, up to 13 weeks, were included in this study. A detailed history was taken and clinical examination of these women was done. After getting a detailed written informed consent, these women were given 200milligram of Mifepristone on outpatient basis. These patients were admitted in the hospital 48 hours later and 800 microgram of Misoprostol (PGE1) was introduced vaginally and applied in the posterior fornix. These patients were observed for 3 hours for the onset of bleeding. If there was no bleeding within 3 hours, another dose of 400 microgram of PGE1 was given per vaginally in the posterior fornix. Immediate surgical evacuation was done if there was excessive bleeding following single dose or second dose of PGE1.These patients were discharged after 3 hours of observation. Follow up was given at 2 weeks. These patients were asked to report earlier in case of excessive bleeding, pain or any evidence of infection like persistent fever, abnormal discharge. At the time of follow up at 2 weeks, repeat ultrasound was done to confirm complete abortion. If the ultrasound done at two weeks showed evidence of retained products of conception, then surgical evacuation by suction was done. Collected data was analyzed using SPSS.

RESULTS:

The study population was in the age group 18-40 years.7% (6 cases) were 19 years or less, 42% (39 cases) belonged to 20-24 years age group,31% (29 cases) belonged to 25-29 years age group,9% (8cases) belonged to 30-34 years age group and 11% (10)cases were between 35 and 40 years of age.[table1].

Table 1. Age group

Age in years	Number of patients	Percentage
<19 years	6	7%
20-24	39	42%
25-29	29	31%
30-34	8	9%
35-40	10	11%

51% [47 cases] belonged to less than 9 weeks gestational age and 49% [45 cases] belonged to gestational age between 9 and 13 weeks.[table2].

Table 2. Gestational age

Gestational age in weeks	Number of patients	Percentage
Less than 9 weeks	47	51%
9-13 weeks	45	49%

In this study, 49% [45 cases] required only single dose of 800 microgram of PGE1 and 51% [47 cases] required a repeat dose of 400 microgram of PGE1. Of the 45 cases who received single dose of PGE1, 7% [3 cases] underwent surgical evacuation immediately as they developed excessive bleeding.4% [2 cases] of the 47 cases that required repeat dose also underwent immediate surgical evacuation because of excessive bleeding. Retained products of conception, confirmed by ultrasound at 2 weeks were found in 10% [9 cases][table 3]

Table 3. Misoprostol doses and surgical intervention

Number of doses of Misoprostol	Number of patients		Complete abortion		Surgical evacuation		
					Immediately due to excess bleeding		Due to RPOC at 2weeks
Single dose	45	49%	38	84%	3	7%	4 (9%)
Repeat dose	47	51%	40	85%	2	4%	5 (11%)
Total	92		78	85%	5	5%	9(10%)

Oral Mifepristone and vaginal Misoprostol appeared to be well tolerated. Out of the 8 patients with minor complaints, 49(4%) had pain, 2(2%) patients developed low grade fever with no evidence of infection and 2(2%) patients developed mild nausea and vomiting. None of the patients developed any major complications like perforation of uterus, rupture of uterus or coagulopathy. [Table 4].

Table 4. Complications

Complications	Number of patients	Percentage
Bleeding requiring immediate evacuation	5	5%
RPOC at 2 weeks	9	10%
pain	4	4%
fever	2	2%
Nausea and vomiting	2	2%
Rupture uterus	nil	-
infection	nil	-
coagulopathy	nil	-

Completeness of abortion without the need for surgical evacuation was seen in 85% (78 of the 92 cases). Immediate suction evacuation due to excessive bleeding was done in 5% (5 cases) and retained products of conception (RPOC) at 2 weeks were found in 10% (9 cases).

DISCUSSION:

Our study suggests that combination of Mifepristone and Misoprostol is a safe and effective method of managing first trimester missed abortion. Effectiveness of the regimen as defined by complete abortion without the need for surgical intervention was achieved in 85% of patients in our study. No major complications were observed in our study. Minor complications were observed in 8% of patients and the most common side effect reported was pain (4%).

Although incomplete miscarriage can be managed with Misoprostol alone, in cases of missed abortion, priming with Mifepristone, makes the regimen more effective. In or study, overall success rate was 85%. Wagaarachichi *et al* [3], reported a success rate of 84.1%. Nielson *et al*[4]., (1997) reported a success rate of 52%, using a combination of Mifepristone 400 mg and Misoprostol 400 microgram, both taken orally with 13% requiring emergency surgical evacuation. The success rate was slightly lower because Misoprostol was used orally rather than vaginally. Plasma concentration and bioavailability of Misoprostol tend to be higher when administered vaginally rather than orally. (Zieman *et al*., 1997[5]).

It has been shown that for termination of early pregnancy, a single dose of 200mg of Mifepristone is as effective as 600 mg, when used in combination with Misoprostol (WHO Task Force 1993[6]). Our study confirms that single dose of 200mg Mifepristone is useful for the management of missed abortion. Most published studies using Misoprostol alone for medical management of delayed miscarriage have a success rate of 13 to 83 %. Should Mifepristone be unavailable, regimen using Misoprostol alone may also be used.

Table 5 summarizes published data with reference to medical regimen and success rates

Study	Regimen	Efficacy (%)
Demetroulis *et al.*[7], 2001[b]	Misoprostol 800 µg (PV)	82.5
Nielsen *et al.*, 1997[c]	Mifepristone 400 mg	52
	Misoprostol 400 µg (PO)	
	Misoprostol 800 µg (PV)	88
Herabutya and O-Prasertsawat[8], 1997[c]	Misoprostol 200 µg (PV)	83.3
Hughes *et al.*[9], 1996[c]	Mifepristone 200 mg	89.1
	Misoprostol 400 µg, 600 µg, 400 µg (PO)	
Chung *et al.*[10], 1997[b]	Misoprostol 400 µg, 400 µg, 400 µg–over 48 h (PO)	70.6
de Jonge *et al.*[11], 1995[a]	Misoprostol 400 µg (PO)	13
Lelaidier *et al.*[12], 1993[c]	Mifepristone 600 mg	82
El–Rafeay *et al.*[13], 1992[c]	Mifepristone 600 mg	96

a. incomplete miscarriage

b. incomplete miscarriage, missed miscarriage and anembryonic pregnancy

c. missed miscarriage and anembryonic pregnancy

po=per oral; pv= per vaginal

Split analysis of Demetroulis *et al.*, showed that failure of Misoprostol alone for management of missed abortion and anembryonic pregnancy as 23.1%. This confirms our study findings and previous studies that priming with Mifepristone makes the regimen more effective. (El Rafeay *et al.*, 1992).

Side effects of this regimen were also assessed. The most common side effect reported was pain (4%). 2% had nausea and vomiting and 2% had low grade fever. These are generally in the lower range than similar study. (Nguyen Thi Nhu Ngoc *et al.* [14],). This may be because of lower dose of Mifepristone used and the vaginal route of Misoprostol administration. Excessive bleeding requiring immediate evacuation was reported in 5% of patients.

Side effects are common among medical abortion clients but this does not affect the safety of the method and the vast majority of patients find it tolerable. Proper counseling is effective in preparing them for the methods' side effects.

CONCLUSION:

From this small study, it is anticipated that medical management of missed abortion will prove to be good alternative to surgical management.

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