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COMPARISON OF MIFEPRISTONE (200mg) FOLLOWED BY MISOPROSTOL (800µg) 6 HRS LATER WITH 24 HRS LATER IN EARLY PREGNANCY FAILURE

Obstetrics & Gynecology

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ABSTRACT

INTRODUCTION: Early pregnancy failure (EPF) is an inclusive term that comprises incomplete, complete, or inevitable spontaneous abortion; anembryonic gestation (blighted ovum); and embryonic demise (missed abortion) at less than 14 weeks 1. It is one of the most common complications of pregnancy, accounting for approximately 15% to 20% of clinically recognized pregnancies 1,2. Many EPFs occur before pregnancies have been clinically recognized (that is, women mistake them for "late cycles").

AIMS & OBJECTIVES: To compare the efficacy between mifepristone 200mg orally followed by misoprostol 800µg vaginally 6 hrs later with mifepristone 200mg orally followed by misoprostol 800µg vaginally 24 hrs later in early pregnancy failure for termination up to 9 weeks of gestation. To reduce unusual blood loss. To reduce surgical intervention in case of early pregnancy failure.

MATERIALS & METHODS: Hospital based Prospective randomiSe comparative single centre study. Department of Obstetrics and Gynecology Midnapore Medical College and Hospital. One year from January 2019 to February 2020 for data collection and six month for data analysis. Mother attended the Gynae OPD clinic and Obstetrics emergency with features of early pregnancy failure. The sample size was 50, with 25 patients in each group.

RESULTS: We found that the table 4 shows the distribution according to gestational age. The main indication for which medical abortion was done in our study is early pregnancy failure (Blighted ovum) and missed abortion. Majority of patients were in the gestational age between 8-9 weeks with 48 % of women who underwent 6 hour interval regimen and 40% of women who underwent 24 hour interval regimen. P value documented is 0.849 which is not significant. There was no significant difference between two groups regarding gestational age (p value=0.849).

SUMMARY AND CONCLUSION: Vaginal Misoprostol can be safely administered 6 hours following Mifepristone instead of waiting for 24 hours. Efficacy in achieving complete abortion rate is almost equal to 24 hours regimen and most acceptable from patient's side also. Additionally, women are less likely to experience side effects the earlier the misoprostol is used. Women can now have more flexibility when using mifepristone and vaginal misoprostol for medical abortion.

KEYWORDS

Mifepristone (200mg), Misoprostol (800µg) And Early Pregnancy

INTRODUCTION

Early pregnancy failure(EPF) is an inclusive term that comprises incomplete, complete, or inevitable spontaneous abortion; anembryonic gestation (blighted ovum); and embryonic demise (missed abortion) at less than 14 weeks [1]. It is one of the most common complications of pregnancy, accounting for approximately 15% to 20% of clinically recognized pregnancies [1,2]. Many EPFs occur before pregnancies have been clinically recognized (that is, women mistake them for "late cycles"). One in 4 women will experience a pregnancy loss over the course of her life. EPF can be further defined by the subtypes of pregnancy abnormality including intrauterine embryonic/fetal demise, anembryonic pregnancy, inevitable abortion, and incomplete abortion diagnosed at <12 weeks' gestation.

It is estimated that up to 60% of all conceptions end in early losses. Chromosomal abnormalities, most commonly translocations and aneuploidy, are responsible for more than half of all spontaneous EPFs. Other genetic defects that are currently impossible to discern by simple karyotype may be the cause of many spontaneous losses.

An EPF that is characterized by a history of a positive pregnancy test, vaginal bleeding without passage of tissue, and an open cervical os is termed an inevitable abortion [3]. Anembryonic pregnancy, which was previously termed "blighted ovum," [1] describes the absence of a visible yolk sac with a mean sac diameter (MSD) of 13 mm, the absence of an embryonic pole with MSD of 20 mm, or the presence of an empty amnion. Embryonic or fetal demise, previously termed "missed abortion," describes the failure of a previously identified embryo to grow or show cardiac activity, or the absence of cardiac motion in embryos ≥5 mm.[4]

For many years, surgical treatment (dilatation and curettage, D&C) has been standard treatment. However, surgical management is associated with risks of complications (uterine perforation, pelvic infection, excessive bleeding, anaesthesia, intra-uterine adhesions, cervical injury or cervical insufficiency in following pregnancies) and high costs.

The Royal College of Obstetricians and Gynecologists as well as the "American College of Obstetricians and Gynecologists" recommend medical methods as a safe, effective and acceptable alternative (evidence level A).

Misoprostol is used off-label for several obstetric and gynaecologic indications, including EPF, due to uterotonic properties leading to ripening and dilatation of the cervix and myometrial contractions. For medical treatment, the International Federation of Gynecology and Obstetrics (FIGO) recommends the prescription of two doses misoprostol 800 µg administered vaginally (3 hrs apart) or two doses misoprostol 600 µg sublingual (3 hrs apart).

Since the introduction of mifepristone in combination with misoprostol for legal medical abortion, many regimens and routes of administration and dosages have been suggested and tested. The FDA-approved regimen of medical abortion consists of 600 mg mifepristone administered orally and 400 mg oral misoprostol administered 48h later. However, many reported different administration regimens of misoprostol, either orally or vaginally and at different intervals from the mifepristone administration have been proposed, in an attempt to find a more successful and convenient regimen [5].

Multiple investigators have evaluated alternative medical abortion regimens to simplify the treatment process and extend the gestational age range. These regimens have included using lower doses of mifepristone, home administration of the misoprostol, varying the dose of misoprostol, use of vaginal misoprostol, and decreasing the dosing interval between mifepristone and misoprostol.

The present study was designed to compare the efficacy, side effects, and acceptability of the administration of 200 mg of mifepristone followed 6 hours later or 24 hours later by 800 µg of misoprostol administered vaginally in women up to 63 days gestation.

These regimens with a shorter interval between mifepristone and misoprostol administration, if effective, would shorten the amount of time necessary for a medical abortion to occur and, potentially, increase acceptability.

The present study was aimed:

- To compare the efficacy between mifepristone 200mg orally followed by misoprostol 800µg vaginally 6 hrs later with mifepristone 200mg orally followed by misoprostol 800µg vaginally 24 hrs later in early pregnancy failure for termination up to 9 weeks of gestation.
- To reduce unusual blood loss.
- To reduce surgical intervention in case of early pregnancy failure.

MATERIALS & METHODS

Study Design: Hospital based Prospective randomization comparative single centre study.
Place of Study: Department of Obstetrics and Gynecology Midnapore Medical College and Hospital.
Periods of Study: One year from January 2019 to February 2020 for data collection and six month for data analysis.
Study population: Mother attended the Gynae OPD clinic and Obstetrics emergency with features of early pregnancy failure.
Sample size: The sample size was 50, with 25 patients in each group.
Sample Design: Eligible patients satisfying inclusion and exclusion criteria were selected.
Case Control required or not: Required.

INCLUSION CRITERIA:

- Primigravida or multigravida with singleton pregnancy with features of early pregnancy failure up to 63 days.
- Early pregnancy failure criteria-

1. Intrauterine gestation with gestational sac>20mm with no evidence of an embryo/yolk sac.
2. Intrauterine gestation with CRL>6mm without cardiac activity.

EXCLUSION CRITERIA:

- Previous history of LSCS
- Severe anaemia <8gm/dl.
- Patient with hyper sensitivity to drugs.
- Patients with cardiac disease, renal failure, Chronic Lung Disease
- Bleeding disorder
- Infection

RESULTS

Our study showed that the table 2 shows the distribution of study subjects according to gravidity in both groups. 72% of women who underwent 24 hour interval regimen and 64% of women who underwent 6 hour interval regimen were of multigravida. 28 % of the patients who underwent 24 hour interval regimen and 36% of the patients who underwent 6hour interval regimen were primigravida. No significant difference was observed between two groups regarding gravidity (p value= 0.544). Table 3 shows the distribution of study subjects according to parity in both groups. 36% of women who underwent 6 hour interval regimen and 32% of women who underwent 24 hour interval regimen were nulliparous. 28% of the patients of both groups were primiparous. Regarding parity two groups were comparable with a p value of 0.98.

We found that the table 4 shows the distribution according to gestational age. The main indication for which medical abortion was done in our study is early pregnancy failure (Blighted ovum) and missed abortion. Majority of patients were in the gestational age between 8-9 weeks with 48 % of women who underwent 6 hour interval regimen and 40% of women who underwent 24 hour interval regimen. P value documented is 0.849 which is not significant. There was no significant difference between two groups regarding gestational age (p value=0.849). Table 5 shows the socio-demographic characteristics of the study subjects. Majority of the study participants of both groups belonged to rural area; most of the study subjects were educated with a level of higher secondary education while most of them were housewives. Majority of the study participants belonged to lower middle class irrespective of groups.

We showed in table 7 shows the comparison of mean hemoglobin level pre and post treatment in both groups. There was no statistically significant difference regarding pre and post treatment hemoglobin level (p value = 0.7 and 0.71 respectively). Table 9 shows the success rate of abortion of both groups. Out of 50 patients who underwent medical abortion, 3 patients did not turn up for check scan, thus their expulsion status was not known. Out of 47 patients who underwent check scan 76% of women in group A and 80% of women in group B had complete expulsion. Side effect profile of both groups is documented in Table 11. Regarding side effects we found no significant difference between two groups (p value= >0.05).

DISCUSSION

Several factors affect the successful abortion rate with mifepristone and misoprostol: gestational age, parity, previous termination of pregnancy and the initial β-HCG plasma levels. The time interval between mifepristone and the prostaglandin analogue may also affect the success rate of medical termination. Simultaneous administration of mifepristone and misoprostol during the first 63 days of gestation was associated with an overall abortion rate of 71.4 % after 24 h [6].

The present study was conducted in the Department of Obstetrics and Gynaecology, Midnapore Medical College & Hospitalupto all pregnant women with gestational age of less than 63 days diagnosed with intrauterine pregnancy failure as confirmed by ultrasonography and undergoing medical abortion and who were willing for follow up during the study period. Our study aimed to demonstrate equivalence between mifepristone 200mg orally followed 6 hrs later and 24 hrs later by misoprostol 800µg vaginally in early pregnancy failure for termination up to 9 weeks of gestation.

The sample size was 50 criteria-25 in group A and 25 in group B). Group A included women who were given Vaginal Misoprostol 6 hours following Mifepristone whereas 24 hours interval between Mifepristone and Misoprostol stands as group B.

In our study mean value for age in group A was 25.6 and in group B it was 26.6 years. Regarding socio-economic status we found 48% of patients of 6 hr regimen group and 40% of patients in 24-hr regimen group who underwent medical abortion belong to lower middle class.

In terms of gravidity we observed that 72% of women who underwent 24 hour interval regimen and 64% of women who underwent 6 hour interval regimen were of multigravida. In the present study 36% of women who underwent 6 hour interval regimen and 32% of women who underwent 24 hour interval regimen were nulliparous.Table-2 An interval of 6-8 hrs and even simultaneous administration do not result in a clinically relevant loss in effectiveness. A recent study by Creinin and colleagues showed that for a regimen of 200 mg mifepristone and 800µg buccal misoprostol, the effectiveness was 95.2% for women administering the drug simultaneously and 96.7% for women administering the drugs 24 hrs apart.[7]

Regarding gestational age; majority of patients were in the gestational age between 8-9 weeks with 48 % of women who underwent 6 hour interval regimen and 40% of women who underwent 24 hour interval regimen. Table-4 Medical methods of abortion guidelines frequently recommend ultrasonography to determine gestational age and confirm the outcome of treatment when the medical history and physical examination are inconclusive. Most we medical abortion trials have used a trans vaginal approach for these indication. Vaginal ultrasonography allows for precise dating, particularly of very early pregnancies. It is also an efficient and accurate means of verifying expulsion of gestational sac after a medical abortion.

The study done by K Prema et al determined the effect of abortion on hemoglobin status in 303 urban women of low socioeconomic status in India. Before abortion, Hb levels ranged from 9.4-14.6gm/dl: mean Hb levels were 12.2 in the first trimester, and 12 in the second trimester.24.5% of these women were anaemic(Hb 11gm/dl) before their medical termination of pregnancy. Hb estimations done after 40 days of abortion showed that there was no alteration in the mean Hb levels either in first or second trimester patient. No significant difference between the initial and follow-up Hb. [8]

In the present study in terms of success rate we observed that out of 50 patients who underwent medical abortion, 3 patients did not turn up for check scan, thus their expulsion status was not known. Out of 47 patients who underwent check scan 76% of women in 6 hr regimen group and 80% of women in 24-hr regimen group had complete

expulsion.Table-9 The difference between our results and those of, who reported a 95.1 % success rate after simultaneous administration of mifepristone and vaginal misoprostol, compared to 96.9 % when administered 24 h apart, may be attributed to the different route of administration of misoprostol. According to El-Refaey et al.[9] 87 % of patients receiving misoprostol orally will abort, while vaginal administration of misoprostol will result in a 95 % abortion rate[9].

Importantly, this equivalent efficacy is achieved with fewer side effects. Significant complication not found. Regardless, women found both treatment regimens equally acceptable. The high efficacy in the 6 hour group is not a reflection solely of misoprostol action because studies using misoprostol alone achieve much lower rates of efficacy when administered in a single dose vaginally[10].

SUMMARY AND CONCLUSION

- The present study was conducted in the Department of Obstetrics and Gynaecology, Midnapore Medical College & Hospital. We included all pregnant women with gestational age of less than 63 days diagnosed with intrauterine pregnancy failure as confirmed by ultrasonography and undergoing medical abortion and who were willing for follow up.
- Sample size was 50 criteria-25 in group A and 25 in group B). Group A included women who were given Vaginal Misoprostol 6 hours following Mifepristone whereas 24 hours interval between Mifepristone and Misoprostol stands as group B.
- Vaginal Misoprostol can be safely administered 6 hours following Mifepristone instead of waiting for 24 hours. Efficacy in achieving complete abortion rate is almost equal to 24 hours regimen and most acceptable from patient's side also.
- Additionally, women are less likely to experience side effects the earlier the misoprostol is used. Women can now have more flexibility when using mifepristone and vaginal misoprostol for medical abortion.
- Because misoprostol can be used as soon as 6 hours after Mifepristone administration, women can now have a medical abortion in a single day with a high level of efficacy, safety, and acceptability.

Table: Obstetric Index, Parity and Misoprostol application to Abortion Interval (hours)

		Group A		Group B	
		Frequency	Percentage	Frequency	Percentage
Obstetric Index	Multigravida	16	64.0	18	72.0
	Primigravida	9	36.0	7	28.0
	Total	25	100.0	25	100.0
Parity	0	9	36.0	8	32.0
	1	7	28.0	7	28.0
	2	5	20.0	6	24.0
	≥3	4	16.0	4	16.0
	Total	25	100.0	25	100.0
Misoprostol application to Abortion Interval (hours)	<8	17	68.0	18	72.0
	8-12	5	20.0	4	16.0
	13-24	3	12.0	3	12.0
	Total	25	100.0	25	100.0

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