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Original Research Paper

Gynecology

A COMPARATIVE STUDY OF MIFEPRISTONE PLUS MISOPROSTOL VS MISOPROSTOL ALONE IN MID TRIMESTER TERMINATION OF PREGNANCY

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ABSTRACT

Background: Medical methods of abortion are those induced by abortifacient pharmaceuticals. Medical methods of abortion have become an alternative method of abortion with availability of prostaglandin analogues and anti-progesterone mifepristone. The present comparative study is undertaken to analyse the efficacy of mifepristone plus misoprostol vs misoprostol alone in mid-trimester termination of pregnancy. **Aims And Objectives:** To know induction abortion interval in both regimens and to study possible side effects of drugs and effective cost of both drug regimens. **Methods:** The present study was undertaken in Department of OBG, at MRMC, Kalaburagi over a period of 18 months. The study was conducted by dividing women approaching for mid trimester termination of pregnancy into two groups each consisting of 30 women. After admission, women assigned to GROUP A was given mifepristone 200 mg orally.24hours after administration of mifepristone, started with misoprostol 600mcg per vaginally followed by misoprostol 400mcg sublingually every 3rd hourly until termination or maximum of 5 doses. women assigned to GROUP B were given misoprostol 600mcg pervaginally followed by misoprostol 400 mcg sublingually every 3rd hourly until termination or maximum of 5 doses. The outcome were studied in terms of induction-abortion interval, expulsion time, total dose of misoprostol, side effects and cost effectiveness of both regimens. **Results:** The Mean induction abortion interval was 29.23 hours in GROUPA whereas 6.21hours in GROUP B. Mean expulsion time was 6.19 hours GROUPA whereas 8.37hours GROUP B. It is statistically significant with p value of 0.014. Mean dose required in GROUP A was 1242.86 mcg which was less when compared to GROUP B,1613.33 mcg with p value of 0.004. There was no statistically significant difference between side effects in two groups. Mean cost for drugs in (GROUP A) was 516.33 rupee and 158.67 rupee in misoprostol group (GROUP B). **Conclusion:** Pretreatment with mifepristone resulted in shorter expulsion time and reduced dose misoprostol required compared with misoprostol only group.

KEYWORDS : mifepristone, misoprostol, mid trimester termination

INTRODUCTION:

Abortion is defined as the spontaneous or induced termination of pregnancy before fetal viability.[1] World Health Organization define abortion as loss or termination of a pregnancy with a fetus aged younger than 20 weeks gestation or weighing <500 grams.

In india, about 2% of pregnancy are terminated. About 85% of the induced abortions are in the first trimester and 15% in the second trimester[2]. Ideally if the termination is in 1st trimester prognosis is better, Morbidity and mortality rates for mid-trimester termination are 3 -4 times higher than termination of pregnancy in 1st trimester of pregnancy.

The timespan that defines a mid-trimester fetal loss extend from the end of first trimester until the fetus weighs < 500 grams or gestational age reaches 20 weeks.

Medical methods of abortion are those induced by abortifacient pharmaceuticals. Medical methods of abortion have become an alternative method of abortion with availability of prostaglandin analogues and anti-progesterone mifepristone.

Misoprostol a newer synthetic prostaglandin E1. It is superior to all other available prostaglandins as it is stable at room temperature, requires no refrigeration, is cost effective, has fewer side effects, is a potent uterotonic and cervical ripening agent. It can be used by both the oral, vaginal and sublingual route and in concurrence with other drugs as well.

Mifepristone, (RU486, a substitute 19- norethisterone derivative) by blocking the progesterone receptors It causes estrogen dominance and results in intrauterine fetal death. At the same time it sensitizes the uterus to the activity of the prostaglandin.

The World Health Organization (WHO) recommends this drug combination, with an initial dose of mifepristone followed by misoprostol 1to 2 days later, for medical management of abortion.[3] The World Health Organization approved both mifepristone and misoprostol for termination of pregnancy by including them in the list of Essential Medicines in 2005

Medical methods of abortion have the advantage over surgical methods as it is non- invasive and with minimal side effects. Anesthesia related complications occurring in surgical method can be avoided. There is need for a safer, quickest, cost effective convenient and feasible medical method of termination of pregnancy in second trimester.

The present comparative study is undertaken to analyse the efficacy of mifepristone plus misoprostol vs misoprostol alone in mid-trimester termination of pregnancy

AIMS AND OBJECTIVES:

1.To know induction abortion interval in both regimens
2.To study possible side effects of drugs and effective cost of both drug regimens.

MATERIALS AND METHODS:

Women who fulfilled the criteria for the study were given explanation of the study, informed written consent was obtained and recruited into study. Detailed personal information, obstetric, menstrual, family and past history was recorded. A detailed general physical examination followed by systemic examination was done. Obstetric examination includes inspection, palpation, auscultation and per vaginal examination. It was prospective interventional study with sample size of 60.(30 subjects in each group) After admission, women assigned to GROUP A was given mifepristone 200 mg orally.24hours after administration of mifepristone, started with misoprostol 600mcg per vaginally

followed by misoprostol 400mcg sublingually every 3rd hourly until termination or maximum of 5 doses.

Immediately after admission, women assigned to GROUP B were given misoprostol 600mcg per vaginally followed by misoprostol 400mcg sublingually every 3rd hourly until termination or maximum of 5 doses. The blood pressure, pulse rate, temperature, frequency of uterine contractions was monitored every 3rd hourly. The side effects like nausea, vomiting, diarrhea, chills and fever were recorded.

After expulsion, the products of conception(fetus and placenta with membranes) were examined to see whether the abortion was complete and bedside ultrasonography was done to ensure completeness.

After fetal expulsion, if spontaneous expulsion of placenta did not occur within 60 minutes of delivery of fetus it is termed as incomplete abortion. Digital exploration of uterine cavity and blunt curettage under general anesthesia in the operating room is reserved for incomplete abortion cases.

After 5th dose of misoprostol, if products of conception are not expelled within 3 hours then it is termed as failure. In these cases women were managed by other methods of mid trimester abortion.

The procedure was considered as successful if there was complete abortion.

Incomplete abortion and failure cases are considered as unsuccessful.

In GROUP A, The induction abortion interval was defined as the interval between the time of administration of mifepristone to the time when product of conception were expelled.

Expulsion time is defined as the interval between the time of administration of 1st dose of misoprostol to the time when product of conception were expelled.

In GROUP B, induction abortion interval and expulsion time are same. The number of doses of misoprostol required are calculated and recorded.

Inclusion Criteria:

- Any pregnant women up to gravida 3 with live singleton pregnancy from 14weeks to 20 weeks of gestation requiring termination of pregnancy (including one previous LSCS).
- Pregnant women with anomalous baby up to 24weeks of gestation.
- Women with obstetric complications or medical disorder (hypertension, thyroid disorder, diabetes etc) requiring termination of pregnancy.

Exclusion Criteria:

- Previous allergic reactions to drugs used in the study.
- Women with known chronic or acute adrenal disease, hepatic disorder, renal failure and cardiovascular disease.
- Women with vaginal bleeding during pregnancy.
- Women with inherited porphyria.
- Women on anticoagulation.

RESULTS:

Majority of patients were between 26-30years of age group in both groups. The mean gestational age is 18.09 weeks in GROUP A and 17.19 weeks in GROUP B. In mifepristone and misoprostol group(GROUPA), indications for abortion included anamalous baby in 56.7% (n=17) ,failure of contraception in 23.3%(n=7), medical disorder in 10%(n=3),severe oligohydramnios in 6.7%(n=2) and pregnancy in unmarried women in 3.3% (n=1) of patients. In misoprostol only group(GROUP B) failure of contraception being most common cause in 56.7% (n=17) followed by anomalous baby in 30%,severe oligohydramnios in10%(n=3) and medical disorder in 3.3 %(n=1) of patients. Mean induction abortion interval was 29.23 hours in the mifepristone and misoprostol group(GROUPA) whereas 6.21hours in misoprostol group(GROUP B).It is statistically significant with p value of 0.001.

DISCUSSION

In the present study, mean duration of third stage was 5.1minutes in the study group and

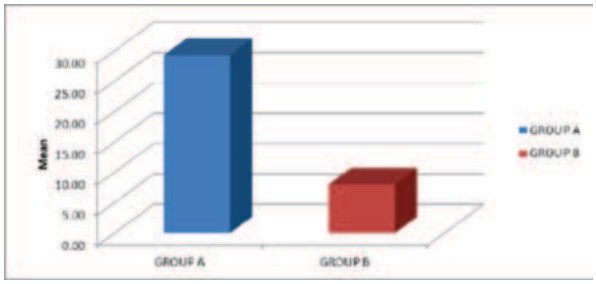

Figure1: Bar Diagram Showing Difference In Induction Abortion Interval Between Two Groups.

Mean expulsion time was 6.19 hours in the mifepristone and misoprostol group (GROUPA) whereas 8.37hours in misoprostol group(GROUP B).It is statistically significant with p value of 0.014

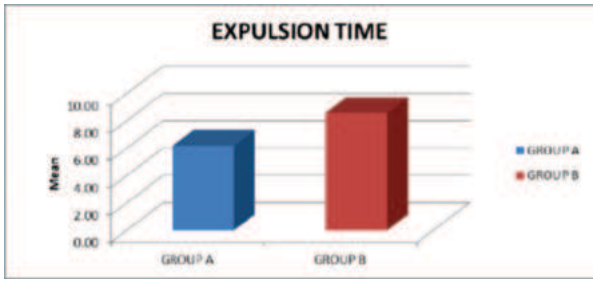

Figure 2: Bar Diagram Showing Difference In Expulsion Time Between Two Groups

Mean dose required in mifepristone and misoprostol group (GROUP A) was 1242.86 mcg while that in misoprostol group (GROUP B) was 1613.33 mcg. The difference was statistically significant.

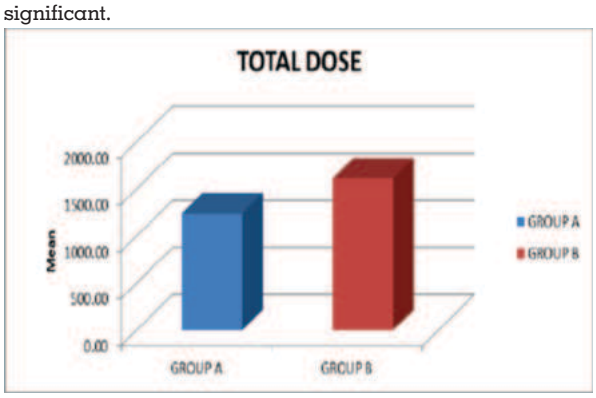

Figure 3: Bar Diagram Showing Comparison Of Mean Misoprostol Dose Required For Abortion

The repeat doses of sublingual misoprostol was required in 73.4% (n=22) of patients in mifepristone and misoprostol group (GROUP A) and 96.71%(n=29) of patients in misoprostol group (GROUP B). The difference between two groups was statistically significant.

Table1: Comparison Of Number Of Repeat Doses Of Sublingual Misoprostol Required For Abortion In Both Groups.

		GROUP A		GROUP B		Total	Chi-suare value	p-value
		No. of cases	%age	No. of cases	%age			
REPEAT DOSE OF SUBLINGUAL MISOPROSTOL	0	8	26.7%	1	3.3%	9	19.717	0.001
	1	8	26.7%	3	10.0%	11		
	2	9	30.0%	9	30.0%	18		
	3	0	0.0%	12	40.0%	12		
	4	5	16.7%	5	16.7%	10		
Total	30	100.0%	30	100.0%	60			

The percentage of complete abortion in mifepristone and misoprostol group (GROUPA) was 90% while that in misoprostol group (GROUP B) was 83.3%. The difference between two groups was not statistically significant. The percentage of incomplete abortion in mifepristone and misoprostol group (GROUPA) was 3.3% while that in misoprostol group (GROUP B) was 6.7% which was not statistically significant. The percentage of failure in mifepristone and misoprostol group (GROUPA) was 6.7% while that in misoprostol group (GROUP B) was 10% which was not statistically significant.

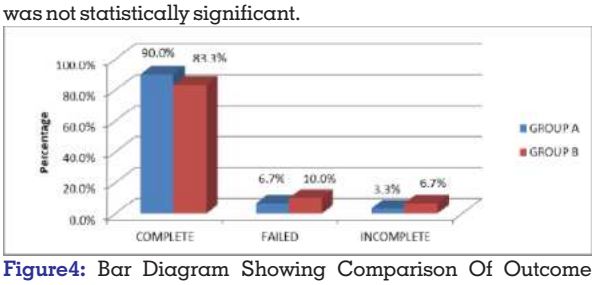

Figure4: Bar Diagram Showing Comparison Of Outcome Between Two Groups.

There was no statistically significant difference between side effects in two groups. Side effects were treated symptomatically and no major complications were found in both groups.

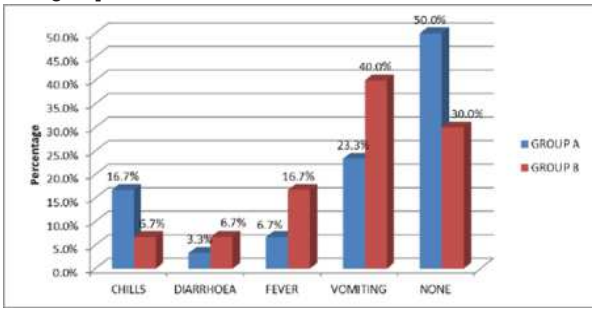

Figure 5: Bar Diagram Showing Comparison Of Incidence Of Side Effets Between Two Groups.

Mean cost for drugs in mifepristone and misoprostol group (GROUP A) was 516.33 rupee and 138.67 rupee in misoprostol group (GROUP B).The difference between two groups was statistically significant with p value of 0.001.

Table 2: Bar Diagram Showing Comparion Of Cost Of Drugs Used In Both Groups

	GROUP A		GROUP B		T	p-value
	Mean	SD	Mean	SD		
COST	516.33 rupee	80.95	138.67 Rupee	50.90	21.632	0.001

DISCUSSION:

The various medical methods of abortion for mid trimester have been proved to be safe and effective. Misoprostol alone although being used routinely for mid trimester termination has the disadvantage of long induction-abortion interval, more chances of incomplete abortion and high failure rate but, mifepristone and misoprostol combination has been found to be very effective with short induction-abortion interval and high success rate in spite of its high cost. The present study evaluated the method of mifepristone plus misoprostol and misoprostol alone for mid trimester termination of pregnancy by sublingual administration of misoprostol after loading dose of vaginal misoprostol.

The present study done was Prospective Interventional comparative study of 60 patients with gestational age between 14 weeks to 24 weeks admitted for mid trimester termination of pregnancy.

Abortion was complete in 90% (n=27) of cases in mifepristone and misoprostol group (GROUP A) and 83.3% (n=25) in misoprostol group (GROUP B) with failure rate being 6.7% (n=2) in GROUP A and 10% (n=3) in GROUP B, which is comparable to study done by PRASANNA LATHA AKKENAPALLY ET AL, JANE E DICKINSON ET AL, ROSE SB SHAND ET AT, OI SHAN TANG ET AL AND SANGEETA RAMAN JOGI E.

Abortion was incomplete in 3.3% (n=1) of cases in mifepristone and misoprostol group (GROUP A) , 6.7% (n=2) in misoprostol group(GROUP B).

Mean expulsion time was 6.19 hours in the mifepristone and misoprostol group (GROUPA) whereas 8.37hours in misoprostol group (GROUP B).It is statistically significant with p value of 0.014.this was comparable to study done by PRASANNA LATHA AKKENAPALLY ETAL,NGUYEN THI NHU NGOC ET AL, Rash ET AL.

In Present study, mean dose of misoprostol required was 1242.86 mcg in GROUP A and 1613.33 mcg in GROUP B which was comparable to study done was comparable to study done by PRASANNA LATHA AKKENPALLY ET ALAND JAN E DICKINSON ET AL.

CONCLUSION:

Comparing mifepristone plus misoprostol vs misoprostol alone in mid trimester termination of pregnancy, it was observed that

- Mifepristone and misoprostol combination group (GROUPA) has shorter expulsion time, higher success rate, and need for Number of repeat dose of misoprostol was reduced.
- Due to shorter expulsion time and increased success rate chances of sepsis, morbidity was reduced.
- Misoprostol alone group (GROUPB) is cost effective, hence still can be considered as alternative method.
- Drawback of GROUP A is anxiety or uneasiness associated for 24 hours following mifepristone administration.
- Side effects like vomiting, chills, diarrhea and fever were more in group B.
- The complete abortion rate, success rate and side effects are comparable in both groups.

Since study size is small, furthers studies in larger sample size is required before forming any definitive guidelines.

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