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Original Research Article

Efficacy and safety of mifepristone-misoprostol combination with extraamniotic ethacridine lactate-misoprostol for termination of second trimester pregnancy

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ABSTRACT

Background: Mid trimester termination of pregnancy is one of the most controversial areas of gynecological practice. It has moral, emotional, social and technical issues. This study was designed for comparison of efficacy and safety of Mifepristone-Misoprostol combination with exrtaamniotic Ethacridine Lactate-misoprostol for termination of second trimester pregnancy.
Methods: The present was undertaken among the patients admitted to hospitals attached to J.J.M. Medical College; Bapuji hospital, Women and Children hospital and Chigateri general hospital Davangere during the study period from November 2016 - October 2017. Patients coming for second trimester abortion to above mentioned hospitals were assigned serial number from 1 to 80 and all patients with even number will be allocated to group 1 and all patients with odd number will be allocated in group 2, each group comprising 40 women each.
Results: Majority of the cases in both the groups were between 21-25 yrs. Majority of the cases in both the groups were multigravidas. 11 cases from group 1 and 12 cases from group 2 were of gestational age between 14-16 wks. 29 cases from group 1 and 28 cases from group 2 were of gestational age between 18-20 wks. In the present study the mean induction abortion interval for group 1 was 19.56±1.82 hours and group 2 was 14.13±2.72 hours. This was statistically significant. Of the 40 cases in each group, 37 had complete abortion i.e. 92.5% 3 cases (7.5%) from both the groups had incomplete abortion. The side effects were relatively more in more in group 1 when compared to group 2.
Conclusions: It was concluded that with this combination success rate was high (92.5 %), with Short induction abortion interval, less rate of incomplete abortion without any major complications.

Keywords: Abortion rate, Ethacridine lactate, Induction-abortion interval, Mifepristone, Misoprostol, Side effects, Second trimester abortion

INTRODUCTION

Mid trimester termination of pregnancy is one of the most controversial areas of gynecological practice.[1,2] It has moral, emotional, social and technical issues.[1,2] Various surgical and medical methods have been tried for second trimester MTP with varying success and induction abortion interval.[3] Advances in fetal diagnosis has resulted in increased number of second trimester pregnancy terminations. It is debatable which method is safest, most effective and having least complications.[1,2]

A combination of Mifepristone, a progesterone antagonist, and Misoprostol, a synthetic prostaglandin

E1 analogue, is effective for medical abortion in second trimester. Pre-treatment with Mifepristone adds to the effectiveness of Misoprostol as an abortifacient.[3]

Cohen first described the use of Ethacridine lactate for second trimester abortion by extraamniotic route in 1946, since then it has been extensively used for midtrimester MTP.[4]

The optimal regimen is still under investigation but is required to be characterized by high abortion rate, short induction- abortion interval, low incidence of side effects, decreased surgical intervention and high acceptability.[5,6]

This study is therefore designed for comparison of efficacy and safety of Mifepristone-Misoprostol combination with exrtaamniotic Ethacridine Lactate-misoprostol for termination of second trimester pregnancy.

METHODS

The present was undertaken among the patients admitted to hospitals attached to J.J.M. Medical College; Bapuji hospital, Women and Children hospital and Chigateri general hospital Davangere. Patients admitted to the above-mentioned hospitals during the study period of 1 year from November 2016-October 2017 are included in the study. Permission for the study was obtained from the College authorities prior to commencement. Patients are randomized in two groups. Patients coming for second trimester abortion to above mentioned hospitals were assigned serial number from 1 to 80 and all patients with even number will be allocated to group 1 and all patients with odd number will be allocated in group 2, each group comprising 40 women each.

Inclusion criteria

- Healthy women aged between 21 to 35 years with singleton intrauterine pregnancy between 13 and 20 weeks of gestation admitted for termination of pregnancy.

Exclusion criteria

- Multiple pregnancies, grand multipara, Cardiac, renal and liver disease, scarred uterus, ruptured membranes, Placenta previa, Hemoglobin less than 8 g%, hemorrhagic disorders and treatment with anticoagulants, intolerance to misoprostol and ethacridine lactate.

Gestational age is determined from first day of last menstrual period (LMP), Pelvic and bimanual examination.[1,4] Urinary pregnancy test if done during early pregnancy.[1] Obstetric ultrasonography is done when date of LMP is not known or where LMP and clinical findings differ.[1,4]

Informed written consent will be obtained from each patient. Selected patients will be registered, detailed history noted, routine investigations will be sent, and gestational age confirmed.

Group 1: A single oral dose of Mifepristone 200mg given on admission after 12 hours 400µg of Misoprostol inserted vaginally and thereafter 400µg repeated every 4 hourly if no response for maximum of 5 doses. Vaginal examination done every 4 hours

Group 2: Extraamniotic ethacridine lactate 0.1% (10 ml per week of gestation to maximum of 150ml instilled using Foleys catheter, bulb inflated with 20ml of distal water) followed 6 hours later by intravaginal misoprostol 400µg repeated 4 hourly if no responses for maximum of 5 doses. Vaginal examination done every 4 hourly,

Foley's catheter removed after 24 hours if not expelled out spontaneously. Patient in each group will be explained regarding the dosage schedule, side effects like nausea/vomiting, diarrhea, headache, fever, chills, abdominal cramps and complications such as hyperstimulation, cervicovaginal tear, uterine rupture.

Pulse rate, blood pressure, uterine contraction will be noted every 4 hours.

- The induction-abortion interval is calculated as time taken from initial insertion of Mifepristone/ Ethacridine lactate to time when fetus and placenta aborted.[4]
- Complete abortion is defined as the expulsion of fetus and placenta without operative interventions.[4]
- If placenta appears complete, no further interventions will be undertaken.
- If placenta is incomplete or fails to get expelled, suction evacuation or check curettage will be done.[7]
- Those who did not expel fetus by 48 hours are considered failures.[1,4]

Statistical analysis

Results are presented as Mean±SD, and Range values for continuous data and Number and percentages for categorical data. Unpaired t test was used to compare the mean values between two groups. Chi-square test was used to analyses the categorical data. A P-value of 0.05 or less was considered for statistical significance. SPSS (version 16) software was used for all the analysis.

RESULTS

Majority of the cases in both the groups were between 21-25 yrs. The mean age was 24.7±4.0 years in group 1 and 25.8±4.4 years in group 2. Range in both the groups was 21-35 years. There was no significant statistical difference in the age distribution in both the groups (P=0.25) Table 1.

Table 1: Distribution of Cases according to their age.

Age group (years)		Group 1	Group 2	Total
21-25	No.	25	22	47
	%	62.5	55.0	58.8
26-30	No.	11	12	23
	%	27.5	30.0	28.8
31-35	No.	4	6	10
	%	10.0	15.0	12.5
Total	No.	40	40	80
	%	100	100	100
Mean age±SD (years)		24.7±4.0	25.8±4.4	-
Range		21-35 years	21-35 years	
Group 1 v/s Group 2		t = 1.17, P = 0.25, NS		
Unpaired t test, P >0.05, Not Sig.				

Table 2: Induction to abortion interval.

Induction-abortion interval (hours)		Group 1	Group 2	Total
<12 hours	No.	0	7	7
	%	0.0	17.5	8.8
12-18 hours	No.	5	28	33
	%	12.5	70.0	41.3
18-24 hours	No.	35	5	40
	%	87.5	12.5	50.0
Total	No.	40	40	80
	%	100	100	100
Mean age±SD (hours)		19.56±1.82	14.13±2.72	-
Range		16-23 Hours	9-21.5 hours	
Group 1 v/s Group 2		t = 10.50, p < 0.001, HS		
Unpaired t test				

Table 3. Side effects.

Side effects		Group 1	Group 2	Total
Abdominal cramps	No.	1	0	1
	%	2.5	0.0	1.3
Chills	No.	4	2	6
	%	10.0	5.0	7.5
Fever	No.	4	2	6
	%	10.0	5.0	7.5
Nil	No.	31	36	67
	%	77.5	90.0	83.8
Total	No.	40	40	80
	%	100	100	100

Majority of the cases in both the groups were multigravidas. In group 1 42.5% were primigravida and 57.5% were multigravida. In group 2, 30.0% were primigravida and 70.0% were multigravida. There was no statistically significant difference in the gestational age distribution between the two groups. Eleven cases from group 1 and 12 cases from group 2 were of gestational age between 14-16 wks. 29 cases from group 1 and 28 cases from group 2 were of gestational age between 18-20 weeks. In the present study the mean induction abortion interval for group 1 was 19.56±1.82 hours and group 2 was 14.13±2.72 hours. This was statistically significant. Table 2. Of the 40 cases in each group, 37 had complete abortion i.e. 92.5% 3 cases (7.5%) from both the groups had incomplete abortion and was supplemented with check curettage in both groups. The side effects were relatively more in more in group 1 when compared to group 2. Majority of the cases in group 2 did not have any side effects. Number of cases with side effects in group 1 was 9 and group 2 was 4. However, the

difference in side effects between the two groups is not statistically significant p=0.13 Table 3.

DISCUSSION

Mifepristone, a progesterone receptor antagonist is effective in shortening the induction abortion interval when used in combination with prostaglandins. Amongst the prostaglandin's misoprostol, a prostaglandin E1 analogue has been extensively used for induction of abortion in first and second trimester. There are many advantages in using misoprostol instead of other prostaglandins such as its low cost ,easy storage facilities. A wide variety of regimens are being used to effect second trimester pregnancy termination.

Ethacridine lactate for midtrimester abortion has a long history of use in our country and its safety has documented. There are no apparent contraindications for its use.

Its use alone has certain disadvantages like longer induction abortion interval, higher failure rate and more chances of incomplete abortion. However, by combining Ethacridine lactate with tab Misoprostol per vaginally these disadvantages has largely overcome leading to shorter induction abortion time and higher success rates in terms of complete abortion. Hence, this regime is now better alternative for termination the present study is done to compare efficacy and safety of mifepristone – misoprostol (group 1) combination with extraamniotic ethacridine lactate-misoprostol (group 2) for second trimester abortion.

Parity wise there was no statistical difference in the I-A interval between the two groups p=0.09 in group 1, and p= 0.27 in group 2

The induction abortion interval obtained in group 2 is comparable with other studies done by different authors on extraamniotic ethacridine lactate-misoprostol for second trimester termination and found to be shorter than other studies. The successful abortion rate in both the groups were same 92.5%. shown below. Side effects were relatively more in group 1 when compared to group 2. Majority of the cases in group 2 did not have any side effects i.e. 36 cases out of 40 did not have any side effects. Number of cases with side effects in group 1 was 9 and group 2 was 4

However, the difference in side effects between the two groups is not statistically significant p=0.13 (NS).

The cost incurred for procuring an abortion with Ethacridine lactate -misoprostol is less compared to mifepristone-misoprostol. Economic wise there is definitive advantage.

According to present study extraamniotic instillation of ethacridine lactate followed by vaginal misoprostol is effective method of termination of pregnancy with minimal side effects.

Table 4. Comparison of Induction abortion interval with other studies on extraamniotic ethacridine lactate-misoprostol for second trimester termination.

Authors	Extraamniotic ethacridine-vaginal misoprostol
Jyothi IS et al [2]	19.8±10.15 hours
Mamta G et al [8]	18.3±6.1 hours
Siddareddy Y et al [9]	16.44 hours
Present study	14.13±2.72 hours

Table 5. Comparison of complete abortion rate of present study with different studies.

Authors	Mifepristone-Misoprostol	Ethacridine-Misoprostol
Jyothi IS et al[2]	-	72%
Nagaria T et al[3]	95%	-
Nanda S et al[7]	90%	-
Mamta G et al[8]	-	83.33%
Siddareddy Y et al[9]	-	99%
Patil N et al[10]	100%	-
Present study	92.5 %	92.5%

CONCLUSION

The use of Misoprostol had synergistic effect with endogenous prostaglandin released due to stripping of membranes from extra-amniotic Ethacridine. With this combination success rate was high (92.5 %), with Short induction abortion interval, less rate of incomplete abortion without any major complications. The number of patients who aborted in 12-18 hours were many (70%) in the Ethacridine -misoprostol group than mifepristone -misoprostol group in which only few (12.5%) aborted. I-A Interval in Ethacridine-misoprostol group was 14.13±2.72hours. There was significant difference in Induction abortion interval between both groups, with p<0.001. There was no significant difference in Induction abortion interval in relation to Parity. There was no difference in complete abortion rate between the two groups. There were more side effects in group 1 compared to group 2 however it was not statistically significant p=0.13 (NS)

Thus, present study concludes ethacridine lactate instilled extra-amniotically followed by vaginal Misoprostol is effective, safer and with lesser side effects, acceptable, has short induction abortion interval than mifepristone – misoprostol for 2nd trimester termination of pregnancy.

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