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Study of a regimen of medical abortion for second trimester termination of pregnancy using mifepristone and misoprostol

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Abstract
Termination of pregnancy between 13-26 weeks constitutes about 10-15 % of all pregnancy terminations but is responsible for two third of all major complications and 50% of all abortion related maternal deaths This study assesses the efficacy of a newer regimen using oral mifepristone 200 mg followed by misoprostol 800 mcg per vaginum 12 hours and 24 hours later in two groups for second trimester pregnancy termination aiming to increase the acceptability and reduce the hospital stay. A total of 100 pregnant women willing for second trimester termination of pregnancy were assigned two groups according to time interval between administration of mifepristone and misoprostol. In group 1, misoprostol 800 mcg was administered per vaginum 12 hours after oral 200 mg mifepristone and in group 2, misoprostol 800 mcg was given after 24 hours of oral 200 mg mifepristone. Successful abortion occurred in 97% women in group1 and 98.8% women in group 2.The acceptability was found to be better in group 1. The proposed newer regimen has comparable efficacy and acceptability as the older regimen and requires lesser hospital stay which is a major concern for the females. At the same time it reduces hospital burden which stands more important for the developing country like India, where health care facilities are already scarce.

Keywords: mifepristone and misoprostol, pregnancy, medical abortion, second trimester termination

Introduction
There is a gradual increase in second-trimester abortion because of wide scale introduction of prenatal screening programs detecting women whose pregnancies are complicated by serious fetal abnormalities such as cardiovascular and skeletal malformation [3]. Termination of pregnancy between 13-26 weeks constitutes about 10-15 %of all pregnancy terminations but is responsible for two third of all major complications and 50% of all abortion related maternal deaths [4]. The incidence of complications increases with the increase in gestational age. The medical method recommended by the WHO and RCOG is the regimen of mifepristone followed by a prostaglandin analogue [5].

Aims and Objective
To assess the efficacy of a newer regimen using misoprostol 800 mcg per vaginum 12 hours vs 24 hours after oral mifepristone 200 mg for second trimester termination of pregnancy aiming to increase the acceptability and reduce the hospital stay.

Materials and Methods
The present prospective randomized study was carried out in the department of obstetrics & gynecology at Sri Krishna medical college and Hospital, Muzaffarpur, from 1st October 2015 to 30th April 2017. Necessary approval was obtained from the ethical committee of the hospital prior to commencement of study. The inclusion and exclusion criteria were defined before the onset of the study. Women who were eligible for the study were thoroughly counseled and informed written consents were taken.

Procedure
A total of 100 pregnant women wiling for second trimester termination of pregnancy were assigned 2 groups according to the time interval between administration of mifepristone and misoprostol.
In group 1, sample size 50 cases, misoprostol 800mcg is given per vaginum after 12 hours of oral mifepristone administration. In group 2, sample size 50 cases, misoprostol 800mcg is given per vaginum after 24 hours of oral mifepristone administration.

Observations and Results

Table 1: Age

	Group 1(n=50)	Group 2(n=50)
Mean Age (yrs)	26.76	27.38
SD	3.9515	2.7397
P value	0.3641	

Table 2: Outcome

Group	Successful	Failed
1(n=50)	47 (94%)	3(6%)
2(n=50)	46 (92%)	4 (8%)

Table 3: Mean I.A.I.

Group	Mean (hrs)	SD	P Value
1(n=50)	18.91	1.4593	P=<0.0001
2(n=50)	31.48	0.9311	

Table 4: Mean IAI (Hrs) According to Gestational Age

Group	(13-15) wks	(16-18) wks	(19-21) wks
1(n=50)	17.843	18.941	19.882
2(n=50)	31.138	31.304	32.611

Table 5: Side Effects

Side Effects	Group 1(N=50)	Group 2(N=50)	P value
Pain	50(100%)	50(100%)	0.9203
Fever	10(20%)	12(24%)	0.8092
Nausea	20(40%)	24(48%)	0.5456
Vomiting	18(36%)	20(40%)	0.8368
Diarrhoea	4(8%)	5(10%)	1.0000

Table 6: Distribution of Cases According to Blood Loss

	Group 1	Group 2	P value
MILD(<100 ml)	19	9	P=0.0450
MODERATE(100-200 ml)	29	39	P=0.0537
SEVERE(>200 ml)	2	2	P=0.6098

Table 7: Acceptability

Group	Acceptable	Unacceptable
1(n=50)	45 (90%)	44 (88%)
2(n=50)	5 (10%)	6 (12%)

Table 8: Mean Hospital Stay in Hours

Group	Mean (hrs)	SD	P value
1(n=50)	26.51	1.8557	P<0.0001
2(n=50)	40.67	2.5407	

Discussion

This study proposes a newer regimen for second trimester termination of pregnancy where reduced interval between mifepristone and misoprostol from 24 hrs to 12 hrs could reduce the total hospital stay and increase acceptability of the regime without compromising abortion rate and hence success rate.

Age

In the present study the mean age in group 1 was 26.76 and in group 2 it was 27.38. SD was 3.9515 and 2.7397 in group 1 and group 2 respectively. In the study of Chai *et al.* [8], mean age in immediate dosing group was 25.5 and that in conventional dosing group it was 25.1.

Outcome

In the present study, the complete abortion rate in group 1 is 94 % and in group 2 the rate was 92%. The difference in the success rate was not statistically significant (p value=1.0000). As the difference in the success rate was not statistically significant, the newer regimen where misoprostol was administered 12 hrs after mifepristone, could be considered equally effective as compared to other standard regimens. It did not alter the outcome in terms of complete abortion. In the present study the success rate with newer regimen was comparable to the success rates in previous studies and was associated with fewer side effects. The success rate in standard 36 - 48 hrs regimen studied by Guest *et al.* [13] was 96 % and that in one vs two day regimen studied by Nilas L *et al.* [11] was 98%.The difference in success rate here might be because of difference in sample size or different regimen of mifepristone and misoprostol used for second trimester termination of pregnancy. El-Refaey H *et al.* [9] found abortion was achieved in 97% [95% confidence interval (CI) 90-100%] of cases without resort to other prostaglandin agents when a combination of misoprostol and mifepristone was used.

Induction Abortion Interval (I A I)

Mean IAI: Mean induction abortion interval in the present study was 18.61 hrs with SD 1.4593 in group 1 and 31.48 hrs with SD. 9311 in group 2. P value was <.0001 which was statistically significant. The present study has found that the acceptability of the newer regimen was as good as that of previous standard regimens.

Mean Abortion Time: The mean abortion time after Misoprostol administration in group 1 was 6.91 hrs with SD 1.4593 and in group 2 it was 7.48 hrs with SD 0.9311**.** P value =0.0219 which is statistically significant. The abortion time significantly reduced with the newer regimen (12 hrs) without compromising the success rate. In this randomized study both 12hr and 24 hr intervals between mifepristone and misoprostol were suitable for clinical use in second trimester MTOP. But the induction-to abortion time in the 12 hr mifepristone-misoprostol administration interval groups were shorter. In group 1 it increased from 17.843 hrs in (13-15) wks to 19.882 in (19-21) wks. P value =0.0001 which was statistically significant. Similarly in group 2, it increased from 31.138 hrs in (13-15) wks to 32.611 hrs in (19-21) wks. P value was <0.0001 which was statistically significant.

Side Effects: Abdominal pain was the most common side effect seen in all patients (100%) in both the groups**.** Abdominal cramp usually developed after misoprostol administration. Other side effects observed were nausea, vomiting, fever and diarrhoea in both groups. Nausea was the second most common (40% in group 1 and 48% in group 2) side effect experienced followed by vomiting, fever and diarrhoea in both the groups. The present study shows that the differences in incidence of side effects in both the groups were not statistically significant.

Blood Loss: Majority of the patients in group 1 had moderate degree of blood loss which comprised of 58 % but 38 % of patients in group 1 had mild degree of blood loss as compared to only 18 % in group 2.P value was 0.0450 which was statistically significant. Maximum number of patients (78%) in group 2 had moderate degree of blood loss as compared to 58 % in group 1.P value was 0.0537 which was statistically significant. No blood transfusion was required in any of the two study groups. The proposed newer regimen was associated with lesser amount of blood loss as the interval between the administration of mifepristone and misoprostol was shorter.

Acceptability: The table shows distribution of cases on the

basis of acceptability of the two regimens**.** The 12 hr regimen in the present study was more acceptable (90%) than the 24 hr regimen (88%).Although the P value was not statistically significant (P=0.7124) (Table 25) but it may reach level of significance when larger study population is selected.

Hospital Stay: In the present study mean hospital stay in group 1 was 26.51 hrs with SD 1.8557 and in group 2 it was 40.57 hrs with SD 2.5407.P value was <0.0001 which was statistically significant (table 26). This new regimen for the administration of mifepristone and misoprostol for second trimester termination of pregnancy has the potential to minimize hospital visits, shorten the duration of procedure and reduce women's anxiety.

Conclusion

Based on observations and results it can be concluded that the newer proposed regimen of 12 hr interval between the administration of mifepristone and misoprostol for second trimester termination of pregnancy has the potential to minimize hospital visits, shorten the duration of procedure and reduce women's anxiety. It will further reduce the incidences and rate of unsafe and illegal abortions in developing countries where practice of unsafe and illegal abortions is high because of unawareness and limited resources. Reduced interval between Mifepristone and Misoprostol from 24 hrs to 12 hrs could reduce the total hospital stay and acceptability of the regimen without compromising the abortion rate and induction-abortion interval. Administration of Misoprostol 12hrs after administering Mifepristone is as effective as administering it 24 hrs later. It improves the acceptability of the regimen.

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