



COMPARISON OF EFFICACY OF MISOPROSTOL 4 HOURLY WITH MISOPROSTOL 6 HOURLY FOR MEDICAL TERMINATION OF PREGNANCY IN SECOND TRIMESTER.

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ABSTRACT: Termination of Pregnancy (TOP), in our country is carried out only when considerable danger to a fetus due to congenital abnormalities, intrauterine fetal loss or when maternal life is under threat. The principle concerns in providing second trimester termination include safety, efficacy, simplicity, low-cost, and fast acting with minimal side effects. **Objectives:** To compare the efficacy in term of complete abortion within 48 hours between protocol-I (200 µg misoprostol 4 hourly) versus protocol-II (200 µg misoprostol 6 hourly) for second trimester (14-24 weeks) medical termination of pregnancy. **Study Design:** Randomized controlled trial. **Settings:** Gynecology & obstetrics unit-II, Bahawal Victoria Hospital (BVH) Bahawalpur. **Period:** From 1st July 2017 to 30th June 2018. **Material & Method:** A total of 182 patients meeting the inclusion criteria were included in study. Ninety one patients were included in group-A and 91 patients were included in group-B. Women allocated to group-A was given misoprostol 200µg every 4 hour. Similar drug and dose were administered to women of group-B intra-vaginally, 6 hourly. Patients in both groups were monitored up to 48. If abortion occurred within 48 hours of induction, it was labeled as effective abortion otherwise it was regarded as failed abortion. **Results:** The mean age in group-A was 26.71 years 25.49 years in Group-B. In group-A, 89 (97.8%) patients showed efficacy (abortion within 48 hours) and in group-B, 74 (81.32%) patients showed efficacy to misoprostol. **Conclusion:** The regimen of using 200µg of vaginal misoprostol 4 hourly is more efficacious and quick for 2nd trimester TOP with fewer side effects when compared to 200µg of vaginal misoprostol 6 hourly.

Key words: Abortion, Efficacy, Medical Termination of Pregnancy, Misoprostol, Second Trimester

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INTRODUCTION

Globally, more than half of the pregnancies are not willingly achieved while around 20% end up being abortions. Termination of pregnancy (TOP) is quite common around the world.¹ Termination of Pregnancy (TOP), in our country is carried out only when considerable danger to a fetus due to congenital abnormalities, intrauterine fetal loss or when maternal life is under threat.²

Majority of TOPs take place within 13 weeks and 5-15% in the 2nd trimester. Usually, fetal reasons are revealed a bit late, TOP in the 2nd trimester is a topic of interest. Prostaglandins are usually used for TOP whereas some other options are available for 2nd trimester TOP. Heart failure is linked to intra-amniotic hypertonic saline infusion

along with heart failure and septic shock. Infections and uterine perforation are risked with evacuation and curettage. Cervical changes and uterine contractions are caused by misoprostol being a synthetic prostaglandin E1 analogue.^{3,4}

Prostaglandins have changed the traditional management approach for TOP in 2nd trimester. Before the availability of misoprostol, other prostaglandins such as prostaglandin E2 and prostaglandin F2 alpha (PGF2a) were mostly used for the termination of second trimester pregnancies. These agents are efficacious but expensive, require refrigeration and needed higher doses, and present higher numbers with fever, nausea, vomiting and diarrhea.^{5,6}

Many studies have documented results of misoprostol for 2nd trimester TOP since early 1990s. Misoprostol is inexpensive, no special storage for temperature required and has few systemic effects.⁷ In these days of financial constraints, misoprostol is an economical and effective abortifacient drug for second trimester pregnancy termination.^{8,9} Our aim was to compare the efficacy in term of complete abortion within 48 hours between protocol-I (200 µg misoprostol 4 hourly) versus protocol-II (200 µg misoprostol 6 hourly) for second trimester (14-24 weeks) medical TOP.

MATERIAL AND METHODS

This randomized controlled study was done gynecology & obstetrics unit-I of BVH Bahawalpur, from 1st July 2017 to 30th June 2018, using non probability consecutive sampling technique.

Sample size was calculated by taking level of confidence (α) = 5%, power of study (1- β) = 80%, anticipated population proportion P-I = 90.6%^{10,11}, anticipated population proportion P-II = 75%⁹, and sample size turned out 182 patients. Ninety one patients (group-A) were given 200 µg misoprostol 4 hourly and 91 patients (group-B) were given 200 µg misoprostol 6 hourly.

All those women were included who had age between 16-40 years, presented with ultrasonic conformation of fetal death during mid-trimester (i.e. from 14-24 weeks), missed abortion or with sever congenital malformation (e.g. anencephalic, gross hydrocephalus with meningocele etc) not compatible with life, with singleton pregnancy and all were up to para-3. Women with gestation <14 weeks and >24 weeks, having history of previous uterine surgery (scarred uterus), with multiple pregnancies (twins and high multiples), or para-4 or more were excluded from the study.

The study was approved from hospital ethical committee. The procedure was explained to each case and written permission for TOP was acquired. Group-A had misoprostol 200µg in posterior vaginal fornix every 4 hour (maximum 6 doses in 24 hours). Group-B had same drug & dose same way, 6 hourly (maximum of 4 doses in 24 hours).

Patients in both groups were monitored up to 48 hours after the start of induction with misoprostol. If abortion (expulsion of both fetus and placenta) occurred within 48 hours of induction, it was labeled as effective abortion otherwise it was regarded as failed abortion.

SPSS version-20 was used for data analysis. Efficacy was labeled in terms of abortion (expulsion of both fetus and placenta of 14-24 weeks) within 48 hours after start of induction, it was termed as effective if occurred within 48 hours otherwise it was labeled as failed. Efficacy of both groups was compared. Effect modifiers were controlled by stratification of data in term of age, and gestational age. Chi square test was applied to see the effect of these on outcome variables.

RESULTS

The mean age of patients in group-A was 26.71 years with standard deviation of 5.2 years. The minimum age of patients in Group-A was 17 years, maximum age of patients was 36 years. The mean age in group-B was 25.49 years with standard deviation of 5.1 years. The minimum age of patients was 17 years, maximum age 36 years. Amongst all patients, 73 patients were in 16-24 years of age group, 89 patients were in 25-32 years of age group and 20 patients were in 33-40 years.

In group-A, 33 patients of 16-24 years of age group showed efficacy (abortion within 48 hours), 43 patients in 25-32 years of age group showed efficacy (abortion within 48 hours) while 2 patients showed no efficacy (abortion within 48 hours) and 13 patients in 33-40 years of age group showed efficacy (abortion within 48 hours) with insignificant p value of 0.352.

In group-B, 33 patients of 16-24 years of age group showed efficacy (abortion within 48 hours) while 7 patients showed no efficacy (abortion within 48 hours), 36 patients in 25-32 years of age group showed efficacy (abortion within 48 hours) while 8 patients showed no efficacy (abortion within 48 hours) and 5 patients in 33-40 years of age group showed efficacy (abortion within 48 hours) while

2 patients showed no efficacy (abortion within 48 hours) with insignificant p value of 0.781.

In group-A 89 (97.8%) patients showed efficacy (abortion within 48 hours) to misoprostol while 2 (2.2%) showed no efficacy to misoprostol. In group-B, 74 (81.32%) patients showed efficacy (abortion within 48 hours) to misoprostol while 17 (18.68%) showed no efficacy to misoprostol.

In group-A, 44 patients were primigravida while 47 multigravida, and in group-B, 43 patients were in primigravida while 48 in multigravida with insignificant p value of 0.882.

In group-A, 44 patients of primigravida showed efficacy (abortion within 48 hours) and 45 patients of multigravida showed efficacy (abortion within 48 hours) while 2 patients showed no efficacy (abortion within 48 hours) with insignificant p value of 0.166.

In group-B, 36 patients of primigravida showed efficacy (abortion within 48 hours) while 7 patients showed no efficacy (abortion within 48 hours) and 38 patients of multigravida showed efficacy (abortion within 48 hours) while 10 patients showed no efficacy (abortion within 48 hours) with insignificant p value of 0.578.

Age Group of Patients	Efficacy (Abortion within 48 hours) in group-B		Total	P-Value
	Yes	No		
16-24 years of age group	33 82.5%	7 17.5%	40 100.0%	0.781
25-32 years of age group	36 81.8%	8 18.2%	44 100.0%	
33-40 years of age group	5 71.4%	2 28.6%	7 100.0%	
Total	74 81.3%	17 18.7%	91 100.0%	

Table-II. Comparison of efficacy (abortion within 48 hours) in different age groups in group-B (misoprostol 6 hourly).

Group of Patients	Efficacy (Abortion within 48 hours)		Total	P-Value
	Yes	No		
Group-A (misoprostol 4 hourly)	89 97.8%	2 2.2%	91 100.0%	<0.001
Group-B (misoprostol 6 hourly)	74 81.3%	17 18.7%	91 100.0%	
Total	163 89.6%	19 10.4%	182 100.0%	

Table-III. Comparison of efficacy (abortion within 48 hours) in different groups of patients

Age Group of Patients	Efficacy (Abortion within 48 hours) in group-A		Total	P-Value
	Yes	No		
16-24 years of age group	33 100.0%	0 0%	33 100.0%	0.352
25-32 years of age group	43 95.6%	2 4.4%	45 100.0%	
33-40 years of age group	13 100.0%	0 .0%	13 100.0%	
Total	89 97.8%	2 2.2%	91 100.0%	

Table-I. Comparison of efficacy (abortion within 48 hours) in different age groups in group-A (misoprostol 4 hourly)

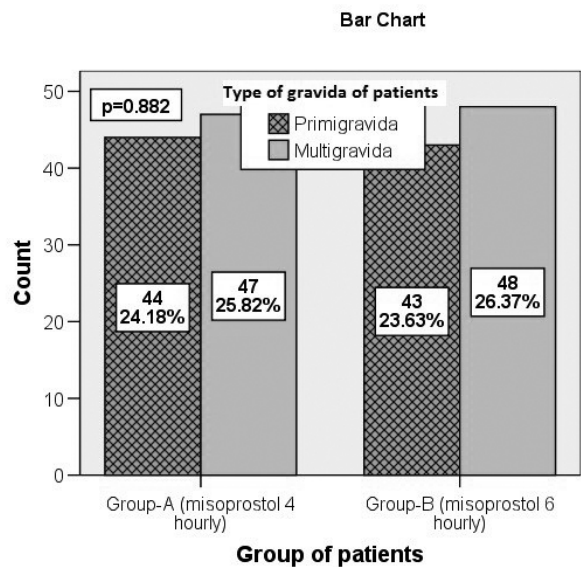


Figure-1. Frequency of primigravida and multigravida in patients of different groups

Gravida of Patients	Efficacy (Abortion within 48 hours) in group-A		Total	P-Value
	Yes	No		
Primigravida	44 100.0%	0 .0%	44 100.0%	0.166
Multigravida	45 95.7%	2 4.3%	47 100.0%	
Total	89 97.8%	2 2.2%	91 100.0%	

Table-IV. Comparison of efficacy (abortion within 48 hours) in patients of primigravida and multigravida in group-A (misoprostol 4 hourly)

Gravida of Patients	Efficacy (Abortion within 48 hours) in group-B		Total	P-Value
	Yes	No		
Primigravida	36 83.7%	7 16.3%	43 100.0%	0.578
Multigravida	38 79.2%	10 20.8%	48 100.0%	
Total	74 81.3%	17 18.7%	91 100.0%	

Table-V. Comparison of efficacy (abortion within 48 hours) in patients of primigravida and multigravida in group-B (misoprostol 6 hourly)

DISCUSSION

We found misoprostol effective and safe. In 1989, Leihair et al¹² initially noted the response of transvaginal misoprostol in the 2nd trimester. A bit later, effects of misoprostol in comparison to other PGs were then documented as effective by Baird et al.¹³

In our study, the efficacy in group-A was 97.8% and efficacy in group-B was 81.32%. This efficacy was comparable to other studies. A study conducted by Herabutya Y et al¹⁴ found 74% & 67% abortion rates respectively in similar groups within twenty four hours while 94% & 92% in forty eight hours. In Group-I, 53% women had fever in comparison to 31% in group-II (P<0.001). In a study conducted by Akhtar S et al¹⁵ found a shorter median induction to abortion time as 14.4 hours with vaginal misoprostol 400ug 4 hourly vs. 18.2 hours when compared to similar dose at 6 hourly (p<0.001). Although similar study noted significantly more women with fever in Group-1.

Both groups witnessed decrease in symptoms associated to pregnancy.

Ruangchainikhom W et al¹⁶ noted that 38% & 57% abortion in Group-I and Group-II respectively (p<0.05). Bhattacharyya and colleagues¹⁷ got no major disparity in time interval at 24 & 48 hours when they compared both regimens. Chaudhuri S et al¹⁸ compared women who were given vaginal misoprostol 400 ug, six hourly (maximum of four doses) with vaginal misoprostol 400 ug every 12 hourly (maximum of four doses). Statistically shorter interval difference was found both the groups (12.59 hours vs 16.41 hours respectively). More (57%) attained abortion in 12 hours in Group-I in comparison to only 26% in Group B. Similar findings were noted by Wong KS and coworkers but with 3 hourly vs 6 hourly regimens.¹⁹

Niroomanesh S et al²⁰ noted more than 80% eviction of conception products while no real difference was found in terms of hospital stay or side effects. Some other researchers also found misoprostol a good option for expulsion of conception products with less side effects.²¹⁻²³

We used a lower dose of misoprostol as compared to many previous studies and noted it to be effective. As the side effects of misoprostol are related to dose, lowest effective dose is advised. Comparison of vaginal misoprostol dosage regarding induction of labor at term has not been extensively evaluated and more studies are required.

CONCLUSION

The regimen of using 200µg of vaginal misoprostol 4 hourly is more efficacious and quick for 2nd trimester TOP with fewer side effects when compared to 200µg of vaginal misoprostol 6 hourly.

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A whole generation worked to **empower** women,
but forget to teach men how to live with **empowered** women.



“Unknown”

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Shamas un Nisa	Review of literature, Data analysis, Study concept.	
2	Farzana Razaq	Data collection, Discussion.	
3	Sadaf un Nisa	Drafting, Proof reading.	