International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Rashmi VR et al. Int J Reprod Contracept Obstet Gynecol. 2023 Sep;12(9):2730-2734
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20232729

Original Research Article

Comparative analysis of vaginal misoprostol 400 and 600 single dose for second-trimester termination of pregnancy- a prospective randomized trial

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Received: 04 July 2023
Accepted: 02 August 2023

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ABSTRACT

Background: This study was done to compare two dosing schedules of tablet misoprostol single dose 600 µg (M600) versus multiple doses 400 µg (M400), kept per vaginally for second termination of pregnancy and to analyze induction to abortion time, side effects, and failure to achieve termination of pregnancy.
Methods: Women admitted for second-trimester pregnancy termination were considered. Inclusion and exclusion criteria were followed. The women were randomized into two groups, with one group receiving single dose of M600 per vaginal and the other one multiple doses of M400, and the two groups were compared in their outcomes.
Results: In the present study no statistical significance was found between the two dosing regimens with regard to induction abortion interval, post-expulsion need for suction, and evacuation.
Conclusions: The study revealed that the dose between M400 and M600 has not shown significance compared with two dosing regimens. Single dose M600 can be considered for second-trimester pregnancy termination due to better compliance.

Keywords: Misoprostol, Multiple dose, Post-expulsion, Second-trimester, Single dose

INTRODUCTION

According to World Health organization (WHO), 73 million induced abortions take place each year across the world.[1] WHO declared abortion services as an essential health service in 2020. Access to safe abortion services is a necessity in today's world. Majority of the abortion occurs in first trimester. And most of the second trimester induced abortions are either due to failed contraception or congenital anomalies. Out of all the abortions that took place in the USA in 2008, 6.2% took place between 13 to 15 weeks of gestation and about 4.0% were at more than 16 weeks of gestation.[2] 15·6 million abortions (14·1 million 17·3 million) occurred in India in 2015 with a rate of 47.0 abortions per 1000 women was reported by Singh et al.[3] To offer safe abortion services to women all over the country, the Medical Termination of Pregnancy (MTP) Act was amended in India in 2021.[4] The most common methods used for second-trimester abortions in India include a combination of mifepristone and misoprostol, foley mechanical dilatation followed by misoprostol use, and extra amniotic saline infusion.[5] All these methods have their own advantages and disadvantages. The different dosing regimens of misoprostol have been rarely compared in their efficacies for second-trimester abortions and hence the novelty of this led to the need for this study in this part of Karnataka.

METHODS

It was a randomized trial conducted for a period of 1 year.

Inclusion criteria

Women getting admitted to Shri Dharmasthala Manjunatheshwara College of Science and Hospital, Dharwad for termination of pregnancy between 13-20 weeks of gestation with a uterine height between 12-24 weeks, regardless of parity were considered.

Exclusion criteria

Women with scarred uterus, women with incomplete miscarriage, Hypersensitivity to misoprostol, and women who don't consent to the study.

Failure criteria

If expulsion does not occur even after 24 hours of a single dose M600 or 5 doses of M400.

Patients were divided into two groups: group 1- receiving a single dose of M600. Group 2- receiving multiple doses of M400.

Sample size and sampling technique

A total of 80 patients were included by using simple random sampling technique.

Randomization method

A random number was chosen (N). Every N^{th} person received M400 4^{th} hourly for a maximum of up to 5 doses and the other group received M600 of a single dose.

Treatment protocol

Informed written consent was taken from enrolled patients for the present study. Study participants were divided into two groups, 50% of the participants were given M600, and another 50% with M400 in multiple doses (maximum up to 5 doses) by simple randomization. The outcome was recorded with primary outcomes like induction to abortion interval, need for blood and blood products, hysterotomy, and retained products of conception were studied and compared in both the groups and data will be analyzed.

RESULTS

Patient characteristics

The mean age in both groups was similar. In the M400 group mean age was 27.8 years and in the M600 group, it was 26.27 years. The majority of patients in the M600 group belonged to the below 25 years age group (50%) whereas most of the subjects in M400 group belonged to the 25-30 years age (37.5%) as represented in the Table 1.

Table 1: Age wise distribution.

Age	M400	Percentage	M600	Percentage	Total	Percentage
<25	13	33	20	50	33	41
25-30	15	38	13	33	28	35
>30	12	30	7	18	19	24
Mean age	27.8		26.27			
Standard deviation	5.79		5.57			

Table 2: Parity distribution.

Parity	M400	Percentage	M600	Percentage	Total	Percentage
Nulliparous	24	60	23	58	47	59
Multiparous	16	40	17	43	33	41

Table 3: Indication for termination.

Indication	M400	Percentage	M600	Percentage	Total	Percentage
Anomaly	27	68	31	78	58	73
failed contraception	7	18	5	13	12	15
maternal indication	5	13	1	3	6	8
Anhydramnios	1	3	3	8	4	5

Table 4: Induction abortion interval.

I-A interval	M400	M600	P value
Mean	7.46	9.42	0.769698
Standard deviation	3.39	4.69	Not significant at p<0.05

Parity distribution

Of the total sample size, majority of the cases were of nulliparous women (58.75%) versus 41.25% of the women who were multiparous. There was no significant difference between the parity distribution in the two groups observed.

Indication for termination

A total of 73% of all the terminations in the study were due to anomalous fetus. The anomalies ranged from complex cardiac anomalies to neural tube defects to raised nuchal translucency (NT). Failed contraception was the second most common cause for termination in the study with 15%. 8% of the patients had pregnancy termination due to maternal comorbidities like idiopathic thrombocytopenic purpura (ITP) and severe pulmonary artery hypertension (PAH) (Table 3).

Induction abortion interval

The mean duration in M400 group was 7.4 hours and the mean induction to abortion interval in M600 group was 9.4 hours (excluding the failure cases).

Induction abortion interval and parity

The mean induction to abortion interval was 7 hours and 8 hours in primigravidae and multigravidas respectively in the M400 group. Whereas the average induction to abortion interval was 9 hours and 10 hours respectively in primigravidae and multigravidae respectively in the M600 group. These findings were statistically insignificant.

Table 5: Induction abortion interval in hours and parity.

Mean I-A interval	M400	M600	P value
Primi	7hours	9 hours	0.729797 Not significant at p<0.05
Multi	8 hours	10 hours	

Induction abortion interval and gestational age

The mean induction to expulsion interval in the M400 group for gestational age <17 weeks was 7.5 hours whereas >17 weeks. was 7.3 hours whereas in the M600 group was 8 and 10.4 respectively. There was no statistically significant difference between the two groups.

Table 6: Induction abortion interval and gestational age.

I-A interval	Mean duration in hours		P value
	M400	M600	
>17 weeks	7.3	10.4	0.61093 not significant at p<0.05
<17 weeks	7.5	8	

Table 7: Parity versus indication for termination.

Condition	Nulliparous	Multiparous	Total	P value
Anomaly	32	20	52	0.316553 Not significant p<0.05
Failed contraception	03	09	12	

Table 8: Comparison between the two groups in the time from first dose to expulsion.

I-A interval	M400	%	M600	%	P value
<6 hours	14	35	6	15	0.097942. Not significant at p<0.05.
6-12 hours	20	50	21	21	
>12 hours	6	15	11	11	

Table 9: Expulsion rate at induction abortion at intervals of 6 hours.

Miso to expulsion	M400	M400	M600	M600	P value
<6 hours	14	35%	6	15%	0.038867. Significant at p<0.05.
>6 hours	26	65%	34	85%	

Table 10: Comparison between the two groups suction evacuation.

Suction evacuation	M400	Percent	M600	Percent	P value
Required	13	32.5	18	145	0.251193 Not significant at p<0.05
Not required	27	67.5	22	55	

Parity versus indication for termination

In both nulliparous and multiparous women, the most common cause for pregnancy termination was an anomaly in the fetus while a higher number of patients terminated pregnancy for failed contraception in a multiparous group.

Comparison between the two groups in the time from first dose to expulsion

At less than 6 hours I-A interval, 35% in the M400 group and 15% in the M600 group underwent expulsion. A total of 50% and 21% were expelled in the M400 and M600 groups respectively between 6 to 12 hours and 15% and 11% were expelled beyond 12 hours in either group after 12 hours. This was not statistically significant.

When the I-A cut-off was taken to be six hours, 35% of the M400 group and only 15% of the M600 group were expelled completely. This was statistically significant at p value <0.05

Comparison between the two groups with respect to need for additional procedures for complete expulsion (suction evacuation)

Although statistically not significant, additional procedures like suction evacuation were required in around 33% of cases in M400 group and about 45% in the M600 group.

DISCUSSION

The ideal dosing schedule for second-trimester pregnancy termination is under appraisal the world over. Although routinely used, misoprostol also has certain disadvantages such as a higher induction-abortion interval, higher failure rates, and requirement of additional procedures for complete abortion. Mifepristone as an add-on has been used which has proven to have better success rates but the higher cost is of concern in developing countries.

The present study evaluated two dosing schedules of per vaginal misoprostol and the effectiveness of each schedule in causing a complete abortion in the second trimester. The present study was a randomized trial of 80 patients admitted at a tertiary care hospital for termination of pregnancy in the second trimester. Group 1 (40 patients) received M400 every fourth hour for a maximum of five doses and group 2 (40 patients) received a single dose of M600.

Age

In the present study the average age in the M600 group was 26.27 years with a range of 47-19 years whereas the average age in the M400 group was 27.82 years with a range of 42-19 years. This was slightly higher than the mean ages in the study reported by Carbonell et al where the mean age was 23.3±7.5 in the M600 group and 21.7±6.4 in the M400 group.[6] A study carried out by Dickinson, the mean age in the M600 group was 29.3 years and in the M400 group was 29.7 years.[7]

There was no significant difference between the age distribution in the two groups similar results reported study conducted by Carbonell et al and Bhattacharya et al.[7,8]

Parity

58.25% of the women in the study were nulliparous while 41.25% were multiparous. There was no statistical significance between the parity-wise distribution in the two groups. This finding was consistent with the results in the studies conducted by Carbonell et al, Bhattacharya et al, Ruangchainikhom et al.[6,8,9]

Indication for termination

The most common indication for termination in the study was a fetal anomaly (72.45%), followed by failed contraception at 15%. The other indications for termination of pregnancy were maternal indications including 1 case each of severe mitral stenosis, severe PAH, maternal ITP, dilated cardiomyopathy, and 4 cases of anhydramnios. 68.08% of the indications for termination in nulliparous women was anomalous fetus whereas only 60.6% of the terminations in the multiparous women were because of fetal anomalies. This finding was not statistically significant. 6.3% of the nulliparous women terminated. pregnancy in view of failed contraception whereas 27.27% of the multiparous women terminated because of failed contraception.

Induction-abortion interval

The average time to expulsion in the M600 group was 9.42 hours (excluding the failure cases) whereas it was 7.48 hours in the M400 group which was not statistically significant. These values were considerably lower than the durations in the study conducted by Herabutya et al, where the average duration of expulsion was 15.2 hours in the M600 group, and the studies conducted by Tang et al and Dickinson, where the average duration in the M400 group is 10.5 hours and 15.1 hours respectively.[10-12] The induction-abortion intervals was longer in multiparous women as compared to nulliparous women which was in contrast to other studies where multiparous women had shorter induction-abortion interval. In our study, with increasing gestational age the I-A interval was prolonged in M600 group but this was not statistically significant. While comparing the time from first dose of misoprostol to the time of expulsion, it was found that 35% of the patients in the M400 group underwent expulsion in less than 6 hours as compared to only 15% in the M600 group. The success rates at less than 6 hours were statistically

significant. However, final success rate at 24 hours was 100% in the M400 group but it was 95% in the M600 group. 45% of the women in the M600 group required suction evacuation post-expulsion whereas only 32.5% of the women in the M400 group required suction and evacuation. But this was statistically insignificant.

CONCLUSION

Second-trimester abortions two regimens of misoprostol dosing can be used i.e. multiple doses of M400 and a single dosage of M600. Multiple studies have shown better efficacy of a single dosage of M600 over multiple dosages of M400 with respect to shorter induction to abortion interval and the need for post-expulsion suction and evacuation. This study did not find a significant difference between the two dosing regimens and hence this study concluded that both the dosing regimens are equally efficient and hence recommends a single dosage regimen of M600 as the compliance will be better as it avoids multiple pervaginal examinations.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Rashmi VR, Jai A, Neha GY, Sunil Kumar KS. Comparative analysis of vaginal misoprostol 400 and 600 single dose for second-trimester termination of pregnancy- a prospective randomized trial. Int J Reprod Contracept Obstet Gynecol 2023;12:2730-4.