



## Role of misoprostol 4 hourly versus 6 hourly in medical termination of pregnancy in 2<sup>nd</sup> trimester.

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**ABSTRACT... Objective:** To determine efficacy of misoprostol given in 4 hourly versus 6 hourly intervals in second trimester for termination of pregnancy. **Study Design:** Cross sectional study. **Setting:** Study was conducted at the department of Obstetrics and Gynecology of Jinnah Medical and Dental College Karachi. **Period:** March to August 2020. **Material & Methods:** Pregnant ladies in second trimester, requiring abortion due to medical reasons, were planned for termination of pregnancy. Two groups were made. Patients in Group-A were given misoprostol 4 hourly and those in Group-B were given misoprostol 6 hourly. Similar dose of drug (200ug) was given in both groups and monitoring was done. If abortion done in 48 hours, it was considered effective abortion and if not happened in 48 hours, it was considered a failed abortion. Consent was taken from all ladies in study group. Ethical approval was taken from ethical review committee. **Results:** Total 140 cases were studied, 70 cases in each group, A & B. Age range of cases was 16-40 years with mean age of 26.4±3.5 years. Most of the cases were having age between 20-30 years (63.5%). Group-A (N=70) was given misoprostol 4 hourly, where abortion was done in 94.3% cases while abortion failed in 5.7% cases. In Group-B (N=70) misoprostol was given 6 hourly, induced abortion in 82.8% and failed in 17.1% cases. **Conclusion:** Misoprostol dose of 20ug given via vaginal route is much effective drug for medical termination of pregnancy when given 4 hourly instead 6 hourly, with low failure rate.

**Key words:** Abortion, Misoprostol, Second Trimester, Termination of Pregnancy.

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## INTRODUCTION

All over the world annually 20% pregnancies end up in abortions.<sup>1</sup> Planned abortions are very common globally. Causes may be will of the parents, unintentional pregnancy or medically indicated. In our country abortions are carried out in government hospitals only when it is medically required and it is harmful to mother health.<sup>2</sup> Misoprostol has been approved by FDA for the treatment of gastric ulcers taken orally. Due to its uterotonic and cervical ripening actions it is also used for medical termination of pregnancies. It is used for evacuation of uterus in case of fetal death and also used for induction of labor. It can be used to treat or prevent post-partum hemorrhage. Most of the time medical termination of pregnancy (TOP) is done in first trimester while in 5-15% cases in second trimester.<sup>3</sup> In our study TOP is related to second trimester of pregnancy. There are

surgical and medical methods for abortions. But here we are concerned with only medical method. Prostaglandins are commonly used for TOP, while other drugs are also available for this purpose.<sup>4</sup> Intra amniotic hypertonic saline injection causes heart failure and fetal death. Uterine evacuation and curettage is associated with infection and uterine perforation. Misoprostol is a synthetic E1 prostaglandin and induce uterine contraction and cervical changes.<sup>5</sup> It is commonly used in second trimester for TOP. When misoprostol was not introduced, prostaglandins E2 and F2 alpha were usually used for medical TOP in 2<sup>nd</sup> trimester. Prostaglandins E2 and F2 alpha are costly, used in high doses, require refrigeration to store them and are associated with high rate of complications like nausea, vomiting, diarrhea and fever.<sup>6</sup> Misoprostol have been in use for TOP in 2<sup>nd</sup> trimester of pregnancy since 1990s.

It is cost effective, easy to use, easy to store, no refrigeration required and minimum side effects reported.<sup>7,8</sup>

Misoprostol is used orally and vaginally. Vaginal route has been reported more effective in inducing abortion. According to a study rate of abortion via vaginal route is 90% as compared to oral route 69%.<sup>9</sup> Few studies also recommend its use via sublingual route, with maximum efficacy.<sup>10</sup> Misoprostol is stable at room temperature and is effective with or without mifepristone. Mifepristone is expensive and not available in some developing countries.<sup>11</sup> Few studies reported that misoprostol in combination with mifepristone has great efficacy with short induction period.<sup>12</sup> Previously many studies have been done on the use of misoprostol for TOP in first trimester, but there is very little data available regarding its efficacy in second trimester of pregnancy. Hence this study was conducted to determine efficacy of misoprostol when used alone via vaginal route in second trimester for termination of pregnancy.

## MATERIAL & METHODS

This cross sectional study was conducted at Obstetrics and Gynaecology Department, Jinnah Medical and Dental College, Karachi from March to August 2020. Pregnant ladies in second trimester of pregnancy admitted in Obstetrics and Gynecology department of Jinnah Medical and Dental College Karachi, in which medical termination of pregnancy was indicated for the sake of health issues of mothers like hypertension, diabetes mellitus or due to fetal death, missed abortion, congenital malformation of fetus, anencephaly or hydrocephalus with meningocele not likely to survive were included in this study. After taking proper history obstetrical examination was done. History of drug allergy was taken in detailed. Those cases in first or third trimester of pregnancy, or where surgical abortion was indicated, having abnormal placenta position, fetal macrosomia, or had previous uterine surgery now having scarred uterus, with multiple pregnancies or para-4 or more were excluded from the study. Cases were divided into two groups. Cases in group-A were given misoprostol 4 hourly, while those in group-B were given misoprostol 6

hourly. Misoprostol 200ug was given via vaginal route. Effect of the drug was monitored for 48 hours. Induction of abortion within 48 hours was labelled as effectiveness of the drug otherwise it was considered as failure of the drug. Cases were monitored for any complication of the drug like nausea, vomiting, fever or abdominal pain, tenderness denoting uterine rupture. Data collected was analyzed using SPSS-20. Sample size was calculated using WHO sample size calculator. Non-probability consecutive sampling technique was used for selection of study sample. Chi square test was applied on the data. Results were displayed in tabular and graphical form. Consent was taken from all women in study sample and ethical approval was also taken from ethical committee of the study hospital. (IRB0389)

## RESULTS

Total 140 cases were included in the study, which were divided into two equal groups with 70 cases in each, Group-A and Group-B. Cases in group A were given misoprostol 4 hourly for induction of abortion. Age range of cases was 16-40 years with mean age of  $26.4 \pm 3.5$  years. Most of the cases were between 20- 30 years of age. Abortion was induced in 66(94.3%) cases while failure was reported in 4(5.7%) cases. Mean time for induction of labor was  $12.3 \pm 2.7$  hours and mean gestational age was  $19.52 \pm 4.6$  weeks in both group-A and group-B.

Age Groups	Total Cases (N=70)	Abortion within 48 hours		P-Value
		Yes	No	
16-20	08 (11.4%)	08 (11.4%)	00 (00%)	0.413
21-25	20 (28.6%)	19 (27.1%)	01 (1.4%)	
26-30	25 (35.7%)	23 (32.8%)	02 (2.8%)	
31-35	12 (17.1%)	11 (15.7%)	01 (1.4%)	
>35	05 (7.1%)	05 (7.1%)	00 (00%)	
Total	70 (100%)	66 (94.3%)	04 (5.7%)	

**Table-I. Efficacy of Misoprostol in Group-A relative to various age groups.**

In Group-B 70 cases were included, mostly (37.1%) between 26-30 years. Misoprostol was given 6 hourly to these cases via vaginal route. Successful abortion was reported in 58 (82.8%)

while failure reported in 12 (17.1%) cases. Those showing drug failure were mostly between 20-30 years of age while cases with <20 years and >30 years of age showed good response.

Age Groups	Total Cases (N=70)	Abortion within 48 hours		P-Value
		Yes	No	
16-20	12 (17.1%)	10 (14.3%)	02 (2.8%)	0.426
21-25	18 (25.7%)	15 (21.4%)	03 (4.3%)	
26-30	26 (37.1%)	22 (31.4%)	04 (5.7%)	
31-35	10 (14.3%)	08 (11.4%)	02 (2.8%)	
>35	04 (5.7%)	03 (4.3%)	01 (1.4%)	
Total	70 (100%)	58 (82.8%)	12 (17.1%)	

**Table-II Efficacy of Misoprostol in Group-B relative to various age groups.**

In our study sample there were 59 (42.1%) primigravida and 81 (57.9%) multigravida cases. In group-A out of 33() primigravida misoprostol showed efficacy in 32() cases while failure reported in one case only. While out of 37 multigravida cases failure was reported in 03(8%) cases.

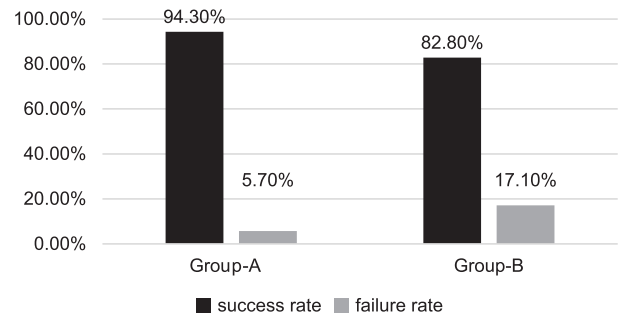
Gravida of Women	Efficacy of the drug within 48 hrs		Total Cases	P-Value
	Yes	No		
Primigravida	32 (97%)	01 (3%)	33	0.538
Multigravida	34 (92%)	03 (8%)	37	

**Table-III. Comparison of efficacy of the drug among primigravida and multigravida in Group-A.**

In group-B out of 70 cases, 26(37.2%) were primigravida and 44(62.8%) were multigravida cases. In 88.5% primigravida and in 79.5% multigravida cases abortion happened while failure rate was 11.5% and 20.5% respectively in primigravida and multigravida cases in this group.

Gravida of Women	Efficacy of the drug within 48 hrs		Total Cases	P-Value
	Yes	No		
Primigravida	23 (88.5%)	03 (11.5%)	26	0.326
Multigravida	35 (79.5%)	09 (20.5%)	44	

**Table-IV. Comparison of efficacy of the drug among primigravida and multigravida in Group-B.**



**Figure-1. Comparison of misoprostol efficacy in both Group-A and Group-B.**

**DISCUSSION**

Misoprostol is an effective drug and safe while given trans-vaginally for inducing medical termination of pregnancy in second trimester of pregnancy.<sup>13</sup> A study conducted in Nishtar Hospital Multan by Ashraf S et al on efficacy of misoprostol given vaginally and judged within 72 hours of induction of labor. They reported success rate of 84.8% and failure rate of 15.1%.<sup>14</sup> These results are comparable to our study where we found success rate of 88.6% and failure rate of 11.4%. Bansal et al reported mean induction time of labor 10.7 ± 2.2 hours after giving misoprostol vaginally.<sup>15</sup> This is similar to mean induction time of 12.3±2.7 hours in our study. In their study mean age of patients was 24.56 ± 4.21 years and mean gestational age was 17.21 ± 3.22 weeks. This is comparable to our study where mean age of patients was 26.4±3.5 years and mean gestational age was 19.52±4.6 weeks. A study conducted by Karande et al reported 100% success rate of intra vaginal misoprostol in second trimester. In their study primigravida were 23.3% and multigravida 76.7%.<sup>16</sup> In our study 42.1% were primigravida and 57.8% were multigravida women. This difference may be due to cultural and social differences as in our community mostly females marry in young age and due to unavailability of proper maternal healthcare services in periphery they experience many complications during first pregnancy and many times abortion is indicated due to negligence of mother and their caretakers. A similar study was conducted in India by Kusumam et al, they included 43.6% primigavida and 56.4% multigravida mothers, mean gestational age was 18.6 weeks, success rate was 78.3% and failure rate was 21.7% and mean induction abortion

interval was 14.64 hours, similar to our study results.<sup>17</sup> Previously a local study conducted in Bahawalpur (a city of Pakistan) reported success rate of 97.8% and failure rate of 2.2% among cases using misoprostol 4 hourly per vaginally, as compared to those using 6 hourly with success rate of 81.3% and failure rate of 18.7%.<sup>18</sup>

In early pregnancy failure misoprostol is used to evacuate uterus for dead fetus components. A study conducted in Netherland reported efficacy of misoprostol in complete evacuation rate of about 50% in such cases.<sup>19</sup> In case of abortion If women do not evacuate spontaneously dead fetus immediately, medical or surgical methods are required for uterine evacuation. Surgical methods are associated with many complications, hence medical termination of pregnancy (TOP) is used. American College of Obstetricians and Gynecologists recommend medical method as safe, for TOP.<sup>20</sup> In this study we used lower dose of misoprostol as compared to previous studies for TOP, and we observed good results. Misoprostol has dose related side effects, hence lowest effective dose causes minimum side effects. Previous literature is mostly about oral efficacy of misoprostol and very little data is present about its per-vaginal use, that's why more studies are required in this aspect.

## CONCLUSION

Medical termination of pregnancy within 48 hours in second trimester using minimum effective dose of misoprostol 200ug given via vaginal route with 4 hourly intervals has been proved much effective with minimum side effects and low failure rate as compared to misoprostol given with 6 hourly intervals associated with relatively higher failure rate.






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No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
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2	Shazia Aftab	Topic selection and data collection, Abstract and recording.	
3	Reena	Data collection, Found additional literature for information.	
4	Huma Baloch	Data collection.	
5	Devi Kumari	Data collection, Data analysis.	
6	Samina Ayaz	Data analysis, Drafting and composing.	