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Original Research Article

Comparative study of combination of misoprostol with Foley's bulb compared with misoprostol alone for termination of second trimester pregnancy

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ABSTRACT

Background: Second trimester abortion is termination of pregnancy in a period from 13 to 28 weeks of gestation. Second trimester losses may be due to maternal factors such as uterine malformation, growths in the uterus (fibroids), or cervical problems. These conditions also may contribute to premature birth. Aims and objectives were to compare the efficacy, safety and suitability of combination of misoprostol with intracervical Foley's catheter v/s misoprostol alone for termination of second trimester pregnancy.
Methods: This randomized controlled trial study was conducted on 100 study subjects who passed our inclusion and exclusion criteria. Group A: received misoprostol with intracervical Foley's catheter. Group B: received misoprostol alone. The groups were compared with respect to the patients' characteristics, gestational age, indication for termination of pregnancy, rate of complications, etc.
Results: Mean value of age (years) of study subjects was 27.12±4.5. Mean induction to delivery time (hours) in P0 was 17.73±6.46 and in P1-P2 was 14.78±4.9 which was significantly higher as compared to ≥P3 (11.46±3.82). (p=0.0004). Mean induction to delivery time (hours) in 14 to 18 weeks was 15.25±5.4 and >18 weeks was 15.02±5.84. (p=0.854). Distribution of side effect between group A and B. (6% vs 20% respectively) (p=0.041).
Conclusions: We conclude that intracervical Foley catheter and vaginal misoprostol is a safe and effective method for second trimester abortion as compared to misoprostol alone group with no additional risks.

Keywords: Foley's catheter, Misoprostol, Second trimester, Mifepristone, Cerviprime gel

INTRODUCTION

Second trimester abortion is termination of pregnancy in a period from 13 to 28 weeks of gestation, which again is subdivided into early period between 13 and 20 weeks and late period between 20 and 28 weeks.[1,2]

Abortion-related complications account for approximately 13% of maternal deaths worldwide, roughly estimated as 47000 deaths per year. Second trimester abortion carries a higher risk of morbidity and mortality as compared to the first trimester abortion specially in the developing countries.[3]

Nowadays due to widespread use of antenatal screening techniques in detecting pregnancies complicated by serious central nervous system and skeletal malformations, genetic abnormalities, there is gradual increase in second trimester termination of pregnancies.[4]

A miscarriage in the second trimester is a pregnancy loss that happens specifically between 13 to 20 weeks of gestation. Second trimester losses may be due to maternal factors such as uterine malformation, growths in the uterus (fibroids), or cervical problems. These conditions also may contribute to premature birth. Unlike first-trimester miscarriages, second-trimester miscarriages are less likely

to be caused by a genetic abnormality; chromosomal aberrations are found in a third of cases.[3]

A miscarriage can result in anxiety, depression, stress and many of those experiencing a miscarriage go through a grieving process. Second-trimester abortion is associated with more morbidity and mortality and, for some women, more social or emotional challenges than first-trimester abortion.[5]

Comprehensive abortion care (CAC), a term "rooted in the belief that women must be able to access high-quality, affordable abortion care in the communities where they live and work", was first introduced in India by Ipas in 2000.[6] The concept of Comprehensive abortion care encompasses care through the entire period from conception to post abortion care and also includes pain management. It is suggested that induction delivery interval has significant psychosocial impact on women and also affects maternal morbidity that's why this study is being done to compare the efficacy of different methods of termination of pregnancy so as to choose the optimal method of termination.[3]

Second-trimester pregnancy termination may be performed with medication or surgery. There are various methods available for second trimester termination of pregnancy.[3]

Medical methods

Medical methods included-1. Mifepristone and misoprostol; 2. Extraovular instillation of drugs like ethacridine lactate, hypertonic saline and prostaglandins; 3. Intracervical or extraovular instillation of cerviprime gel.

Mechanical method

Mechanical methods included Foley catheter.

Surgical methods

Surgical methods included 1. Dilatation and evacuation and 2. Aspirotomy

Surgical methods have more morbidity, may be complicated by incomplete evacuations, uterine perforation and cervical trauma, therefore the medical methods seem to be better alternative to surgical methods.[3] The most efficacious regimen for second trimester termination was combination of mifepristone followed by misoprostol. This regimen had 97 to 99 percentages success rate of abortion within 24 hours.[7] However, mifepristone shows a plethora of side effects such as abdominal cramping, back pain, allergic reactions, excessive uterine bleeding etc.[8] so misoprostol is being tried in combination with other methods of abortion like mechanical methods.

In countries where mifepristone is not available or affordable gemeprostol or misoprostol alone have shown to be effective, although a higher total dose is needed and is less effective than the combined regimens.[9] Misoprostol is a fabricated analog of prostaglandin E1, which was developed as a gastro cytoprotective agent.[10] It can be used by sublingual, vaginal, oral, buccal or rectal route. Cervical ripening and vaginal delivery rate improve significantly within 24 hours via the vaginal route.[11] It is used widely for labor induction, abortion and prevention and treatment of postpartum hemorrhage. It binds to myometrial cells to cause strong myometrial contractions leading to expulsion of tissue.[12]

It has been proposed and researched that combined use of intracervical Foley's catheter and vaginal misoprostol is a novel safe, effective and acceptable method for termination of second trimester pregnancy.[8]

Aim and objectives

The aim and objectives were to compare the efficacy, safety and suitability of combination of misoprostol with intracervical Foley's catheter v/s misoprostol alone for termination of second trimester pregnancy.

METHODS

After getting approval from our institutional ethical committee, this randomized controlled trial study was conducted in department of obstetrics and gynaecology from 1st Jan 2021 to 31st June 2021 at PDRMC, RNT medical college, Udaipur on 100 study subjects who passed our inclusion and exclusion criteria.

Block randomization

Block randomization with sealed envelope system: In this, we prepared ten randomly generated treatment allocations within sealed opaque envelopes assigning A and B in 5 envelopes each, where A represents misoprostol and Foleys combination group and B represents misoprostol group. Once a patient consented to enter a trial an envelope was opened and the patient was then offered the allocated group. In this technique, patients were randomized in a series of blocks of ten.

Two groups included-Group A: received misoprostol with intracervical Foley's catheter as well as the group B: received misoprostol alone.

Inclusion criteria

Pregnant women who need termination between 14 to 24 weeks were included. Gestational age is calculated from the date of the first day of last menstrual period and confirmed by ultrasonography. Who fulfills the indications defined in the MTP act and who have given informed written consent to participate in the study.

Exclusion criteria

Patients who have contraindication to misoprostol, coagulation disorder, disseminated intravascular coagulopathy, chorioamnionitis and vaginal infections were excluded from the study.[10]

METHODS

Hundred pregnant women attending the OPD for second trimester MTP who fulfill the inclusion and exclusion criteria were selected for the study. Ultrasound examination was used for the gestational age confirmation and their eligibility. Selected patients were advised to admit in labour ward and to stay in hospital till pregnancy was terminated. Complete evaluation of each patient was done at the time of admission. Detailed history as well as findings on medical and obstetric examination was recorded.

In the group A, after taking informed and written consent, under all aseptic measures Foley's catheter (14-16 Fr) was introduced through cervix to the extra-amniotic space and balloon was inflated with 30 ml normal saline. At the same sitting 200 µg misoprostol was kept in posterior fornix and the dose was repeated every 6th hourly till the catheter got expelled out or till maximum five doses.

In the group B only misoprostol (200-400 micrograms) was kept in posterior fornix aseptically and the dose was repeated every 6th hourly till maximum five doses. Cervical reassessment was done and if needed oxytocin infusion was started.

Maternal vitals were monitored and side effects like chills, nausea, vomiting, diarrhoea, headache, severe pain abdomen, excessive bleeding p/v were observed. Failure of this method was considered if there occur serious side effects or no delivery of the fetus after 48 hours. Effectiveness was determined by complete expulsion of fetus and placenta, need for surgical intervention (D/E, hysterotomy, hysterectomy) and rate of the complications.[3]

The groups were compared with respect to the patients' characteristics, gestational age, indication for termination of pregnancy, rate of complications, etc.

Appropriate method of statistical analysis was applied to study the efficacy of each method of induction. Descriptive statistics were used to calculate the means, frequencies and S. D. Chi square test was used to compare categorical variables of significance.

RESULTS

In 76.00% of patients belonged to age group 20-30 years followed by >30 years (20%) and only 4 out of 100 patients (4%) were in age group <20 years. Mean value of age (years) of study subjects was 27.12±4.5 (Table 1).

In maximum patients (39 %), misoprostol dose required was 600 mcg followed by 800 mcg (27%), 400 mcg (24%) and 1000 mcg (7%) and only 3 out of 100 patients (3%) required 200 mcg dose (Table 2).

Table 1: Distribution of age (years) of study subjects.

Age (Years)	Frequency	Percentage (%)
<20	4	4
20-30	76	76
>30	20	20
Mean ± SD	27.12±4.5	

Table 2: Distribution of dose of misoprostol among study subjects.

Dose of misoprostol (mcg)	Frequency	Percentage (%)
200	3	3
400	24	24
600	39	39
800	27	27
1000	7	7
Total	100	100

Proportion of patients with induction to delivery time (hours): 10-20 hours was significantly higher in P0 and P1-P2 as compared to ≥P3. (10-20 hours: 56.25%, 59.18% vs 52.63% respectively). Proportion of patients with induction to delivery time (hours): >20 hours was significantly higher in nulliparous (P0) as compared to P1-P2 and ≥P3. (>20 hours: 34.38%, 18.37% and 0% respectively). Proportion of patients with induction to delivery time (hours): <10 hours was significantly higher in ≥P3 as compared to P0 and P1-P2. (<10 hours: 47.37%, 9.38% and 22.45% respectively) (p=0.004) (Table 3).

Mean ± SD of induction to delivery time (hours) in P0 was 17.73±6.46 and in P1-P2 14.78±4.9 which significantly higher as compared to ≥P3 (11.46±3.82) (p=0.0004).

Distribution of induction to delivery time (hours) was comparable between gestational age (14 to 18 weeks and >18 weeks), (<10 hours: 18.75% and 25% respectively, 10-20 hours: 62.50% and 54.41% respectively, >20 hours: 18.75% and 20.59% respectively) (p=0.72) (Table 4).

Mean±SD of induction to delivery time (hours) in 14 to 18 weeks was 15.25±5.4 and >18 weeks was 15.02±5.84 with no significant association between them (p=0.854).

Proportion of patients with induction to delivery time: <10 hours was significantly higher in Group A as compared to group B. (<10 hours: 36% vs 10% respectively). Proportion of patients with induction to delivery time: 10-20 hours, >20 hours was significantly lower in group A as compared to group B. (10-20 hours: 52% vs 62% respectively, >20 hours: 12% vs 28% respectively) (p=0.004) (Table 5).

Table 3: Comparison of induction to delivery time (hours) with parity.

Induction to delivery time (Hours)	P0 (nulliparous), (n=32) (%)	P1-P2, (n=49) (%)	≥P3, (n=19) (%)	Total, n (%)	P value
<10	3 (9.38)	11 (22.45)	9 (47.37)	23 (23)	
10-20	18 (56.25)	29 (59.18)	10 (52.63)	57 (57)	0.004†
>20	11 (34.38)	9 (18.37)	0 (0)	20 (20)	
Mean±SD	17.73±6.46	14.78±4.9	11.46±3.82	15.1±5.67	0.0004§
Range	7.17-30.25	6.25-23.83	6.5-20	6.25-30.25	

†Fisher's exact test, §ANOVA

Table 4: Comparison of induction to delivery time (hours) with gestational age (weeks).

Induction to delivery time (Hours)	14 to 18 weeks, (n=32) (%)	>18 weeks, (n=68) (%)	Total, n (%)	P value
<10	6 (18.75)	17 (25)	23 (23)	
10-20	20 (62.50)	37 (54.41)	57 (57)	0.72‡
>20	6 (18.75)	14 (20.59)	20 (20)	
Mean±SD	15.25±5.4	15.02±5.84	15.1±5.67	0.854*
Range	7.17-28.17	6.25-30.25	6.25-30.25	

*Independent t test, ‡ Chi square test.

Table 5: Comparison of induction to delivery time (hours) between group A (Foleys and misoprostol) and group B (Misoprostol alone).

Induction to delivery time (Hours)	Group A, (n=50) (%)	Group B, (n=50) (%)	Total, n (%)	P value
<10	18 (36)	5 (10)	23(23)	
10-20	26 (52)	31 (62)	57 (57)	0.004‡
>20	6 (12)	14 (28)	20 (20)	
Mean±SD	12.66±4.89	17.53±5.39	15.1±5.67	<0.0001*

*Independent t test, ‡Chi square test.

Mean ± SD of induction to delivery time in group B (misoprostol alone) was 17.53±5.39 which was significantly higher as compared to group A (Foleys+Misoprostol) (12.66±4.89) (p<0.0001).

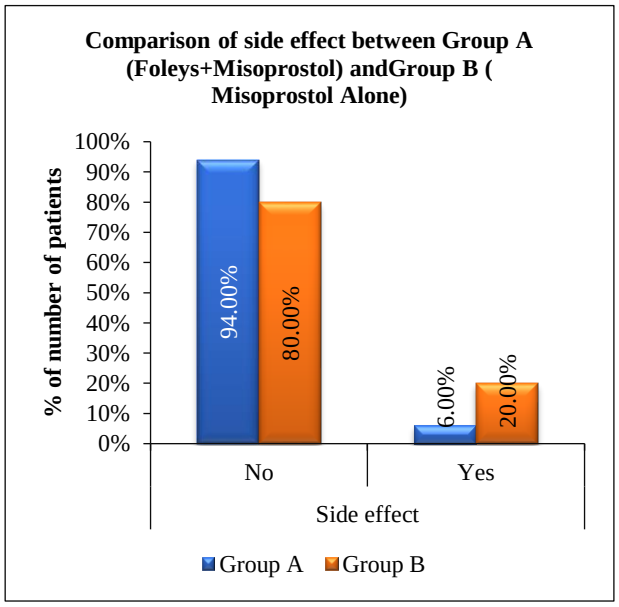

Figure 2: Comparison of side effect.

Distribution of side effect between group A and group B. (6% vs 20% respectively) (p=0.041). Most common side effect among both of them is severe abdominal pain followed by fever with chills (Figure 1).

DISCUSSION

We observed mean age as 27.12±4.5 years that shows most of women having an abortion are between age of 20-30 years which is similar as found by Rezk et al and Mahajan et al.[13,14]

Out of 100 cases in our study, 39 cases required misoprostol dose 600 mcg and showed the maximum abortion rate within 24 hours. It suggests that 600 mcg misoprostol dose is required in maximum number of patients with high rate of abortion success. The results were same as found by Dickinson et al which showed that 600 mcg vaginally administered misoprostol dose is superior as compared to orally administered 200 mcg dose and 800 mcg of misoprostol, which is likely to have more side effects also, especially diarrhea.[15,16]

Our study showed that only 13 cases report side effects out of 100 cases. The result was compared with Dickinson et al study which showed that there is very less side effects

of misoprostol and varied among the patients (0-8.8%), this is due to difference in administered doses of misoprostol.[15] So, study suggests that misoprostol administration for second trimester pregnancy termination is suitable due to the occurrence of less side effects.

In our study, none of the cases reported to have uterine rupture which is similar to the study by Rezk et al only 7% cases reported complications by the use of misoprostol.[13] It suggests that misoprostol can be used for the termination of second trimester pregnancy. Data which we found in our observational study were almost similar as shown by Jamali et al study where 13.2% cases reported complications.[17] These include bleeding, need for blood transfusion and curettage. Teratogenic effects were reported with failed abortion and attempted to continue pregnancy after administration of misoprostol.

Our finding was similar to Manninen et al that multiparous women are more likely to complete the termination faster.[18] Our finding was same as found by Odeh et al that previous confinement positively affects the success of termination of pregnancies so, induction to delivery time is significantly higher in nulliparous group.[19]

Our study on 100 patients revealed that majority of patients in our study require 600 mcg misoprostol dose in all group of parity (p=0.083). Present study was compared with Manninen et al which showed that 800 mcg administration followed by 400 mcg dose is required in majority of patients to abort the second trimester pregnancy and Rettenmaier at al showed that women with no previous pregnancy (p=0.02), no previous live birth (p=0.0001) and gestations 17-21 weeks (p=0.001) required more misoprostol doses. From this discussion, it was observed that there is no statistically significant relationship between misoprostol dose and parity for termination of second trimester pregnancy.[18,20]

Current study showed that medical termination of pregnancy in second trimester generally takes 10-20 hours irrespective of gestational age. P=0.72 which was not significant so it was shown in this study that induction to delivery time doesn't depend much on gestational age. Results were compared with Manninen et al study where induction to delivery time was 4.6 hours in <18 weeks of gestation and it is >8 hours in >18 weeks of gestation which showed that more time required in termination of higher weeks of gestation which was not supported by our study.[18]

Foley catheter plus misoprostol method is more effective at >18 weeks of gestation (58.82%) and misoprostol alone is effective at 14 to 18 weeks of gestation age (68.75%). This finding was same as given by Allen et al study in which misoprostol alone is effective under <16 weeks of gestational age and it reduces its effectiveness by increasing gestational age, additional mechanical dilation is required to achieve the same degree of effectiveness.[21]

Comparison of side effects between group A and group B

Present study revealed that there is no side effects in 94% of the cases in combined misoprostol and Foley catheter group and 80% in misoprostol alone group. Only 6% and 20% of cases reported side effects in both groups respectively. Many adverse effects of misoprostol use have been reported include diarrhea, abdominal pain, headache, menstrual cramps, nausea and flatulence, chills, shivering, and fever (easily disappeared after cooling and antipyretic), all of them are dose-dependent. The most common side effects are chills/shivering (38%), fever (35%), and diarrhea (24%). Results were compared with Rezk et al study which showed that side effects were comparable in both the groups which comprised of severe abdominal pain, fever with chills and diarrhea.[13] Thus it was observed that Treatment by misoprostol during the second and third trimesters makes it possible to terminate a pregnancy easily and quickly without significant side effects.

In our study, none of the cases reported uterine rupture in both groups which is similar to the study of Rezk et al current study showed that 4% cases reported complications in combined misoprostol and Foley catheter group and 10% cases reported complications in misoprostol alone group in termination of second trimester pregnancy.[13] These findings were compared to studies of Rezk et al and Samantaray et al.[13,22] According to them, there was significant difference in two groups in terms of complications but the sample size was not enough for a conclusion. The most common complication seen in our study is excessive bleeding per vagina followed by need of blood transfusion.

Comparison of induction to delivery time with parity

In our study comparative analysis was done in nulliparous women between both groups and it was observed that mean induction to delivery time was 19.06±6.02 in group A and 17.13±6.69 in group B which is not statistically significant.

In parity P1-P2 women, mean induction to delivery time was 11.6±2.91and 19.4±3.21 in group A and group B respectively. This showed that group B patients took much more time as compared to group A which is statistically significant (p<0.0001).

In parity ≥P3 mean induction to delivery time was 9.66±2.6 in group A and 13.94±3.97 in group B which is also statistically significant (p<0.01).

So, it was observed from our study that combined method (Foleys catheter with misoprostol) is more effective in higher parity women as compared to nulliparous women. Thus, it may be concluded that induction to delivery time, parity and method adopted for termination of second trimester pregnancy are dependent on each other.

Comparison of induction to delivery time with gestational age

In our study, it was observed that in women with gestation age <18 weeks, mean induction to delivery time was 16.4±5.53 in group B which was significantly higher as compared to group A (11.8±3.24) (p<0.009) results were similar to Shabana et al study in which mean induction to delivery time was 10.8±3.91 in combined method and 14.6±2.67 in misoprostol alone method.[5]

Present study showed that in termination of pregnancy with gestation age >18 weeks, mean Induction to delivery time was 18.57±5.14 in group B which was significantly higher as compared to group A (12.83±5.16) (p<0.0001).

However, there is still need to find out the best route and dose with minimum side effects and complications. In order to shorten the induction to abortion interval and to minimize the side effects of repeated doses of misoprostol, combining it with Foley catheter is a good alternative option.

CONCLUSION

Thus, it may be concluded from our study that combined Foleys catheter with misoprostol method is more effective as compared to misoprostol alone method in termination of second trimester pregnancy irrespective of gestational age. The combined use of intracervical Foley's catheter and vaginal misoprostol is a safe, effective and acceptable method for termination of second trimester pregnancy. The use of Foley catheter with misoprostol for termination of pregnancy is cheaper and very convenient methodology for both patients and obstetricians. This study supports the use of misoprostol combine with Foleys catheter.

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