Comparison of intravaginal misoprostol alone and in combination with intracervical Foley's catheter for termination of second trimester pregnancy- 3 years study at a tertiary care hospital.

Subha Ranjan[1], A Sarojini[2], Ipsita Mohapatra[3], A Vivekanand[4], Smruti Ranjan[5]

[1,3]Assistant Professor,[2]Professor, [4]Professor and Head, Department of Obstetrics and Gynecology, Prathima Institute of Medical Sciences, Karimnagar, Telangana. [5]Assistant Professor, Department of Community Medicine, Jawaharlal Nehru Medical College, Wardha.

Address for correspondence: Dr Subha Ranjan, Assistant Professor, Department of Obstetrics and Gynecology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.

Email: drsubha2009@gmail.com

ABSTRACT

Introduction: Termination of pregnancy in second trimester is one of the greatest challenges in modern obstetrics practice and is more risky than during first trimester. Now the main concern of the obstetrician is to provide the most effective, safest, and cost effective regimen with least or no complications.

Objectives : To compare the effectiveness and safety of misoprostol alone and its combination with intracervical Foley's catheter for second trimester termination of pregnancy.

Material and Methods: 100 women of 14-28 weeks of pregnancy were enrolled for termination for any indication and were randomized into two groups. Group I (study group): received 200 mcg of misoprostol 6 hourly and intracervical Foley's catheter. Group II (control group): received only 200 mcg of misoprostol 6 hourly, upto a maximum five doses. The outcomes are measured in terms of success rate of abortion within 48 hours, induction to delivery interval and maternal side effects.

Results: The induction to abortion interval was 13.84±5.37 hours in the combined group compared to 22.68±4.82 hours in the misoprostol group (P value<0.001) with success rate of 90% in the combined group and no major complications reported.

Conclusion:

Use of intracervical Foley's catheter improves the efficacy of vaginal misoprostol for termination of midtrimester pregnancy with shorter induction to delivery interval with no significant increase in side effects.

Keywords: Foley's catheter, misoprostol, second trimester pregnancy termination

INTRODUCTION

Termination of pregnancy in second trimester is one of the greatest challenges in modern obstetrics practice. Dimension of problems are social, medical and medico-legal. Termination of pregnancy (TOP) in second trimester is more risky than during first trimester[1]. Despite of the advances in prenatal diagnosis in first trimester, TOP in second trimester due to congenital anomaly and intrauterine fetal death still accounts for large number of abortionn[2,3]. Globally the incidence of unavoidable second trimester TOP is about 10-15%[1,4]. It accounts for 2/3rd of all major termination related complications[4,5].

Now the main concern of the obstetrician is to provide the most effective, safest, and cost effective regimen with least or no complications. Till date there is no consensus or recommendations on the safest method of termination in these women[6]. Termination of second trimester pregnancy is more risky and as surgical methods have more morbidity, therefore the medical methods of TOP seem to be better alternative to surgical methods[7,8]. Surgical methods are gradually getting replaced by mifepristone, prostaglandins, oxytocin and mechanical methods.

Development of medical approaches using mifepristone and prostaglandin analogue is providing a better alternative since last two decades[9]. Mifepristone is a progesterone antagonist, which sensitizes myometrium to prostaglandin induced contraction and cervical ripening. It is expensive to use in developing country. PGE2 and PGF2 also have a high cost and need temperature control for storage and transportation[10]. On the other hand misoprostol, a synthetic PGE1 analogue, is a stable and cheaper formulation, which is easily available and quite effective with little or no gastrointestinal side effects. It is in use since 1988 and now it is a proven drug for its cervical ripening and has a potent oxytocic action[11]. It can be used via oral, vaginal and rectal route but when used vaginally, there are fewer or no gastrointestinal side effects[12]. Vaginal misoprostol has slow onset but sustained effect with peak action after 60 minutes. So small doses are equivalent to high dose of oral misoprostol. Scared uterus is not a contraindication to its use in second trimester.

Mechanical dilatation of cervix with Foley's catheter to induce labour was first described by Krause in 1833[13]. Embry and Mollison in 1967 reported 94% successful induction with Foley's catheter[14]. Foley's catheter is one of the cheapest, safest and effective mechanical methods of induction verified in various studies[8,15]. In developing countries like India use of Foley's catheter has been recommended by WHO and many studies have shown excellent results with it either alone or in combination with misoprostol or PGF2. Apart from direct mechanical dilatation, it stimulates the paracervical plexus of nerves, releases PGs and increases excitability of uterus resulting in cervical ripening and uterine contraction[16].

We conducted this study to determine the frequency of indications and to compare the efficacy of misoprostol alone and its combination with Foley's catheter balloon for therapeutic termination of second trimester pregnancy.

MATERIALS AND METHODS

This randomized controlled study was carried out in the Department of Obstetrics and Gynaecology, of Prathima Institute of Medical Sciences, which is basically a referral centre, during a period of 3 years from August 2012 to July 2015. Ethical committee approval was obtained. Pregnant women needing termination between 14 to 28 wks were enrolled. Gestational age was calculated from the date of the first day of last menstrual period and confirmed by ultrasonography. Women having history of two or more previous caesarean section, contraindication to misoprostol, low lying placenta, multiple pregnancy, grand multipara, coagulation disorder, disseminated intravascular coagulopathy, PROM, chorioamnionitis, and vaginal infections were excluded from the study.

The cases were randomized into two groups by lottery method. Group I: received misoprostol and intracervical Foley's (study group) and Group II: received misoprostol alone (control group).

In the study group (Group I), after taking informed and written consent, under all aseptic measures Foley's catheter (14-16 Fr) was introduced through cervix to the extraamniotic space and balloon was inflated with 30 ml normal saline. Catheter was placed inside the patient's thigh and firmly attached. At the same sitting 200µg 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 control group (group II) only misoprostol (200µg) 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. Antibiotic coverage was given with IV cefotaxime and IV metronidazole. Maternal vitals were monitored and side effects like chills, nausea, vomiting, diarrhoea, headache, severe pain abdomen, excessive bleeding p/v were observed. Bleeding was assessed by counting the number of completely soaked sanitary pads changed. It was considered average if less than 200cc and excessive if more than 200cc. Failure of this method was considered if there were 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 complications, excessive bleeding p/v.

The data was collected on a structured questionnaire. The groups were compared with respect to the patients characteristics, gestational age, indication for termination of pregnancy, rate of complications, etc. Descriptive parameters were expressed as mean ± standard deviation and range. Frequencies were expressed as percentage. Comparison of mean values among two group performed by student's t test of independent mean, where as ?2 test used for comparison of proportions. 'P' value of less than 0.05 was considered statistically significant.

RESULTS

Total 100 women were randomly selected who were in second trimester (14-28 weeks), presenting either with missed abortion (before 24 weeks), intrauterine death (24-28 weeks) or with gross congenital anomalies incompatible with life. They were divided into two groups. Study group received Foley's and misoprostol. Control group received misoprostol alone.

The descriptive statistics of demographic variables of patients are described in Table1. Both groups are comparable and showing no significant differences. (P>0.05)

Obstetrical characteristics are described in Table2, showing that majority of the cases were primigravida (54% and 50% in study and control groups respectively). Most of the cases belonged to gestational age of 22 weeks and more (55% and 40%) with a mean of 22.7weeks and 23.4 weeks in study and control groups respectively. Out of 100 cases, 9 cases in study group and 7 cases in control groups had a history of caesarean section in previous pregnancy. Both groups are comparable with respect to gravidity, gestational age and showing no statistically significant difference (P>0.05).

The most common indication was fetal demise, which accounts for 48% and 40% in study and control groups respectively. Second common indication was gross congenital anomaly incompatible with life, like anencephaly, hydrops fetalis, hydrocephalus, and anhydramnious (28 % and 36%). Maternal indications include 3 cases of severe preeclampsia and one case of eclampsia.(Table-3)

The outcome of both methods is described in Table 4. In study and control group respectively, success rate were 90%

and 82%, with mean induction to delivery time were 13.84 hours and 22.6 hours in the successfully complete termination cases. In 1st 24 hours the termination of pregnancy achieved in 82 % and 56% cases among study and control groups respectively. These observation were found to be statistically significant (P<0.001).

Table 5 summarizes the various complications and its relative frequency. The complications observed were nausea, vomiting, severe abdominal pain, headache and dizziness, etc and was not statistically significant in these groups. Excess bleeding (>200 ml) observed in 18% and 10% of the cases in the study and control group respectively. No maternal mortality and no uterine rupture was observed in either group.

Table 1: Demographic characteristics of study groups

		Group I (n=50)	Group II (n=50)
1. Age in years{(mean±SD) & (Range)}		23.4±4.1 (19-33)	
2. Socio economic status			
	Lower	34(68%)	32(64%)
	Middle	14(28%)	17(34%)
	Upper	2(4%)	1(2%)
3. Booking status			
	Booked	11(22%)	13(26%)
	Unbooked	39(78%)	37(74%)

Table 2: Obstetrical characteristics of study groups

		Group I (n=50)	Group II (n=50)
1. Gravidity			
	Primi	27(54%)	25(50%)
	G2	17(34%)	22(44%)
	≥ G3	6(12%)	3(6%)
2. Gestational age (weeks)			
	14-18	6(12%)	8(16%)
	18-22	19(38%)	20(40%)
	>22	25(50%)	22(44%)
	Mean	22.72±3.4	23.42±3.8
	Range	(14-28)	(14-28)
3. Previous caeserean section			
	Yes	9(18%)	7(14%)
	No	41(82%)	43(86%)

Table 3: Indication for Termination of pregnancy (TOP)

Indications	Group I (n=50)	Group II (n=50)
1. Missed miscarriage	9(18%)	11(22%)
2.Fetal anomaly	14(28%)	18(36%)
3.Fetal demise	24(48%)	20(40%)
4.Maternal indication	3(6%)	1(2%)

Table 4: Outcome of Termination of pregnancy (TOP)

Outcome		Group I (n=50)	Group II (n=50)
TOP in 1st 24 hours		41(82%)	28(56%)
TOP in 48 hours		4(8%)	13(26%)
TOP after 48 hours		5(10%)	9(18%)
Successful TOP in hours:			
	Mean	13.84±5.37	22.68±4.82
	Range	7-26	12-37
Successful TOP		45(90%)	41(82%)
Failure		5(10%)	9(18%)

Table 5: Complications of intervention

Complications	Group I (n=50)	Group II (n=50)
1. Nausea & Vomiting	9(18%)	6(12%)
2. Headache & Dizziness	8(16%)	6(12%)
3. Abdominal pain	6(12%)	9(18%)
4. Fever	4(8%)	6(12%)
5. Excess bleeding(>200ml)	8(16%)	5(10%)
6. Uterine rupture	0(0%)	0(0%)
7. Maternal mortality	0(0%)	0(0%)

DISCUSSION

Midtrimester termination of pregnancy (TOP) has a global incidence of 10-15%[1,4,17]. Most of the time it is unavoidable. There is a gradual increase in incidence because of wide scale introduction of prenatal screening programme[18].

The most efficacious regimen for medical termination of second trimester pregnancy appears to be use of mifepristone followed by misoprostol[4,9,19]. This regimen has an abortion rate of 97-99% in first 24 hours[19, 20]. In low resource setting mifepristone is non affordable or non available. Misoprostol is widely used for second trimester termination of pregnancy. However there is still a debate about the best route and dose with minimum induction to delivery interval and minimum side effects [21]. In order to shorten the induction to delivery interval and to minimize the side effects of repeated dose of misoprostol, intracervical Foley's catheter combination is one of the better options[22].

The purpose of our study was to compare the efficacy and outcome of misoprostol alone and in combination with intracervical Foley's catheter for medical termination of second trimester pregnancy. In this study the induction to delivery

interval (IDI) was 13.84±5.37 hours in combined group which is significantly shorter than misoprostol alone group (22.68±4.82 hours) {P<0.001}. The success rate was higher in combined group (90%) as compared to misoprostol (82%). Surgical evacuation was needed in 10% of the cases in combined group as compared to 18% in the misoprostol group.

The side effects and complication was comparable without any significant difference. Our study included nine cases of previous caesarean section in combined group and seven in misoprostol alone group and we observed greater failure rate (29%) in misoprostol alone group as compared to combined group (11%) but the sample size was not enough for a conclusion. No uterine rupture observed in our study.

Similar induction to delivery interval was observed by Shabana A et al., a study conducted at Egypt, in which induction to delivery interval in combined group was 15.6±5.4 hours which significantly shorter than misoprostol alone group (21.9±4.9) and P<0.05[8]. The success rate was 100% at early gestational age and as gestation increases, a fall in the success rate observed. They concluded that, as misoprostol dose in both group was similar the decrease in induction to delivery interval was attributable to use of intracervical Foley's catheter. The catheter may exert its effect by disrupting the integrity of amnion-chorion and myometrium and release prostaglandin and cytokines, which alters the collagen and extracellular matrix rendering the uterus susceptible[23-25].

The induction to delivery interval of misoprostol alone showed marked variation among various studies. It varies from 9 -30 hours, with success rate of 60-100%. A study conducted by Imran F et al., at Karachi, used 200 mcg misoprostol with hydroxyl ethyl gel for termination of pregnancy between 14-24 weeks, found a success rate of 96% and induction to delivery interval 9.02±4.57 hours[15]. Another study by A koury HA and et al., on 217 women of 15-24 weeks of gestation, compared the outcome of vaginal and oral misoprostol[26]. The induction to delivery interval observed was longer for oral misoprostol group (30.5±14.4 hours) as compared to vaginal route (18.3±8.2hrs). Kooper smith study observed a low success rate of 60-70%[27]. Ghorab et al., and Shabana A et al., observed a success rate of 100%[8],[28]. These large variations in the outcome may be due to difference in the regimens used, routes of administration, indication, parity and the gestational age at the time of presentation.

There are very limited studies which compares the use of prostaglandin E1 tablet alone versus its combined use with Foley's catheter in terminating Midtrimester pregnancy. A study by Toptas et al., was conducted in a total of 91 pregnancies. Women between 13 to 26 gestational weeks were included in the study. Study participants received intravaginal misoprostol in combination with Foley's catheter (n=46) or intravaginal misoprostol alone (n=45). The authors concluded that combination of intravaginal misoprostol and extra amniotic Foley catheter for second trimester pregnancy termination does not provide additional efficacy with one case experiencing uterine rupture in the catheter group[29].

Recently Razk et al., conducted comparative study including 90 pregnant women between 13 and 24 gestational weeks. Enrolled women were equally allocated into three groups. The first received vaginal misoprostol (n=30), the second received intracervical Foley catheter alone (n=30) and the third received both (n=30)[30]. The induction to abortion interval was 7.5±1.25 h in the combined group, compared to 11.76± 1.63 h in the misoprostol group and 19.76±1.52 h in the catheter alone group (p value<0.001) with a success rate of 100% and no major complications reported.

In our study we found a significant reduction in induction to delivery time in combined group as compared to misoprostol alone group. But the mean duration of delivery in both the groups are greater than that observed by razk et al., taptas et al., but closely resembles with the study conducted by Shabana A et al. Increased duration may be due to greater mean gestational age in our study and we used a comparatively low dose of misoprostol with a longer dosing interval as compared to above mentioned studies. This was in agreement with the finding of Gomez et al., they found that the induction to abortion interval increased by 4 hours after 20 weeks[31]. Another study on Midtrimester termination of pregnancy by Ashok et al. concluded that the induction to abortion interval was significantly longer in higher gestational age pregnancy[32].

CONCLUSION

Use of intracervical Foley's catheter improves the efficacy of vaginal misoprostol for termination of midtrimester pregnancy with shorter induction to delivery interval with no significant increase in side effects.

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