ORIGINAL RESEARCH PAPER

Gynaecology

A COMPARATIVE CLINICAL EVALUATION OF INTRAMUSCULAR CARBOPROST TROMETHAMINE WITH INTRAVAGINAL MISOPROSTOL FOR SECOND TRIMESTER TERMINATION OF PREGNANCY.

KEY WORDS: Mid trimester abortion, Carboprost tromethamine,Misoprostol

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ABSTRACT

Objective To comparatively evaluate the success rate of abortion, the induction abortion interval and the side effects associated with intravaginal Misoprostol and intramuscular Carboprost in an endeavour to find safe and effective method for second trimester pregnancy termination.

Material and methods : A prospective randomised non blinded study conducted in the Department of Obstetrics at Dr Baba Saheb Ambedkar Hospital over a period of two years on 60 pregnant women seeking termination of pregnancy between 13 weeks to 20 weeks of gestation.

Results Demographic and Obstetric characteristics of both the groups in terms of age, education, socio economic status,religion, parity, period of gestation and number of previous abortions were similar.Success rate at 24 hours for Misoprostol was significantly higher than that of Carboprost (p =0.004) but no statistically significant difference was observed at 48 hours. The mean induction abortion interval was less for misoprostol (12.24 hours) as compared to carboprost (16.82 hours),this difference was statistically significant(p=0.0198). The side effects reported,headache ,nausea vomiting diarhoea and fever were much lower with Misoprostol and the difference was statistically significant.

Conclusion Intravaginal Misoprostol at a dose of 400 mcg 3 hourly is a superior method of termination of second trimester pregnancies in view of its shorter induction abortion interval, fewer side effects and cost effectiveness.

INTRODUCTION

At the core of reproductive rights is the principle that a woman has the right to decide whether and when to have a child. – Centre for Reproductive Rights

Worldwide, forty two million induced abortions take place annually, of which thirty five million are conducted in developingcountries like India.[1] In India, despite thirty seven years of liberal legislation in place, the number of unsafe procedures being carried out is staggeringly high. According to Government of India estimates, 8.9% of maternal deaths are caused by unsafe abortions.

Majority of terminations occur in first trimester of pregnancy,mid trimester abortions constitute 10-15 %, but are responsible for two-third of abortion related complications as per World Health Organisation estimates. Complicating factors associated with midtrimester pregnancy termination include the larger foetal-placental unit, increased uterine blood flow, and an unfavourable cervix. India's second trimester abortion rate is thought to be among the highest in the world.[2]Compared with the maternal mortality rate for procedures performed at 8 weeks gestation, the relative risk for mortality increases substantially in the second trimester, with a 7.7-fold increase at 13 to 15 weeks, and 9.3-fold increase at 16 to 20 weeks.[3]Unsafe second trimester abortions contribute disproportionately to abortion related morbidity and mortality.

In India, ignorance and inability to take an early decision regarding abortion and inaccessibility of services and providers as well as paucity of abortion facilities[4]compels a large number of women to seek termination of pregnancy in second trimester. Also, recent advancements in the field of foetal diagnostics have led to a greater degree of detection of foetal anomalies and thus have contributed significantly to midtrimester abortions. Thus women continue to need second trimester pregnancy termination services The variousmethods for second trimester termination are: dilatation and evacuation,Intra amniotic instillation of saline, urea or prostaglandins, extra amniotic instillation of ethacridine lactate or prostaglandins, vaginal, oral or sublingual administration of prostaglandins and analogues; hysterotomy etc. Therehave been continuing efforts to improve the technology for second trimester termination in terms of effectiveness, technical ease of performance, acceptability, reduced cost and reduction of side effects and complications.

Carboprost tromethamine was approved by the FDA as far back as 1979 for aborting pregnancies between the 13 and 20 weeks ofgestation. It is a synthetic methyl analogue of prostaglandin F2alpha, which is resistant to enzymatic degradation and has a long half-life. However it is reported to have high incidence of side effects and needs refrigeration for storage. Misoprostol is a synthetic analogue of prostaglandin El. Good results in second trimester abortions have been reported with the use of Misoprostol. It is a cheap drug with minimal side effects and can be used with oral, sublingual and vaginal routes.

The quest for safer methods for second trimester pregnancy termination without jeopardising ssubsequent reproductive life, is on and this study, a comparative evaluation of intramuscular Carboprost tromethamine with intravaginal Misoprostol, has tried to make a little step ahead in the same direction.

MATERIAL AND METHODS

This was a prospective randomised nonblinded study conducted in the Department of Obstetrics and Gynaecology at Dr Baba Saheb Ambedkar Hospital and Medical College over a period of two years after taking approval from the scientific and ethical committee of the institute A total of 60 pregnant women who were seeking termination of pregnancy between 13 weeks to 20 weeks of gestation as per the MTP Act and those with intra uterine dead foetus were thoroughly evaluated. Women meeting the inclusion and exclusion criteria were enrolled in the study after taking informed consent.

Inclusion criteria

- Singleton pregnancy
- Period of gestation between 13 to 20 weeks

Exclusion criteria were

- Pregnant women with multiple pregnancies.

- Maternal infection.
- Uterine anomalies like fibroid or bicornuate uterus.
- History of previous uterine surgeries.
- Those with contraindication to prostaglandin like history of bronchial asthma or allergy.
- History of medical disorders like hepatic, renal or cardiac disease.

Detailed histories including socio-demographic details along with obstetric, medical and surgical history were recorded followed by complete general, systemic and obstetric examination. The women were randomly divided into two groups of 30 women each and the first group received 250 microgram of Carboprost by intramuscular route at 3 hourly interval till the abortion was induced up to maximum 10 doses. The second group received 400 micrograms of Misoprotol vaginally every three hours till the abortion was induced up to maximum 5 doses. The outcomes were noted in terms of procedure success (at least foetus or both foetus and placenta expelled within 48 hours), completeness of abortion, abortion induction interval, side effects/complications and cost effectiveness. Abortion was termed complete if both foetus and placenta were expelled completely without operative intervention.

STATISTICAL ANALYSIS The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 17.0.categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Regression analysis was performed to know the effect of various factors on complications and p value <0.05 was considered statistically significant.

Table 1 Sociodemographic parameters

Socio demographic parameter		Carboprost Group I		Misoprostol Group II	
		Number	Percentage	Number	Percentage
Age (in Years)	<= 20	2	6.67	3	10
	21-25	14	46.67	14	46.67
	26-30	11	36.67	6	20
	31-35	2	6.67	5	16.67
	>=36	1	3.33	2	6.67
Education	Illiterate	13	43.3	10	33.3
	Undergraduate	16	53.3	16	53.3
	Graduate	1	3.3	4	13.3
Socio economic Status	Lower	16	53.3	17	56.7
	Upper lower	4	13.3	2	6.7
	Lower middle	9	30.0	10	33.3
Religion	Hindu	30	100	27	90
	Muslim	0	0	2	6.7
	Sikh	0	0	1	3.3

RESULTS

The sociodemographic profile of patients are depicted in Table 1.The mean age + standard deviation for the two groups was 26.10 ± 3.79 years and 26.57±5.69 years. Most of the women belonged to 21- 25 years of age group. Majority of the women in Carboprost and Misoprost groups belonged to lower socioeconomic class (53.3% and 56.7% respectively) and 95% of the study population were Hindu by religion.

The mean parity ± S.D in Carboprost group was 1.70 ± 1.44 and that of Misoprostol group was2.00 ± 1.72 while the mean number of abortions in the two groups were 0.43 ± 0.73 and 0.33 ± 0.80 respectively. The mean period of gestation for Carboprost group was 16.99 ± 2.16 weeks and 17.04 ± 2.30 weeks for the Misoprostol group. The main reason for termination in both the groups was to limit the family size. Intra uterine foetal death constituted approximately one third of the reason for termination in both the groups.(Table 2)

Table 2 Obstetrical Parameters

		Carboprost Group I		Misoprostol Group Ii	
		Number	Percentage	Number	Percentage
Gravidity	Primigravida	4	13.33	7	23.33
	Multigravida	26	86.67	23	76.67
Previous abortion	0	20	66.7	23	76.7
	1	8	26.7	6	20
	2	1	3.3	0	0
	3	1	3.3	0	0
	4	0	0	1	3.3
Periods of gestation (in weeks)	13-16	14	46.67	14	46.67
	17-20	16	53.33	16	53.33
Reason for Termination	IUD	10	33.3	9	30
	Fetal malformation	8	26.7	6	20
	Limit family	11	36.7	13	43.3
	Space Children	1	3.3	1	3.3
	Maternal Indication	0	0	1	3.3

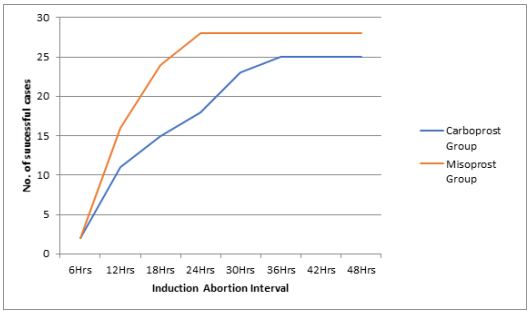
The outcome of treatment is depicted in [Table3]. The mean induction abortion interval in Carboprost group was16.82 hours and for Misoprostol group was 12.24 hours with p value 0.019 which was statistically significant. Misoprostol group had significantly more success rate after 24 hours (93.33% vs 60% p value 0.0048).However success rate after 48 hours, though higher in Misoprostol group than Carboprost group, was not statistically significant. The cumulative success with time interval is depicted in [Figure 1]. The side effects reported were headache, nausea, vomiting, diarrhoea and fever. The Misoprostol group had significantly lower rates of nausea, vomiting and diarrhoea (p value 0.025,0.0003 and 0.0001 respectively) as compared to the Carboprost group. The mean expenditure per case was Rs 695.57 and Rs 151.45 for Carboprost and Misoprostol groups respectively and the difference was statistically significant (p value 0.0001).

Table 3 Outcome Variables

		Carboprost Group I		Misoprostol Group II		P -value
		Number	Percentage	Number	Percentage	
Outcome after 24 Hrs	Success	18	60	28	93.33	0.0048
	Failure	12	40	2	6.67	
Outcome after 48 hours	Success	25	83.3	28	93.33	0.4238
	Failure	5	16.7	2	6.67	
Induction Abortion Interval Mean ± SD		16.82 ± 8.90		12.24 ± 4.48		0.0198
Completeness Of Abortion	Complete	19	76	20	71.43	0.7632
	Incomplete	6	24	8	28.57	
Side Effects/Complications	Headache	2	6.67	2	6.67	1
	Nausea	14	46.67	5	16.67	0.0251
	Vomiting	17	56.67	3	10	0.0003
	Diarhoea	16	53.33	2	6.67	0.0001
	Fever	1	3.33	1	3.33	1

	Excessive Bleeding	1	3.33	2	6.67	1
Cost in Rupees Mean ± SD		695.57 ± 315.70		151.45 ± 34.22		0.0001

Fig 1 Cumulative Successful Outcomes at Time Intervals



DISCUSSION

Worldwide efforts are on to formulate an ideal method for second trimester termination of pregnancy. The present study had attempted to take this quest a step ahead. Prostaglandins have emerged as the most commonly employed method in the present times though the analogue type, the dose, the dose interval and route continue to be researched. In the present study,Intramuscular Carboprost 250 mcg at 3 hourly interval, an approved method was compared with intra vaginal Misoprostol 400 mcg at 3 hourly interval.

Demographic characteristics of both the groups in terms of age, education, socio economic status and religion were comparable (p value 0.70,0.40,0.28 and 0.09 respectively). Obstetrical parameters of the two groups in terms of parity, period of gestation and number of previous abortions were also similar (p value 0.46,0.93 and 0.67 respectively)The most common reason reported for termination in both the groups was limiting family size followed by intra uterine death and foetal malformation.

After 48 hours, Twenty five out of thirty women aborted in the Carboprost group and twenty eight aborted in the Misoprostol group making the success rate of 83.3%and 93.3% for the two groups respectively but the difference was not significant (p=0.42).However, success rate after 24 hours for Misoprostol was significantly higher than that of Carboprost (p value0.004). The mean induction interval was lower for misoprostol (12.24 hours) as compared to Carboprost (16.82 hours),this difference was statistically significant(p=0.0198). As expected a much shorter induction abortion interval was reported in multigravidas in group II (11.96hours) ascompared to group I (17.04 hours), p value being 0.0207.

The side effects reported were headache, nausea, vomiting diarrhoea and fever. There were no cases of uterine rupture or cervical trauma. Nausea, vomiting and diarrhoea were significantly lower with misoprostol (p value 0.025,0.0003 and 0.0001 respectively).Only two women underwent hysterotomy when they failed to abort and they both belonged to the carboprost group. Misoprostol had a cost advantage of almost 5 times lower cost as compared to Carboprost and did not require refrigeration.

Borgida et al (1995) used 250 mcg Carboprost every 3 hours[5], the success rate of 94.55% was reported after 24 hours with a mean induction abortion interval of 11.3 hours as compared to 60% success rate and a mean abortion induction time of 16.82 hours obtained in the present study with carboprost at the end of 24 hours. Uterine curettage was required in 15% as compared to the 24%in the present study.The lower rate of incomplete abortion in their study could be explained by the fact that oxytocin 40U/L was given after thedelivery of the foetus. The incidence of side effects reported in their study was nausea 71%, headache 33%, fever 92% which were much higher as compared to the Carboprost group in our study. Biswas et al (1996) had a success rate of 97.5% with the use of intramuscular Carboprost for mid trimester abortion between 13 to 20 weeks[6].

Yilmaz et al (2005) reported a 100% success rate and a median induction abortion interval of 10 hours by using 800mcg Misoprostol intravaginally every 6 hours either moistened with acetic acid or normal saline [7]. The induction abortion interval noted was 8hours and 14 hours in the two groups, retained placenta was noted in3.l% and 9.4%. Nausea was reported in 27.2% and 26.1%, vomiting in 8.3% and 2l.8%, fever in 30 .3% and 25% and diarrhoea in 24.2% and2l.5%. As compared to the present study , their success rate is higher and abortion induction interval shorter but the side effects observed also show a higher incidence probably due to the higher dose of Misoprostol used.

A success rate of 98.59% and a mean induction interval of 12.9hours was reported with the use of 400 ug of intravaginal misoprostol every 3 hours by Bhattacharya et al (2006) which is comparable to thepresent study [8].Similarly, a success rate of 95% was reported with the use of 400 ug of misoprostol every 12 hours by Chaudhuri et al (2006).The mean abortion interval was 15.5 hours and a complete abortion rate of 66.6%.[9]

A success rate of 82.01% with sublingual and a success rate of 79.14% with 400 mcg of intravaginal misoprostol at 3 hours interval was reported by Bhattacharjee et al (2008).[10] The mean induction interval reported in the two groups was of 14.1 and 14.5 hours respectively. Thesevalues are comparable to that in misoprostol group of the present study."

Carbonell et al (2008) reported a success rate of 98. 15% and 94.3%with 600 ug every 6 hours and 400 ug every 4 hours of misoprostol Intravaginally[11].The mean abortion interval was 10.7 hours and 11.5 hours. The results are comparable to the present study with the use of Misoprostol. In their study, 81.6% and75.65% had complete abortions. The side effects reported were chills(70% and 71%), diarrhoea (38.1 % and48.8%), fever (32.4%and l%),vomiting (22.9% and 23.8%) and nausea (8.6% and l7.l%). A lower incidence of side effects was reported in the present study with the use of intravaginal misoprostol.

Result of this prospective study suggest that 400 mcg intra vaginal misoprostol every 3 hours is more effective agent for termination of pregnancy in second trimester as compared to intramuscular carboprost every 3 hours as it has shorter induction abortion time interval with fewer side effects and is more cost effective. The success rate of both regimen are same after 48 hours but significantly higher success rates are observed after 24 hours with misoprost regimen as compared to carboprost regimen.

CONCLUSION

Women will continue to need second trimester termination of pregnancy and it is important to provide safe, accessible standard quality termination services. Both intramuscular Carboprost and intravaginal Misoprostol are quite effective in termination of pregnancy in second trimester .Based on the present study, intravginal misoprostol should be the first line drug in view of its shorter induction abortion interval,fewer side effects and cost effectiveness. Carboprost however can be used as alternative drug for the cases that fail by other methods.

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