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Comparison between the Intracervical Route (Solution form) and Intravaginal Route (Tablet Form) Misoprostol Administration for Cervical Priming in Early Pregnancy Failure.

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ABSTRACT

Background: Misoprostol has been used for cervical priming before suction evacuation in early pregnancy failure. The procedure widely accepted and practised. we evaluate the efficacy of misoprostol in intracevical solution form v/s vaginal tablet form for cervical priming before suction evacuation. **Methods:** A prospective clinical trial was carried out in 200 women presenting with early pregnancy failure between period of gestation (6-12 wks) who were sequencially allocated to two groups of 100 each. Both group received 200ug misoprostol 1 hr prior to suction evacuation by either solution or tablet form. **Results:** Demographically both groups are similar for all period of gestation. misoprostol solution significantly improve cervical dilatation ($p<0.001$) with reduced suction evacuation period compare with tablet form. No major complication occurs in ether groups. **Conclusion:** The solution form is an effective alternative to tablet form of misoprostol of cervical priming. To the best of our knowledge this may be the first study to compare the efficacy of misoprostol in intracervical solution form vs intravaginal tablet form for cervical priming before suction evacuation.

Keywords: Early pregnancy, Cervical priming, misoprotol, Intracervical solution form, Intravaginal tablet form and suction evacuation.

INTRODUCTION

Early pregnancy failure is one of the most common entity in pregnancy, the obstetrician meet in day to day professional life. Up to 50% of conception, up 15% of clinically recognised pregnancy,[1] 2-6%of pregnancy with detectable fetal heart rate ended in failure. It will affect one in 4 women during their life time. Historically D&C was the commonly acceptable treatment option for early pregnancy failure. Though medical abortion is the other option. Now a days misoprostol mifepristone available to the field, Still D&C is the worldwide acceptable procedure for early pregnancy failure. The combination of mifepristone and misoprostol is one of the most effective regimen.[2]

Many times the procedure become difficult as the cervix is unyielding. To make the cervix primed (soft & dialatable), dinoprostole gel &recently misoprostole is being applied intravaginally. Various studies available to evaluate the efficacy of misoprostol in various route (buccaly, orally, intravaginally). But this study is design to compare between application of misoprostole intravaginally, tablet form and solution form. The effect of misoprostole on cervical priming have been extensively studied. Pharmakokinetics studies have shown that misoprostol is readily absorbed after sublingual, buccal, vaginal, rectal administration. But data are lacking on the pharmacokinetics as intra vaginal misoprostole in solution form.

Misoprosol is widely used in obstetrics for medical abortion, cervical priming and induction of labour.[3-13] It is a prostaglandin E1 analogue originally developed for the treatment of peptic ulcer. It was licenced for oral use, however vaginal administration become more popular & widely used for medical abortion & cervical priming. Many clinical studies have found that vaginal administration is more effective than oral administration.[5,8] There has been suggestive evidence showing that absorption through the vaginal route is inconsistence and absorption could be improved by adding water/NS to the misoprostol tablet.[10,11] It was not uncommon to find that the majority of the misoprostol tablet was still not completely dissolved several hours after vaginal

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administration.[12,13] As the misoprostol tablet is soluble in water so this study was desingned to evaluate the efficacy of misoprostol in solution form. The aim of this prospective comparative study was to assess the efficacy of intra vaginal misoprotol in tablet form vs solution form for cervical priming in management of early pregnancy failure.

MATERIALS AND METHODS

200 patients attending to the OPD having early pregnancy failure (missed abortion, incomplete abortion) and viable pregnancy(<12 wks) requesting for termination were recruited in to the study during the period from March 2017 to February 2018. These 200 women were recruited for surgical evacuation (S/E). The study was approved by the ethics committee of the Hi-Tech Medical College & Hospital, Rourkela & Shanti Memorial Hospital & IVF Center, Rourkela.

Inclusion criteria were healthy women who were pregnant (<12 wks) and women with early pregnancy failure desires for surgical evacuation. Women with history of allergy to misoprostol and major medical problem were excluded from the study.

The patient was randomized by computerised randomisation schedule. 200 ug of misoprostol tablet placed in posterior fornix or 200 ug of misoprostol solution instilled to cervical canal by 10 ml syringe 1 hr prior to the procedure. The diameter of the cervical canal measured with hegar dialator, advers events and any complication were recorded and compared between the two groups.

The diameter of the cervical canal was assessed by negociating no.6 or no.8 hegar's dilators with minimal pressure through cervical canal to a distance of 3 cm. The cervical diameter and snatching present or absent was evacuated by one physician (the co author MP).The vagina of each patient was cleansed by the on duty physician to remove any remaining fragments of the tab & solution, Prior to the PI (principal investigator) assessing the cervical priming to maintained the blindness of the study.

The cervical diameter and snatching (present or absent) was the primary outcome of the study. These condary outcome was any treatment emergent advere effect.

For the statistical analysis was computed by using a two-tailed test with an level as 0.05 and a 95% power.

RESULTS & DISCUSSION

No significant difference observed between the two groups with respect to age, age parity, socioeconomic profile, religion, gestational age, no of previous abortion [Table 1]. Preoperatively, out of 200 patients who were given misoprostol in solution form or intravaginal tablet form, 20(20%) vs 18 (18%) had spotting before the procedure and 12 (12%) vs 10 (10%) complain mild spasmodic pain. None of them had heavy bleeding or passage of conceptus during the waiting period. No pt reported nausea, vomiting, diarrhoea, during pre-operative period. 3(3%) patient in solution form compared with (2%) in oral form developed fever (temp>100°F) after the completion of procedure. A single experienced investigation (MP) conducted all the case of suction evacuation. The initial cervical dialatation of both groups ranged from 0-12 mm [Table 2], with the solution group have significantly higher median value than tablet group. (10+2.8 mm vs 8+2.3mm respectively, p<0.001). The duration of procedure ranged from 2-6 min (4.4+1.5 min) for the solution group compared with 2.5 -7min (5.2+1.8 min) for the tablet group [Table 2]. The solution group having a lower overall mean procedure period. For the operating surgeon suction evacuation was easier in solution form than tablet form. No major complication occurs either of the two groups.

Table 1: Demographic profile Patient characteristics.

Variables	Tablet form (n=100)	Vaginal solution form (n=100)	significance
Maen age±SD	25.6±2.5	26.8±3.4	Not significant
Range (years)	17-38	18-38	
Mean parity	3.8±2	3.5±2.0	
range	P1 -6	P1-6	
Mean G.A (wks)	7.9±2.1	8.0±1.8	
range	6-12	6-12	
Religion (hindu)	48(96%)	46(92%)	
Lower socioeconomic status	47(94%)	47(94%)	
Previous abortion	20(40%)	16(32%)	

Table 2: Pretty operative period.

	Tablet form	Solution form
Vaginal spotting	18[18%]	20[20%]
Mild spasmodic pain	10[10%]	12[12%]

Table 3: Intra operative parameter

POG (6-12 wks) Initial dialation	Tablet form(n=100)	Solution form(n=100)	significance
Median(10 mm)	10±2.8	8±2.3	P<0.001
Range(0-12)	0-12	0-12	
Mean time(min) To complete the procedure s/e	4±1.5	5.2±1.8	0.024

Post operatively side effect was noted in both groups their profile is mentioned in [Table 6]. Incidence of nausea 2% in solution group 1% in tablet group, vaginal bleeding was within normal limit in both groups. There was no episode of diarrhoea, vomiting

in both groups. There was mild rise of temperature 2(2%) in solution group 3(3%) in tablet group. Patient acceptability of medication similar in both groups. 36 patient out of 200 had a previous history of abortion. During follow up 7 days, 1 month none of the patient had any major complain, 6 patients complain low backache, 10 patients complain mild intermittent spotting.

Table 4: Comparison between two groups.

	Misoprostol tablet form(n=100)		Misoprostol solution form(n=100)	
Snatching	Present	Absent	Present	Absent
	(38)38%	(62)62%	(32)32%	(68)68%

Table 5: Post-operative period

	Misoprostol Tablet 200ug(n=100)	Misoprostol Solution 200ug(n=100)
Post medication dialatation(mm)	5.10±1.75 (0-10)	5.60±1.69 (2-10)
Cervical tear	0	0
Repaired cervix	0	0
Uterine perforation	0	0

Table 6: Treatment emergent adverse effect

Variables	Tablet 200ug	Solution 200ug
Nausia	3	3
vomiting	0	0
fatigue	4(13.3)	6(20)
Abdominal pain(cramp)	17(56.7)	19(63.3)
Vaginal bleeding	10(33.3)	9(30)
dizziness	6(20)	3(10)
diarrhoea	7(23.3)	1(3.3
Oral temp(≥37°c)	1(3.3)	1(3.3)

Misoprostol may be administered by various routes: oral, vaginal, rectal and sublingual. In general, the vaginal route appears to be as effective as the other. Intra vaginal application of misoprostol for cervical priming before suction evaluation is a widely accepted procedure. This study we tried to evaluate the efficiency of misoprostol in intra cervical application in solution form. We found the dilatation and procedure is easier in solution group than tablet group.it needs further study to evaluate the effect.

CONCLUSION

This comparative study was between the application of intracervical misoprostol (200ug) in solution form and intra vaginal misoprostol in tablet form (200ug). The study shows comparable side effect in both the groups but cervical priming is better in solution group and the procedure is little bit easier without any major complication in solution form. It needs further study for better co-relation.

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