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EVALUATION OF THE OUTCOME OF ORAL VERSUS VAGINAL MISOPROSTOL IN TERMINATION OF ALL CASES OF INTRAUTERINE FETAL DEATH

Obstetrics & Gynaecology

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ABSTRACT

Introduction: Misoprostol a potent uterotropic and uterotonic agent which causes cervical effacement &dilatation and stimulates myometrial contractions, is effective in terminating intrauterine foetal death. The Objective of the study was to compare the effectiveness of oral misoprostol versus vaginal misoprostol in termination of all cases of intrauterine foetal death and its outcome. Details of induction –delivery interval and maternal morbidities were also analysed. **Methodology:**A prospective comparative study.All pregnant women indicated for termination of intrauterine foetal death satisfying both inclusion and exclusion criteria being admitted in our Labour Room during the period of this study were included.Total 60 patients were included out of which 30 receiving oral misoprostol forms the first group and the other 30 receiving vaginal misoprostol forms the second group. For the first group, 200 mcg of oral misoprostol tablet was dissolved in 200ml water and 25 mcg, ie. 25ml of the solution was given first and then every two hours till pain occurs. Second group was given 25 mcg of vaginal misoprostol every 4 hourly. Induction-delivery interval and maternal morbidities were compared in both groups. **Results:** The mean induction-delivery interval was higher in Oral misoprostol when compared to vaginal route and this difference was found to be statistically significant ($p < 0.001$). However, the oral route was much easier when compared to vaginal route.The maternal morbidities like diarrhoea, fever, PPH, shivering, vomiting and tachysystole were similar in both groups.There were no cases of uterine rupture in the study. **Conclusion:**The effectiveness of different routes of administration was significant in our study with significantly shorter mean induction-delivery interval in vaginal route compared to oral route.Although there were few maternal morbidities seen in both groups, there were no statistically significant differences between two groups

KEYWORDS

Intrauterine Foetal Death; Oral; Vaginal; Misoprostol

INTRODUCTION

Intrauterine foetal demise (IUFD) indicates no foetal heartbeat detected after 20 weeks' gestation.The total estimated number of global stillbirths is 3.2 million annually Within the past two decades, Prostaglandins (PGs) have provided an alternative method for induction of labour in women with IUFD[1,2]. Misoprostol is absorbed rapidly when administered orally, vaginally, rectally or intra-cervical. The vaginal route is advantageous because peak levels are reached slowly and sustained for a long time and this is associated with fewer side effects[3,4]. The vaginal route is also more effective than the oral route[5,6,7]. The greater bioavailability of vaginal Misoprostol probably explains the clinical results. The bioactivity of misoprostol is characterized by rapid absorption, extensive metabolism and rapid excretion. After oral administration, the Tmax of misoprostol acid is 12 ± 3 minutes with a terminal half-life of 20-40 minutes[8].

Thirty eight studies conducted by Reproductive Health Library[9], involving 3490 women out of which 855 women in the vaginal misoprostol versus oral misoprostol trial which concluded that women administered vaginal misoprostol were more likely to deliver within 24 hours and had shorter mean induction to delivery interval compared to women who were administered oral misoprostol. There were no differences for other outcomes such as need for analgesia and side effects including nausea, vomiting, diarrhoea and pyrexia. Many studies have shown that vaginal misoprostol is safe and effective in termination of second and third trimester intrauterine fetal death.[10,11,12.] Hence the purpose of this study was to evaluate the effectiveness and side effects of oral versus vaginal misoprostol for the termination of all the cases of intrauterine foetal death.

Methodology

Study Design : Prospective comparative study
Study Period : 20 months
Sampling: Simple random sampling

(ii) INCLUSION CRITERIA:

1. All patients of age 18 years and above
2. Patients with intrauterine foetal death.
3. Patients who are ready to undergo required follow up and surgical management if required.

(iii) EXCLUSION CRITERIA:

1. Patients with previous uterine surgery, placenta praevia, abnormal lie, multiple pregnancy, parity of five and above,
2. Patients with respiratory tract disease, organic heart disease, renal disease.
3. Patients with pelvic pathology, uterine anomalies and haemorrhagic disorders.
4.Patients with allergy to prostaglandins.
5. Conditions which contraindicates the use of misoprostol like glaucoma, mitral stenosis,sickle cell anaemia, poorly controlled seizure disorders.

Methods of Data Collection

The patients reported to the department for termination of pregnancy with intrauterine foetal death was screened for inclusion in the study.After explaining to the patients about the study and obtaining approval from the Institutional Ethics Committee, a written informed consent was obtained from the patients. Initial assessment includes duration of amenorrhea, age, gravidity, parity, duration of IUFD and an initial Bishop score. Then general and systemic examination was carried out. Vaginal examination was done for all the women in order to rule out the presence of any pelvic pathology. Sonography was done to confirm IUFD. Routine investigations such as hemogram, BT, CT, blood sugar,urine examination, VDRL, serum creatinine and HIV were carried out in all the included patients.

Total 60 patients were included out of which 30 receiving oral misoprostol form the first group and the other 30 receiving vaginal misoprostol forms the second group. For the first group, 200 microgram of oral misoprostol tablet was dissolved in 200ml water and 25 mcg ie. 25ml of the solution was given first and then every two hourly till pain occured. Second group was given 25 mcg of vaginal misoprostol every4hourly. The patients were kept under observation and the outcome was considered as successful if a complete expulsion without surgical intervention was achieved. Induction-delivery interval and maternal morbidities were compared in both the groups.

RESULTS

Demographic Profile

Majority of the patients were in the age group 26 to 30 years old. In that both the groups were having nearly half of the patients in this group. The mean age was higher in the vaginal misoprostol group.

Table 1 : Age Distribution

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)	Chi-square test (p value)
Age at study (N=60)			
18 to 25 years old	07 (23.3)	07 (23.3)	0.051
26 to 30 years old	13 (43.3)	16 (53.3)	
31 to 35 years old	02 (06.7)	06 (20.0)	
36 to 40 years old	08 (26.7)	01 (03.3)	
Age (Mean ± S.D)	29.57 ± 5.4	27.7 ± 4.3	

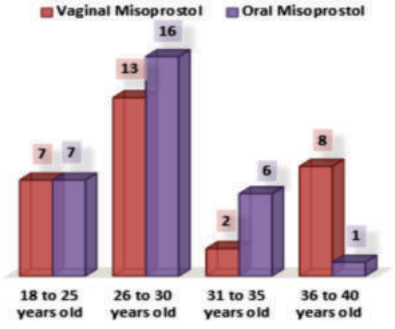


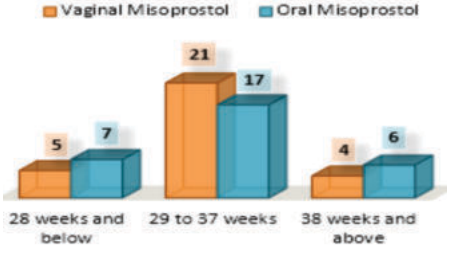
Figure1: Age Distribution Among The Two Groups

Obstetric Score

Primigravida were higher in the study with vaginal group having higher primigravida. Rest of the scores were similar in both groups.

Table 2: Obstetric Score

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)	Chi-square test (p value)
Primigravida	14 (46.7)	11 (36.7)	0.849
Gravida 2 Para 1 Live 1	07 (23.3)	08 (26.7)	
Gravida 3 Para 1 Live 1 Abortion 1	04 (13.3)	05 (16.7)	
Gravida 3 Para 2 Live 2	03 (10.0)	05 (16.7)	
Gravida 3 Abortion 2	02 (06.7)	01 (03.3)	



Gestational Age

Gestational mean age was seen similar in both groups and there were no statistical differences between them.

Table 3: Gestational Age

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)	Chi-square test (p value)
28 weeks and below	05 (16.7)	07 (23.3)	0.561
29 to 37 weeks	21 (70.0)	17 (56.7)	
38 weeks and above	04 (13.3)	06 (20.0)	
Mean ± S. D	32.73 ± 4.2	32.5 ± 4.5	0.897 (T test)

Cause of Intrauterine death

In the vaginal misoprostol group cord around the neck (23.3%) was mostly seen as the cause of IUFD and in oral misoprostol group congenital anomaly and severe preeclampsia (13.3 %) were seen.

Table 4: Cause Of Intrauterine Death

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)
1. Abruption	05 (16.7)	02 (06.7)
2. Cardiac Anomaly	01 (03.3)	01 (03.3)
3. Cause Unknown	02 (06.7)	03 (10.0)
4.Congenital Anomaly	02 (06.7)	04 (13.3)
5.Cord Around Neck	07 (23.3)	01 (03.3)
6.Polyhydramnios	01 (03.3)	01 (03.3)
7.Preeclampsia	01 (03.3)	02 (06.7)
8.Renal Anomaly	00 (00.0)	01 (03.3)
9.Gestational Hypertension	01 (03.3)	01 (03.3)
10.Severe IUGR	01 (03.3)	03 (10.0)
11.Severe Preeclampsia	03 (10.0)	04 (13.3)
12.Thickened Meconium	01 (03.3)	02 (06.7)
13.Gestational Diabetes	04 (13.3)	03 (10.0)
14.Unknown cause	01 (03.3)	02 (06.7)

Bishop score

The bishop score of less than 4 was higher in vaginal misoprostol group when compared to bishop score of 4 to 6 in oral misoprostol group. There were no statistical differences between two groups.

Table 5: Bishop Score (N=60)

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)	Chi-square test (p value)
Bishop Score <4	18 (60.0)	11 (36.7)	0.578
Bishop Score 4 to 6	10 (33.3)	17 (56.7)	
Bishop Score > 6	02 (06.6)	02 (06.6)	

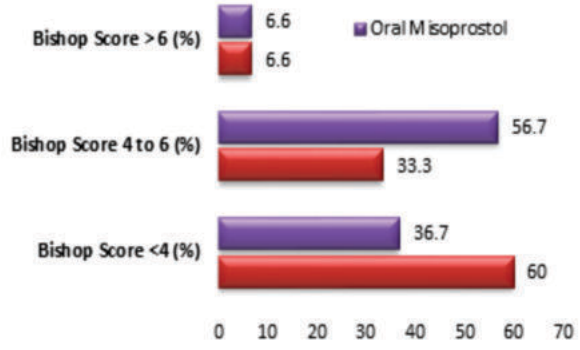


Figure 3: Bishop score

Misoprostol doses given

The doses of misoprostol given were lower in the vaginal group compared to oral group

Table 6: Number Of Doses Of Misoprostol

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)
0 dose	01 (03.3)	01 (03.3)
1 dose	08 (26.7)	04 (13.3)
2 doses	08 (26.7)	11 (36.7)
3 doses	07 (23.3)	06 (20.0)
4 doses	03 (10.0)	03 (10.0)
5 doses	00 (00.0)	03 (10.0)
6 doses	00 (00.0)	01 (03.3)
7 doses	01 (03.3)	00 (00.0)
8 doses	01 (03.3)	01 (03.3)
12 doses	01 (03.3)	00 (00.0)

Augmentation with Oxytocin
In the vaginal group 22 patients and in oral group 21 patients required oxytocin augmentation.

Table 7: Augmentation with oxytocin

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)	Chi-square test (p value)
Yes	22 (73.3)	21 (70.0)	0.774
No	08 (26.7)	09 (30.0)	

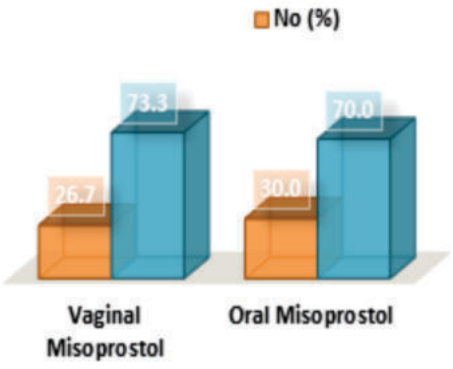


Figure 4: Augmentation with oxytocin

Induction to delivery interval
The vaginal misoprostol group had statistically significant difference with oral misoprostol group, with vaginal group having comparatively lesser time to induce.

Table 8: Induction To Delivery Interval

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)	Chi-square test (p value)
3 to 7 hours	14 (46.7)	00 (00.0)	<0.001
7 to 10 hours	07 (23.3)	01 (03.3)	
11 to 15 hours	05 (16.7)	09 (30.0)	
15 to 20 hours	01 (03.3)	09 (30.0)	
20 to 25 hours	01 (03.3)	07 (23.3)	
Mean ± S. D	9.39 ± 4.8 hrs	16.0 ± 4.1 hrs	<0.001 (T test)
Spontaneous Delivery	01 (03.3)	01 (03.3)	
Failed Inductions	01 (03.3)	03 (10.0)	

The mean induction-delivery interval was higher in the oral misoprostol group when compared to vaginal group and this difference was found to be statistically significant (p <0.001). However, the oral route was much easier when compared to vaginal route, but that advantage does not seem to transfer in the interval time.

There were two patients who had spontaneous delivery, one of each in vaginal and oral misoprostol group. In the vaginal group there was one failed induction and the patient was a primigravida. She was induced with 8 doses of vaginal misoprostol. The patient had established chorioamnionitis and was taken up for caesarean section.

In the oral group, there were 3 failed inductions. One of the patient was a primigravida. She was induced with 12 doses of oral PGE1, the patient had established chorioamnionitis and was taken up for caesarean section. The second case was gravida 3 with 2 Abortions in the past [G3A2] with IUFD at 35 weeks of gestation. She was induced with 10 doses of oral PGE1 but failed. As per patient's own request, she was taken up for caesarean section. The third case was a primigravida with IUFD at 26 weeks of gestation. She was induced with 12 doses of oral PGE1 but failed. so that the patient was taken up for hysterotomy.

Maternal Morbidity
In comparison to maternal morbidity, both groups had similar amount of morbidities and no statistically significant difference found.

Table 9 : Maternal Morbidity

	Vaginal Misoprostol n (%) (N=30)	Oral Misoprostol n (%) (N=30)	Fischer's Exact test (p value)
Nil	10 (33.3)	16 (53.3)	0.689
Diarrhoea	04 (13.3)	03 (10.0)	
Low Grade Fever	04 (13.3)	04 (13.3)	
PPH	05 (16.7)	01 (03.3)	
Shivering	03 (10.0)	02 (06.7)	
Vomiting	04 (13.3)	03 (10.0)	
Tachysystole	00 (00.0)	01 (03.3)	

DISCUSSION

The purpose of this study was to investigate the effectiveness of oral versus vaginal misoprostol in termination of all cases of intrauterine foetal death and its outcome. The majority of the patients with IUFD were in the age group 26 to 30 years old. The mean age was higher in the vaginal misoprostol group.In our study the bishop score of less than 4 was higher in vaginal misoprostol group when compared to bishop score of 4 to 6 in oral misoprostol group. There was no statistical difference between the two groups. In the vaginal misoprostol group cord around the neck (23.3%) was mostly seen as the cause of IUFD and in oral group congenital anomaly and severe preeclampsia (13.3 %) were seen. 22 patients in the vaginal group and 21 patients in the oral group required oxytocin augmentation. Orally treated patients required significantly more doses than vaginally treated patients. In this study the vaginal misoprostol group had shorter mean induction-delivery interval and faster ripening of cervix. The mean induction-delivery interval was higher in Oral misoprostol group (16.0 ± 4.1 hours) when compared to vaginal group (9.39 ± 4.8 hours). However, the oral route was much easier when compared to vaginal route, but that advantage does not seem to transfer in the interval time.

There were several studies reviewed, in that some studies showed better effect for vaginal misoprostol, and some showed no significant differences between them.

In other reviewed studies there were significant differences between the two groups, which was similar to our study. In our study the maternal morbidities like diarrhoea, fever, PPH, shivering, vomiting and tachysystole were similar in both groups.There were no cases of uterine rupture in the study.

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Conflict of interest: None declared

CONCLUSION

The vaginal route of administration of misoprostol when compared to oral route of administration showed significant difference in ripening time of cervix. The effectiveness of different routes of administration was significant in our study with significantly shorter mean induction – delivery interval in vaginal group compared to oral group. Although there were few maternal morbidities seen in both groups, there were no statistically significant differences between two groups.

REFERENCES

1. Osterman MJK, Martin JA. National Vital Statistics Reports. Natl Vital Stat Reports. 2014;63(6):1–17.
2. Kochenour NK. Management of fetal demise. Clin Obstet Gynecol. 1987;30(2):322–30.
3. Hale RW, Zinberg S. Use of misoprostol in pregnancy. N Engl J Med. 2001;344(1):59–60.
4. Gottschall DS, Borgida AF, Mihalek JJ, Sauer F, Rodis JF. A randomized clinical trial comparing misoprostol with prostaglandin E2 gel for preinduction cervical ripening. Am J Obstet Gynecol. 1997;177(5):1067–70.
5. Ho PC, Ngai SW, Liu KL, Wong GCY, Lee SWH. Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy. Obstet Gynecol. 1997;90(5):735–8.
6. Ngai SW, Chan YM, Lam SW, Lao TT. Labour characteristics and uterine activity: Misoprostol compared with oxytocin in women at term with prelabour rupture of the membranes. BJOG An Int J Obstet Gynaecol. 2000;107(2):222–7.
7. Bartley J, Baird DT. A randomised study of misoprostol and gemeprost in combination with mifepristone for induction of abortion in the second trimester of pregnancy. BJOG An Int J Obstet Gynaecol. 2002;109(11):1290–4.
8. Nyende L, Towobola OA, Mabina MH. Comparison of vaginal and oral misoprostol, for the induction of labour in women with intra-uterine foetal death. East Afr Med J. 2004;81
9. Dodd JM, Crowther CA. Misoprostol for induction of labour to terminate pregnancy in the second or third trimester for women with a fetal anomaly or after intrauterine fetal death. Cochrane Database Syst Rev. 2010; 4):179–82.
10. Fadalla FA, Mirghani OA, Adam I. Oral misoprostol vs. vaginal misoprostol for termination of pregnancy with intrauterine fetal demise in the second-trimester. Int J

Gynecol Obstet. 2004;86(1):52–3.
11. Palod S, Nayak T. Use of misoprostol for termination of second and third trimester pregnancy with intrauterine foetal death. Int J Reprod Contraception, Obstet Gynecol. 2016;5(4):1216–20.
12. Bhandekar SS, Chauhan AR, Ambadkar A. Prospective Comparative Study of Oral Versus Vaginal Misoprostol for Second-Trimester Termination of Pregnancy. J Obstet Gynecol India. 2018