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A Comparison of Intravaginal Misoprostol with Intracervical Prostaglandin E_2 Gel for the Management of Dead Fetus in Utero

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ABSTRACT

Objective To compare the effectiveness and side effects of vaginal misoprostol with prostaglandin E_2 gel for induction of labour in intrauterine fetal death.

Design Prospective randomised trial.

Setting Department of Obstetrics and Gynaecology, Ramathibodi Hospital.

Subjects A total of 54 women with antepartum fetal death between 14 and 39 weeks of gestation was randomly assigned to have either 100 μg intravaginal misoprostol or 3 mg intracervical prostaglandin E_2 gel at 24 hours interval.

Results The mean induction to delivery interval was 24.3 hours for misoprostol and 23.0 hours for prostaglandin E_2 gel. The 24 hours success rate was 69% in misoprostol group compared to 64% in prostaglandin E_2 group. The mean dose of misoprostol used was 213.8 μg and for prostaglandin E_2 was 5.6 mg. The number of oxytocin used, the incomplete expulsion of placenta and the side effects were not significantly difference in either groups.

Conclusion Vaginal misoprostol in dose of 100 μg is effective, practical and inexpensive for induction of labour in intrauterine fetal death.

Key words : fetal death, intravaginal misoprostol, intracervical prostaglandin E_2, induction of labour

Fetal death at any stage of gestation is usually followed by spontaneous labour and expulsion of the products of conception in a relatively short time. However, the dead fetus may be retained in utero for several weeks. Besides the psychological burden that it imposes on the

mother, this condition may lead to infection or severe consumptive coagulopathy, especially when the dead fetus has been retained for more than four weeks.[1]

The superiority of prostaglandins over other methods for inducing labour after antepartum fetal death before term is now well recognized.[2] Prostaglandin E_2 (PGE_2) gel has been used effectively in the termination of pregnancy with dead fetus for many years in this institute,[3] but it is still expensive for developing country.

Misoprostol, which is a synthetic analogue prostaglandin E_1, is principally used to prevent peptic ulcer induced by the ingestion of nonsteroidal anti-inflammatory agents. Misoprostol has been found to be equally effective when used instead of prostaglandin E_2.[4,5]

A randomized controlled trial was therefore initiated to compare the effectiveness and side effects of intravaginal misoprostol and intracervical PGE_2 gel for termination of pregnancy with dead fetus.

Materials and Methods

From January 1995 to February 1997, 54 patients in whom a diagnosis of fetal death had been confirmed by clinical and ultrasound evaluation were randomized to have either 100 μg intravaginal misoprostol or 3 mg intracervical PGE_2 gel. All patients studied had normal coagulation profiles, performed on the day of admission for induction of labour with unfavorable cervices.

In the PGE_2 group, dinoprostone 3 mg vaginal tablet (Prostin E_2®, Upjohn) was crushed in a sterile container and mixed with 3 ml of hydro-ethyl cellulose (K-Y jelly,® Johnson and Johnson). The cervix was exposed by mean of bi-valved speculum. The vagina and cervix were wiped clean with a dry swab or cotton wool. The tip of a sterile rubber urine catheter (size 12-14 FR) was then pushed deep inside the external os, using uterine packing or sponge forceps to insert the catheter. The speculum was then removed and the gel was injected, followed by a further 2 ml of air to empty the contents in the rubber catheter. The patient was left in supine position for 20 minutes and subsequently no specific restriction was imposed. In the misoprostol group, half tablet (100 μg) of misoprostol (Cytotec®, Searle) was placed in the posterior vaginal fornix. In both groups, the treatment was repeated at 24 hours interval if it was found that the cervical dilatation had not progressed to three centimetres or more. If the cervix was found to be three centimetres or more dilated after 24 hours of application, intravenous oxytocin (10 units per 1000 ml 5% dextrose in water) was used instead for those patients with uterine size under 24 weeks. Patients with uterine size of 24 weeks or greater were transferred to labour ward and intravenous oxytocin (5 units per 1000 ml 5% dextrose in water) was started for augmentation purpose only. Analgesia (pethidine 100 mg) and antiemetic (promethazine HCl 50 mg) were administrated as required. After the expulsion of fetus and placenta, the placenta was examined for its completeness otherwise an evacuation of uterus was carried out.

All data were analyzed using the unpaired t-test where appropriate with P-value < 0.05 considered statistically significance. Epi info Version 5.01 b and Minitab Release 6.1 data analysis software programme were used.

Results

A total of 54 patients were enrolled in this study. The distributions of patients age, gestational age, and parity were similar in the misoprostol and PGE_2 gel groups (Table 1).

In Table 2, the induction to delivery time (hours) was 24.83 ± 21.47 in the misoprostol group compared to 22.98 ± 15.85 in the PGE_2 gel groups (P = 0.71). The mean dose used for misoprostol group was 0.214 ± 0.17 mg compared to 5.58 ± 4.17 mg in the PGE_2 gel group. The cumulative percentage number of delivery at 12, 24 and 48 hours was 27.6, 69 and 79.3 in the misoprostol group compared to 28, 64 and 88 in the PGE_2 gel group respectively. The number of oxytocin used was 17.2% in misoprostol group and 32% in the PGE_2 gel groups. The incomplete expulsion of placenta was 10.3% in the misoprostol group and 28% in the PGE_2 gel group. In Table 3, the side effects were more or less the same for both groups. The analgesia requirement was 31% in the misoprostol groups compared to 48% in the PGE_2 gel group.

Table 1. Patients' profile

Characteristics	Misoprostol n = 29	PGE_2 gel n = 25	P-value
Maternal age (years), mean ± SD	30.29 ± 5.65	28.48 ± 5.84	0.12
Gestational age (weeks), mean ± SD	26.86 ± 6.53	26.92 ± 6.61	0.97
Range	15-38	14-39	
Nulliparous (%)	13 (44.8)	18 (72.0)	0.08

Table 2. Results of the treatment in both groups

Effects	Misoprostol n = 29	PGE_2 gel n = 25	P-value
Induction - delivery interval (hours), mean ± SD	24.28 ± 21.47	22.98 ± 15.85	0.71
Range	6.42 - 75.83	0.58 - 58.0	
Mean dose used (mg)	0.214 ± 0.17	5.58 ± 4.17	-
Cumulative number delivered within			
12 hours (%)	8 (27.6)	7 (28)	
24 hours (%)	20 (69.0)	16 (64)	
48 hours (%)	23 (79.3)	22 (88)	
Number of oxytocin used (%)	5 (17.2)	8 (32)	
Number of incomplete expulsion of placenta (%)	3 (10.3)	7 (28)	

Table 3. Side effects

Side effects	Misoprostol n = 29	PGE_2 gel n = 25
Nausea and vomiting (%)	3 (10.3)	1 (4)
Temperature > 38.5 °c (%)	0	1 (4)
Analgesic required (%)	10 (34.5)	11 (44)

Discussion

The use of intracervical PGE_2 gel in achieving delivery after antepartum fetal death becomes a routine practice in this hospital since 1991. However, the treatment is expensive and requires skill. Misoprostol, a prostaglandin E_1 analogue, is easy to use and effective when placed the tablet in the vagina.[4,5]

This study has demonstrated that there was no difference whether intravaginal misoprostol or intracervical PGE_2 gel were used for the termination of intrauterine fetal death. All pregnancies were successfully terminated, although the mean induction to delivery time was longer, 24.3 hours in the misoprostol group and 23 hours in the PGE_2 gel groups, when compared with two other recent studies. In the first study, Bugalho et al[4] used 100 μg intravaginal misoprostol applied every 12 hours in 72 women at 18-40 weeks of pregnancy with intrauterine fetal death and the mean induction to delivery time was 12.6 hours. In the second study, Bugalho et al[5] reported 120 women with fetal death starting with 50 μg misoprostol with escalated dose to 800 μg at 6 hours interval compared with 36 women using intravenous oxytocin. The mean induction to delivery time was 14.8 hours in the misoprostol group and 31 hours in the oxytocin group (P-value = 0.001). Certainly, the mean induction to delivery time in each group in this study was better than oxytocin but they were longer than the time reported for misoprostol. Initially, we were not sure about the potency of misoprostol when used with fetal death, where the process itself tends to progress and also the rate of absorption for individual varies thus the time interval was set at 24 hours apart. Nevertheless, the mean induction to delivery time of dead fetus previous reported from this hospital for PGE_2 gel applied at 6 hourly interval twice a day in 74 woman was 17.6 hours compared favourably with 14.8 hours using misoprostol reported by Bugalho et al.[5] The 48 hours success rate can be improved if the time interval of each application is shortened with the minimum dosage remains at 50 μg. Further study is needed to establish the best time interval. In this study the misoprostol group required less oxytocin and appeared to be better at expelling the placenta than the PGE_2 gel group. This is probably due to its analogue property causing better uterine contraction.

Lastly, although misoprostol is inexpensive and can be stored at room temperature, it must be used with caution for being an analogue it is very potent. Its action can be unpredictable especially in multiparity with term pregnancy and the recent fetal death.

References

1. Pitkin RM. Fetal death : diagnosis and treatment. Am J Obstet Gynecol 1987 ; 157 : 538-9.
2. MacKenzie IZ. The therapeutic roles of prostaglandins in obstetrics. In : Studd J, editor. Progress in Obstetrics and Gynaecology. Vol 8. London : Churchill Livingstone, 1990 : 149-73.
3. Herabutya Y, O-Prasertsawat P. Intra-cervical prostaglandin E_2 gel in management of dead fetus in utero. Asia-Oceania J Obstet Gynaecol 1991 ; 17 : 335-9.
4. Bugalho A, Bique C, Machungo F, Faundes A. Induction of labor with intravaginal misoprostol in intrauterine fetal death. Am J Obstet Gynecol 1994 ; 171 : 538-41.
5. Bugalho A, Bique C, Machungo F, Bergstrom S. Vaginal misoprostol as an alternative to oxytocin for induction of labor in women with late fetal death. Acta Obstet Gynecol Scand 1995 ; 74 : 194-8.