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Comparison of The Efficacy of Intravaginal Misoprostol in Second-Trimester Pregnancy Termination between Live and Dead Fetuses

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ABSTRACT

Objective To study the complications and compare the success rate and abortion time interval between the live and the dead fetuses in second-trimester pregnancy termination with intravaginal misoprostol.

Study design A prospective comparative study.

Setting Department of Obstetrics and Gynecology, Chaoprayayommaraj Hospital.

Methods A total of 46 pregnant woman between 14 and 28 weeks of gestation with obstetric, medical, or genetic reasons for termination of pregnancy were recruited to receive 200 μg of misoprostol inserted intravaginally every 12 hours.

Results The rates of successful abortions within 12, 13 - 24 and 25 - 48 hours in dead fetuses were 69.04%, 19.04% and 11.19%, while in live fetuses were 0.00%, 75.00% and 25.00%, respectively. The success rates within 12 hours in live fetus group were significantly lower than those of the dead fetus group (p=0.018). No serious complication occurred in terms of hemorrhage, nausea and vomiting.

Conclusion Intravaginal misoprostol is an effective and safe method for second - trimester pregnancy termination. The success rate is higher and the abortion time is less in dead fetus pregnancy than those in the live fetus pregnancy.

Key words: termination of pregnancy, second trimester, misoprostol

Misoprostol is a synthetic 15-deoxy-16 hydroxy-methyl analog of prostaglandin E1 (PGE1). It is primarily used to inhibit gastric acid secretion and prevent peptic ulcer in patients taking nonsteroidal anti-inflammatory drugs. Because of its prostaglandin activity, it is also very useful for cervical ripening and induction of labor. Neto et al appeared to be the first reporting on the use of misoprostol for termination of fetal death in the second and third trimesters of pregnancy.[1] Intravaginal application of misoprostol in doses ranging from 800 to 1,600 μg was remarkably effective in attaining safe pregnancy interruption without serious complication in second trimester of pregnancy.[2] In case of highly unfavolable cervix, it was found that the intracervical application had significantly more effective results than the intravaginal application. For studying the intrauterine pressure, the intravaginal application could induce more myometrial contractily than the intracervical application and was more comfortable to apply.

Therefore, we chose to apply misoprostol intravaginally to induce abortion. Furthermore, the market price of 200 μg misoprostol (cytotec, Searle, Illinois, USA) is unexpensive compared to other prostaglandin analogs.

The purpose of this study was to evaluate the complications and compare the success rate and abortion time between the live and the dead fetuses in second- trimester pregnancy termination with intravaginal misoprostol.

Materials and Methods

The study population consisted of 46 pregnant women at 14 to 28 weeks, gestation, admitted to the Department of Obstetrics and Gynecology, Chaoprayayommaraj Hospital for termination of pregnancy between dead fetus group and live fetus group. All pateints have the medical, obstetrical and genetic seasons for pregnany termination. Exclusion criteria included 1) cervical bishop score > 4, 2) Lower genital tract infection, 3) maternal history of hypersensitivity to prostaglandin.

The patients were left in supine position for 1 hour after vaginal insertion of misoprostol. Vital signs and side effects were monitored every 4 hours. The progression of abortion was evaluated by cervical examination every 12 hours prior to subsequent dosing. The occurrence of abnormal signs and symptoms, such as diarrhea, fever, pain, nausea and vomiting was recorded. Diphenoxylate HCL 5 mg and acetaminophen 500-1,000 mg were orally given in case of diarrhea and fever respectively. Metoclopamide HCL 10 mg was intravascularly injected if nausea and vomiting occurred. Meperidine 50-100 mg was given intramuscularly on demand as narcotic analgesic for uterine pain. If a favourable cervix was attained but uterine contraction was inadequate (at least 3 contractions in 10 minutes) oxytocin infusion would be started at 1-2 mU/min and was gradually increased in dose increment of 1-2 mU/min at 30 minute interval as necessary. Complete abortion was defined as the expulsion of both the fetus and placenta without any additional operative procedures. If the conceptive products were not completely delivered or instrumental or manual evacuation was required, the condition was considered to be and incomplete abortion. Treatment success was defined as abortion occurred within 48 hours after the initial-dosing and no serious complication was noted. Fever was defined as any temperature $\geq 38^{\circ}C$ after induction. Postabortal hemorrhage was defined as blood loss in excess of 500 ml after abortion of the conceptive products.

The baseline data and outcome variables was installed in the microcomputer progtram SPSS PC+ (SPSS Inc.,Illinois, USA) for analysis. Fisher's exact test with Yate's correction was used to evaluate the success rate, the complete abortion rate, side effects. The differences were regarded as significant at p-value of 0.05.

Result

The characteristics of the patients is presented in Table 1. The two groups had similar mean age and parity. The mean gestational age for patients in the dead fetus group (17.78 weeks) was significantly less than that of the live fetus group (25.00 weeks). The indication for pregnancy termination are blighted ovum 24 cases (52.2%), dead fetus in utero 16 cases (30.4%) and congenital anomalies 6 cases (13.0%). The doses used of misoprostol for termination of pregnancy in the dead fetus group and live fetus group are not difference as shown in Table 2. The interval times to complete delivery of the conceptive products in the dead fetus group were significantly less than those of the live fetus group ($p<0.05$) as shown in Table 3. Cummulative rate of successful abortion within 12 and 13-24 hours was about 69.04% and 88.08% respectively in the dead fetus group, while were significantly more than those in the live fetus group 75.00%. Patients who had live fetus attained all complete abortion. Incomplete abortion was about 64.29% from dead fetus group and required curettage as shown in Table 4. Requirement of oxytocin to augment labor are not different in both group, but requirement of analgesia was more common in the live fetus group and significantly different from the dead fetus group ($p<0.05$) as shown in Table 5. No

severe side effects and complications occurred, only nausea and vomiting in our patients which could be controlled by metoclopamide 10 mg injection. The complication of postabortal hemorrhage was estimated blood loss of more than 500 ml due to uterine atony was observed in 4 patients of dead fetus group.

Table 1. Demographic characteristics of patients between live and dead fetuses

	Dead fetus (N = 42)	Live fetus (N = 4)	p-value
Age (years)	28.40 ± 8.0397	26.00 ± 9.6264	0.921
Parity	1.90 ± 1.1436	3.00 ± 2.8284	0.330
Gestational age (weeks)	17.78 ± 9.1852	25.00 ± 7.8528	0.012 *

Data presented as mean ± S.D. *Sig. p-value < 0.05

Table 2. Dose of misoprostol used for termination of pregnancy compared between live and dead Fetuses

		Dead fetus (N = 42)	Live fetus (N = 4)	p-value
200 Micro gram	(1 tab)	5 (11.90%)	1 (25.00%)	0.565
400 Micro gram	(2 tab)	13 (30.95%)	0 (0.00%)	
600 Micro gram	(3 tab)	18 (42.86%)	2 (50.00%)	
800 Micro gram	(4 tab)	6 (14.29%)	1 (25.00%)	

Table 3. Interval times to complete abortion of the conceptive products compared between live and dead fetuses

	Dead fetus (N = 42)	Live fetus (N = 4)	p-value
Abortion time ≤ 12 hours	29 (69.04%)	0 (0.00%)	0.018 *
Abortion time 13-24 hours	8 (19.04%)	3 (75.00%)	
Abortion time 25-48 hours	5 (11.19%)	1 (25.00%)	

* Sig. p-value < 0.05

Fisher's exact test used for data analysis when N < 5.

Table 4. Type of abortion

	Dead fetus (N = 42)	Live fetus (N = 4)	p - value
- Complete abortion	15 (35.71%)	4 (100.00%)	0.024 *
- Incomplete abortion (required Dilate +Curettage)	27 (64.29%)	0 (0.00%)	

* Sig. p-value < 0.05

Fisher's exact test used for data analysis when N < 5.

Table 5. Requirement of oxytocin and analgesia during termination of abortion

	Dead fetus (N = 42)	Live fetus (N = 4)	p - value
- Oxytocin augmentation	5 (11.90%)	1 (25.00%)	0.440
- Analgesics requirement	15 (35.71%)	4 (100.00%)	0.024 *

* Sig. p-value < 0.05

Data was analysed by using Fisher's exact test.

Discussion

There is significantly more difficulties, side effects, complications and expenses for termination of pregnancy in second trimester than first trimester pregnancies for intrauterine death, medical, obstetric and genetic reason. Surgical dilatation and evacuation of uterine cavity can result in uterine perforation and intestinal injury. Now, medical abortion with local administration of prostaglandins is preferable to dilatation and evacuation. Such treatment has been used to bring about cervical ripening and uterine contraction which is non-invasive and more physiological to expel the conceptive product.[5,6] The action of prostaglandin E2 analogs on cervical ripening by changes in proteoglycan metabolism and composition has been previously elucidated.[4] It is proved that the same local effect could be achieved with misoprostol, the prostaglandin E1 analog. Jain and Mishell has compared the efficacy and safety of 200(g of intravaginal misoprostol applied every 12 hours with those of 20 mg of dinoprostone (PGE2) administered intravaginally every 3 hours. They concluded that misoprostol was at least as effective as dinoprostone for the termination of second trimester pregnancy including both dead and living fetuses, but was less costly, more convenient to apply and asscociated with fewer side effects.[7] The use of intravaginal misoprostol at the dose of 100 μg every 12 hours has been reported to be safe, effective, practical and inexpensive method for induction of labor in intrauterine fetal death.[7] Vaginal administration of 100 μg misoprostol every 14 hours was also highly effective for induction of second trimester abortion.[8]

The comparison of the efficacy of intravaginal Misoprostol in second-trimester pregnancy termination between live and dead fetuses found that the success rates within 12 hours in live-fetus group were significantly lower than those of the dead-fetus group, this result same as the study of Srisomboon J and Pongpisuttinun S, the success rates within 12 and 24 hours in live-fetus group were significantly lower than those of the dead-fetus group.[9]

The present study has demonstrated that intravaginal application of relatively low doses of an analog of prostaglandin E1, misoprostol is an effective and safe method to induce abortion in the second trimester. The success rates were significantly shorter in the dead-fetus group compared with those of the live fetus. After fetal death, intrinsic change may occur in the uterus and cervix that make the myometrial cells sensitive to stimulant and cervical tissues favorable to ripening agent. Therefore, the cervixs of the patients with dead fetus tend to be more readily to efface and dilate when compared with that of the live fetus patient.

When the samples was small (less than 5), the statistics of Fisher's exact test with Yate's correction was used to evaluate the success rate, the complete abortion rate, and side effects. The differences were regarded as significant at p-value of 0.05.[10]

The suggestion for the further research study, if the misoprostol will use in pregnant woman and live fetus for illegal abortion in the second trimester, it should be convinced in the ethical aspect.

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