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Comparison of Intravaginal Misoprostol and Dinoprostone for Cervical Ripening and Labour Induction at Term with Unfavourable Cervix : a Randomized Controlled Study

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ABSTRACT

Objective To study the efficacy of 100 mcg misoprostol and 3 mg dinoprostone, both as intravaginal tablet for cervical ripening and labour induction.

Design A prospective randomized controlled study.

Setting Department of Obstetrics and Gynaecology, Rajavithi Hospital.

Subjects Sixty term pregnant women who had indicatons for labour induction with unriped cervix (Bishop score < 7) and no contraindication to prostaglandins.

Interventions All patients were randomized to receive either 3 mg dinoprostone or 100 mcg misoprostol as vaginal tablet.

Main outcome measures Mode of delivery, Bishop score before medication, after 6 and 12 hours of medication, treatment interval from insertion to delivery, Apgar score, maternal and neonatal complications.

Results There was no statistical difference between both groups with regards to obstetric characteristics and the mean pre-treatment Bishop scores. Bishop scores after 6 and 12 hours of medication and tachysystole were significantly higher in those receiving misoprostol ($P < 0.05$). Induction to delivery interval was significantly lower in those receiving misoprostol ($P < 0.05$). There was no significant difference in mode of delivery, Apgar score, hyperstimulation, neonatal and maternal complications.

Conclusion Intravaginal misoprostol (100 mcg) is more effective agent for cervical ripening and labour induction than intravaginal dinoprostone tablet (3 mg). However, misoprostol is associated with a higher prevalence of tachysystole than dinoprostone but with no difference in maternal and neonatal complications.

Key words : misoprostol, dinoprostone, intravaginal, induction of labour, unriped cervix

Cervical condition is probably the most important factor when deciding which labour induction methods should be used. During the last two decades, the concept of cervical ripening had gained momentum and involved treatment to render the cervix more favourable followed by a formal induction method.[1] Prostaglandin, placed in intravagina adjacent to the cervix, are used clinically to effect cervical softening and ripening to facilitate the induction of labour.[2] Prostaglandin E_2 (dinoprostone) 3 mg vaginal suppository has been used with significant effectiveness than placebo.[3,4]

In this country, we imported dinoprostone (Prostin E_2 ; Upjohn), a very expensive vaginal pessary (7 US$). Many low-socioeconomic patients who need to have labour induced with unriped cervix in Rajavithi Hospital can not afford it.

Misoprostol (Cytotec : Searle), a synthetic prostaglandin E_1 analogue, has been used for treating peptic ulcer and it is cost 0.4 US$ per one oral tablet of 200 μg. Several studies have shown good results in cervical ripening and labour induction.[5-8] Misoprostol was used in this randomized controlled study to compare with dinoprostone for cervical ripening and labour induction in patients with either medical or obstetric indications when the cervix was unfavourable (Bishop score < 7).

Materials and Methods

This study recruited 60 term pregnancy (≥ 37 weeks) who had indications for labour induction and unriped cervix (Bishop score < 7) with no contraindication to prostaglandins. Informed consent was obtained after proper counselling. From March 15 to September 15, 1995, the women were randomized to two groups each with 30 subjects receiving either 3 mg dinoprostone or 100 mcg misoprostol, as vaginal tablet. The initial Bishop score was evaluated and the women were monitored for fetal heart rate and uterine contraction by electronic fetal monitoring. Maternal vital signs were recorded hourly. After 6 and 12 hours, cervices were reevaluated in those women who had not yet delivered. In both groups, the dose was repeated every 12 hours until an adequate contraction pattern (three or more contractions in 10 minutes), satisfied change in Bishop score (three or more). The maximum dose of misoprostol was 200 mcg, or two doses of drug. The maximum dose of dinoprostone was 6 mg, or two doses of drug, oxytocin augmentation was permitted in patients who did not enter active labour within 4 hours after receiving the maximum dose. In case of abnormal labour pattern such as protracted or arrest of cervical dilatation in active phase with poor uterine contraction, oxytocin was recommended.

The data collected included indication for induction of labour, maternal age, gravidity, parity, gestational age, the Bishop scores before 6 hours and 12 hours after drug insertion, insertion to delivery interval, result of electronic fetal monitoring, birthweights and Apgar scores. The data was analysed using Chi-square test (χ^2), unpaired t-test, Fisher exact test and survival analysis. The level of statistical significance was at $P < 0.05$. All data was collected and analysed by using the computer programme strata.

Results

Obstetric characteristics of the studied population are shown in table 1. Thery were similar in both groups. Indications for induction of labour are shown in table 2 and there were no significant difference in both groups. Hypertensive disorders in pregnancy was the most

common indication for induction of labour in both groups (43.3% in misoprostol group and 30% in dinoprostone group).

Table 3 shows Bishop score before, after and medication at 6 and 12 hours. The mean Bishop score in the misoprostol group was significantly higher than those in dinoprostone group, both at 6 and 12 hours after medication.

Treatment intervals (insertion to delivery, insertion to oxytocin and oxytocin to delivery) are shown in table 4, and only the insertion to delivery in the misoprostol group was significantly shorter than those in dinoprostone group.

Table 5 shows the results of electronic fetal monitoring. Tachysystole in the misoprostol group was significantly higher than those in dinoprostone group. Mode of delivery is shown in table 6. The misoprostol group had a higher rate of spontaneous labour, and a significant lower rate of oxytocin augmentation than those in dinoprostone group. The birthweight, Apgar score at one and five minutes were not significantly different in both groups. There was no neonatal and maternal complication.

Discussion

A good randomization was achieved as indicated by the obstetric characteristics, indications for induction of labour, Bishop score before medication were similar in both groups. The less

Table 1. Obstetric characteristics

Characteristics	Misoprostol (N = 30)	Dinoprostone (N = 30)	P
1. Age (y)	27.8 ± 5.85	28.47 ± 4.30	NS
2. Gravidity	2.11 ± 1.30	2.05 ± 1.22	NS
3. Parity	1.73 ± 0.83	1.73 ± 0.83	NS
4. Gestational age (wk)	39.9 ± 1.72	39.8 ± 1.95	NS

Data are presented as mean ± standard deviation

NS = Not significant by unpaired t-test, P > 0.05

Table 2. Indications for induction of labour

Indications	Misoprostol	Dinoprostone	P
1. Postdate	9	12	NS
2. Post-term	5	4	NS
3. Hypertensive disorders in pregnancy	13	10	NS
4. Other	3	4	NS

Data are presented as mean ± standard deviation

NS = Not significant by Chi-square or Fisher Exact test

Table 3. Bishop score

Characteristics	Misoprostol	Dinoprostone	P
- Score before medication	3.97 ± 0.96	4.20 ± 1.06	NS
- Score after 6 hr of medication	9.63 ± 0.265	7.43 ± 1.91	< 0.001*
- Change in score after 6 hr of medication	6.00 ± 2.57	3.23 ± 1.74	< 0.001*
- Score after 12 hr of medication	11.56 ± 2.33	10.17 ± 2.42	0.027*
- Change in score after 12 hr of medication	8.17 ± 1.72	5.97 ± 2.39	< 0.001*

Data are presented as mean ± standard deviation

NS = Not significant by unpaired T-test (P > 0.05)

* = significant by unpaired T-test (P < 0.05)

Table 4. Treatment interval (hr)

Treatment interval	Misoprostol	Dinoprostone	P
- Insertion to delivery (min)	750 ± 311 (N = 30)	1,033 ± 314 (N =30)	0.025*
- Insertion to oxytocin (min)	750 ± 340 (N = 3)	755 ± 127 (N = 17)	NS
- Oxytocin to delivery (min)	363 ± 115 (N =3)	435 ± 213 (N = 17)	NS

Data are presented as mean ± standard deviation

NS = Not significant by unpaired T-test (P > 0.05)

* = significant by unpaired T-test (P < 0.05)

Table 5. Results of electronic fetal monitoring

Results	Misoprostol (N)	Dinoprostone (N)	P
- Normal	14	23	0.034*
- Tachysystole	14	5	0.026*
- Hyperstimulation	1	0	NS
- Hyperstimulation with fetal distress	1	2	NS

NS = Not significant by Fisher exact T-test P > 0.05

* = significant by Chi square test P < 0.05

Table 6. Mode of delivery and oxytocin augmentation

Characteristics	Misoprostol		Dinoprostone		
	N = 30	%	N = 30	%	
Spontaneous labour	27	90	13	43.3	0.00037*
Oxytocin augmentation	3	10	17	56.7	0.00037*
Spontaneous vaginal	24	80	20	66.7	NS
Forceps extraction	0	0	1	3.3	NS
Vacuum extraction	2	6.7	2	6.7	NS
Caesarean section	4	13.3	7	23.3	NS

NS = Not significant by Chi-square or Fisher Exact test

* = significant by Chi-square or Fisher Exact test

expensive misoprostol appeared to be better than that of dinoprostone with regards to cervical ripening and induction of labour. Fletcher et al[8] reported significant different result in the mean change of Bishop score in the misoprostol group. In our study, we had the same significant different results and also a significance better Bishop score and mean change in Bishop score after 6 hours of drug insertion in the misoprostol group. These results might be interpreted that misoprostol was more effective than dinoprostone for cervical ripening and induction of labour. This study also showed more significant different results in the misoprostol group such as : shorter intervals of insertion to delivery time, required less oxytocin augmentation, higher incidence of spontaneous labour and tachysystole than did patients in dinoprostone group.

Herabutya et al[9] reported no significant difference in Bishop score change after 12 and 24 hours of medication in 100 mcg intravaginal misoprostol group compared to 1.5 mg intracervical dinoprostone gel group for the same reason. But in our study, we had significant difference in Bishop score change after 6 and 12 hours after medication.

Srisomboon et al[10] also reported no significant difference in terms of Bishop score change between 100 mcg intracervical and 100 mcg intravaginal misoprostol. Herabutya et al[9] reported one uterine hyperstimulation in the misoprostol group and no significant difference in tachysystole. There was also no significant difference in tachysystole between 100 mcg intracervical and 100 mcg intravaginal misoprostol (24% vs 32%) reported by Srisomboon et al.[10] Wing et al[11] used the lower dose 50 mcg tablet of intravaginal misoprostol every 3 hour for a maximum of 6 doses compared with 0.5 mg of intracervical prostaglanden E_2 in gel form every 6 hour for a maximun for 3 doses. They found that interval from start of induction to vaginal delivery was significanty shorter in the misoprostol group and used significantly less oxytocin than in the dinoprostone group. But there was a significantly high prevalence of tachysystole (36.7%) and meconium passage (27.9%) in the misoprostol group than in the

dinoprostone group.

However, Chuck et al[12] reported the same results as the study of Wing et al[11] but there was no significant difference in adverse maternal, fetal or neonatal effects. When Wing et al[14] decreased the dose of misoprostol to 25 mcg in the same methodology as their previous study,[11] they reported the same effectiveness of misoprostol compared with dinoprostone. But the complications such as tachysystole and thick meconium passage occurred with similar frequency in both groups. Different dosing regimen had influence in the effectiveness for cervical ripening and induction of labour. Patients with the 3 hour dosing schedule had significant shorter intervals from start of induction to vaginal delivery, and less frequently required oxytocin augmentation. There was no significant difference between groups in the frequency of tachysystole and meconium passage.[14]

Varaklis et al[15] used intravaginal misoprostol (25 mcg) tablet every 2 hours for a maximum of 6 doses compared with intracervical gel (0.5 mg) dinoprostone every 6 hours for a maximum of 2 doses. They reported that the patients in misoprostol group had significantly reduced mean time from drug administration to onset of 3 contractions in 10 minutes ($P = 0.007$), mean time to rupture of membranes ($P = 0.01$) and mean time to delivery ($P = 0.006$). Three patients in the misoprostol group experienced uterine hypertonus but no related fetal morbidity.

In conclusion intravaginal misoprostol is more effective agent for cervical ripening and induction of labour than intravaginal dinoprostone tablet. However, intravaginal misoprostol is associated with a higher prevalence of tachysystole than intravaginal dinoprostone but with no difference in maternal and neonatal complications. Further investigation to compare the safety and effectiveness cervical ripening and induction of labour for different dosing regimens is needed in a large number of our Thai patients.

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