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Randomized Controlled Trial of Intravaginal 50 mcg Misoprostol and 3 mg Dinoprostone for Cervical Ripening and Labour Induction at Term with Unfavorable Cervix

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ABSTRACT

Objective To study the efficacy of 50 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 M.O.P.H. Bangkok.

Subjects Eighty term-pregnant women with indicatons for labour induction and unriped cervices (Bishop score < 7) with no contraindications to prostaglandins therapy.

Interventions All patients were randomized to receive either 50 mcg. misoprostol or 3 mg dinoprostone 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 the two groups with regards to obstetric characteristics, pre-treatment Bishop score, 6 and 12 hours after medication. Tachysystole was significantly higher in those receiving misoprostol ($P < 0.05$). Induction to delivery interval, induction to oxytocin stimulation interval and oxytocin stimulation to delivery interval were 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 (50 mcg) is more effective agent for cervical ripening and labour induction than intravaginal dinoprostone tablet (3 mg). However misoprostol is associated with a significant higher prevalence of tachysystole than dinoprostone, but with no significant difference in neonatal and maternal complications.

Key words : controlled trial, misoprostol, dinoprostone, cervical ripening and labour induction

Labour induction in a woman with unfavourable cervix is likely to fail if one cannot prevail the cervix to ripe. This problem, to some extent, has been overcome with the use of prostaglandin. Previously we have reported our success with intravaginal misoprostol, a synthetic prostanglandin E_1 analogue. It is more effective than dinoprostone which is the only drug approved by the Food and Drug Administration for cervical ripening and labor induction in women with Bishop score < 7[1]

In the previously described regimen of misoprostol 100 mcg every 12 hours to a maximum of 2 doses, we found a significant higher frequency of uterine tachysystole in patients treated with misoprostol compared with prostaglandin E_2 vaginal tablet. In this study a lower dose of 50 mcg misoprostal inserted every 6 hours to a maximun of three doses was evaluated. Our objective was to test the hypothesis that misoprostol is as effective as dinoprostone vaginal tablet for cervical ripening and labor induction, and that delivery can accomplished with a reduction of the incidence of uterine tachysystole encountered in our previous study with the higher dosage of 100 mcg of misoprostol.[1]

Materials and Methods

This study recruited 80 term pregnancy (≥ 37 weeks) who had indications for labour induction with unriped cervices (Bishop score < 7) and with no contraindications to prostaglandins therapy. Informed consent was obtained after proper counselling. From December 1, 1995 to August 30, 1996, the women were randomized into two groups receiving either 3 mg dinoprostone or 50 mcg misoprostol as a vaginal tablet by dividing 200 mcg tablet roughly into four 50 mcg doses. The initial Bishop score was evaluated and the women were monitored for fetal heart rate and uterine contraction by electronic fetal monitoring after the insertion of the drugs. 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 6 hours until an adequate contraction pattern (three on more contractions in 10 minutes) with satifactory changes in Bishop score (three or more). The maximum dose of misoprostol was 150 mcg, on three separated doses. The maximum dose of dinoprostone was 9 mg, on three separated doses. Oxytocin augmentation was permitted in patients who did not enter active labor within 4 hours after receiving the maximum dose. In case of abnormal labor pattern such as protracted or arrest of cervical dilatation in active phase with poor uterine contraction, oxytocin augmentation was also commenced.

The data collected included indications for induction, maternal age, gravidity, parity, gestational age, initial Bishop score, Bishop score at 6 and 12 hours after drug insertion, insertion to delivery interval, result of electronic fetal monitoring, birthweights and Apgar score. 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 $P < 0.05$. All data was collected and analysed by using the computer programme strata.

Results

Obstetric characteristics of the studied population are shown in table 1. They were similar in both groups. Indications for induction of labour are shown in table 2 and there were no significant difference in both groups. Postdate was the most common indications for induction of labour in both groups (45% in misoprostol group

and 50% in dinoprostone group)

Table 3 shows Bishop score before and after 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. There were only 3 cases (7.5%) in the misoprostol group and 10 cases (25%) in the dinoprostone group required the second doses.

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

Table 5 shows the results of electronic fetal monitoring. Tachysystole in the misoprostol group was significantly higher than those in the dinoprostone group. Mode of delivery is shown in table 6. The misoprostol group had a significant lower rate of oxytocin augmentation than those in the dinoprostone group. The birth weight and Apgar score at one and five minutes were not significantly difference in both groups. There was one case of postpartum hemorrhage from uterine atony in the misoprostol group. In the dinoprostone group two women had postpartum hemorrhage ; one was due to retained placenta and the other was due to cervical tear after vacuum extraction. However maternal complications were not significantly difference in both

Table 1. Obstetric characteristics

Characteristics	Misoprostol (N = 40)	Dinoprostone (N = 40)	P
1. Age (yrs)	22.45 ± 5.53	24.28 ± 4.87	NS
2. Gravidity	1.58 ± 1.01	1.75 ± 0.84	NS
3. Parity	0.48 ± 0.78	0.60 ± 0.67	NS
4. Gestational age (wks)	40.43 ± 1.28	40.63 ± 1.17	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 (N = 40)	Dinoprostone (N = 40)	P
1. Postdate	18	20	NS
2. Post-term	7	4	NS
3. Hypertensive disorder in pregnancy	10	12	NS
4. Others	5	4	NS

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

Table 3. Bishop score

Characteristics	Misoprostol (N = 40)	Dinoprostone (N = 40)	P
- Score before medication	4.13 ± 0.82	4.23 ± 0.08	NS
- Score after 6 hrs of medication	8.80 ± 1.88	7.50 ± 1.26	< 0.001*
- Change in score after 6 hrs of medication	4.68 ± 1.06	3.28 ± 0.46	< 0.001*
- Score after 12 hrs of medication	11.83 ± 1.53	10.40 ± 1.24	< 0.05*
- Change in score after 12 hrs of medication	7.70 ± 0.71	6.18 ± 0.44	< 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 (hrs)

Treatment interval	Misoprostol	Dinoprostone	P
- Insertion to delivery (min)	689.52 ± 171.60 (N = 40)	967.20 ± 141.42 (N = 40)	< 0.001*
- Insertion to oxytocin (min)	640.0 ± 240.0 (N = 7)	665 ± 200 (N = 15)	< 0.001*
- Oxytocin to delivery (min)	350 ± 150 (N = 7)	410 ± 150 (N = 15)	< 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 5. Results of electronic fetal monitoring

Results	Misoprostol (N = 40)	Dinoprostone (N = 40)	P
- Normal	14	28	0.034*
- Tachysystole	23	11	0.026*
- Hyperstimulation	3	1	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		P
	N = 40	%	N = 40	%	
Spontaneous labour	33	82.5	25	62.5	< 0.001*
Oxytocin augmentation	7	17.5	15	37.5	< 0.001*
→ Spontaneous delivery	31	77.5	28	70.0	NS
→ Forceps extraction	2	5	5	12.5	NS
→ Vacuum extraction	1	2.5	3	7.5	NS
→ Caesarean section	6	15	4	10.0	NS

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

* = significant by Chi-square of Fisher Exact test

groups. There was no neonatal complication in either groups.

Discussion

In this study the misoprostol dose was reduced from 100 mcg to 50 mcg and the interval was shortened to 6 hours with the number of dose limited to three. The incidence of tachysystole in this study (55%) was not difference from our previous study.[1] Inspite of the reduction of the dosage only 3 cases (7.5%) received the second dose of misoprostol.[1] This could be due to the small size of the tablet which was easier to dissolve and one still does not know the correct dose to use. In the meta-analysis of misoprostol for cervical ripening and labour induction,[2] the tachysystole was significantly higher when compared with the use of dinoprostone, but the incidence of hyperstimulation was not significantly difference between the two groups. (The results of this study agreed with that.)

The incidence of tachysystole in this study (55%) is higher than other previous studies which varied from 4.2 to 46.7%.[1-12] Although, the incidence of hyperstimulation was higher in the misoprostol group, this difference did not achieve statistical significance. In this study, women who received misoprostol had similar cesarean rate ($p > 0.05$) as those received dinoprostone. But in the meta-analysis misoprostol group had a significantce lower overall cesarean rate than the dinoprostone group.

The authors of the meta-analysis reported that the significant lower overall cesarean rate in the misoprostol group could be explained from the heterogeneity of treatment effect across the studies. It appeared that the Campos study was an important contributor to the overall heterogeneity due to its large variability in cesarean rate between the misoprostol (3.8%) and the control (25.3%) groups.[8]

In conclusion, 50 mcg intravaginal misoprostol is an effectiveness and safe agent to use for labour induction. Although incident of tachysystole was significantly higher than in dinoprostone group but the hyperstimulation rate was not significantly difference between the two groups.

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