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A Randomised Double-Blind Study of Vaginal Misoprostol vs Dinoprostone for Cervical Ripening and Labour Induction in Prolonged Pregnancy

H Y Lee

ABSTRACT

Background: Dinoprostone, is presently used in our standard protocol for cervical ripening and labour induction. In search for a cheaper alternative, misoprostol has been found to be a good substitute. In view of the potential saving it might offer, we set out to test its efficacy against the standard dinoprostone.

Methods: A randomised double-blind study involving 50 pregnant women with prolonged pregnancy, treated at a government hospital in Malaysia, was carried out. Two hundred µg of intravaginal misoprostol were compared with 3 mg of dinoprostone in each treatment arm.

Results: In the misoprostol group, labour was successfully established in 92% of cases compared to 64% in the dinoprostone group (p=0.04). The induction-delivery interval was shorter with more women delivering within 12 hours (72% vs 28%, p=0.047). Maternal and neonatal complications, mode of delivery, the need for oxytocin and pethidine were quite similar statistically. Polysystole was more frequent (28% vs 12%, p=0.28) in the misoprostol group but it was not associated with fetal distress.

Conclusion: The study showed that misoprostol was a more effective drug in labour induction.

Keywords: misoprostol, prolonged pregnancy, labour induction

INTRODUCTION

Induction of labour is an integral component of any maternity practice. About 5% - 40% of all labours are induced for one reason or another[1-4]. In this part of the world and in the United Kingdom, prostaglandin (PG) E2, like dinoprostone, has been the standard agent used[5]. It was first introduced by Calder and Embrey in 1973[6] and has since established itself in many maternity units inspite of its prohibitive cost.

At the Kuantan General Hospital, Malaysia, we have on average, 3 cases of labour induction a day. Our protocol states the use of 2 doses of 3 mg vaginal dinoprostone at 6-hourly interval. On average, we use about 180 tablets of dinoprostone a month at a cost of SGD100.35 per tablet[7a]. This takes up a significant portion of our drug budget.

Recently, an ulcer-healing drug, misoprostol, has been found to be effective and safe for use in labour induction[8-10]. This agent, an analogue of PG E1, costs only SGD1.88 per 200 µg tablet[7b]. It can be stored at room temperature. Its use is also less cumbersome unlike dinoprostone where after removal from the fridge, requires 30 minutes of warming before use[11].

In view of the possible financial saving, we decided to compare its effectiveness with dinoprostone in the induction of labour for low risk women with prolonged pregnancy. The study was carried out following approval from the local ethical committee of the hospital.

METHODS

From 1 January 1996, all women with prolonged pregnancy (Term +10 or more days) admitted for the induction of labour were screened for suitability to be included in this study.

The selection criteria were: 1) para 3 or less with a single pregnancy and cephalic presentation; 2) no previous Caesarean section or contraindication to prostaglandin and an uncomplicated pregnancy and, 3) a modified Bishop score of 6 or less. The role of PG E2 with a Bishop score of 7 or more is questionable[12]. An informed consent was obtained for every case entered into the study.

Assuming an established labour rate of 100% with the use of 200 µg of misoprostol[8,10] compared to 55% with the use of 3 mg of dinoprostone[10], 25 patients were required in each treatment arm to attain a 95% accuracy in detecting a difference at 5% significance level.

After a case was recruited, randomisation of the treatment was done by drawing a sealed envelope containing a coded number. The author personally assessed all the cases until transfer to the labour room. The cervical favourability was recorded according to the modified Bishop score[13].

An independent clinician not involved in the study was then called in to insert the type of PG allocated to that coded number by referring to a masterlist. The rest of the staff including the author were blinded to the type of treatment given.

Either misoprostol tablet 200 µg or dinoprostone 3 mg was used intravaginally at 6-hour interval with a maximum of 2 doses per patient. A review of the

Department of Obstetrics & Gynaecology
Kuantan General Hospital
Jalan Tanah Putih
25000 Kuantan
Pahang, Malaysia

H Y Lee, MBBS, MRACOG, MRCOG (UK)
Registrar

B11, 5 Jermal Court
Jalan Bagan Jermal
10250 Georgetown
Penang

cervix was done every 6-hourly until the patient was ready for labour and subsequently transferred to the labour room. If no established labour ensued, intravenous oxytocin was then given to the patient. However, if still no cervical ripening was achieved after 24 hours, a Caesarean section was then performed as a result of failed induction.

Throughout the study, regular monitoring of temperature, blood pressure, pulse rates, contraction and fetal heart rates were undertaken. Intermittent cardiotocographic tracings were also done. Both the mother and baby were followed up until discharged.

All the data were duly collected and the type of PG used was revealed only at the end of the study. Statistical analysis was undertaken with the use of either the student t-test or X2 method. This was performed using the statistical package Epi Info version 5, Mac 1991.

RESULTS

Patient characteristics

Patient characteristics in both treatment groups were comparable as depicted in Table I.

Table I - Patient characteristics

Attributes Mean (SD)	Misoprostol N=25	Dinoprostone N=25	p value
Age (years)	26.3 (4.8)	26.5 (4.4)	0.88
Parity	1.3 (1.2)	1.1 (1.0)	0.43
Post-date (days)	12.5 (2.1)	12.6 (2.6)	0.81
Height (cm)	153.2 (5.5)	155.5 (6.2)	0.18
Weight (kg)	63.4 (9.9)	67.7 (10.8)	0.15
Birthweight (gm)	3,134 (463)	3,070 (306)	0.57
Initial Bishop	4.1 (1.1)	4.1 (1.2)	1.00
Malay patient	21 (84%)	18 (72%)	0.49

No significant difference

Table II - Induction outcome

Attributes Freq (%)/Mean (SD)	Misoprostol N=25	Dinoprostone N=25	p value
Established labour rate*	23 (92%)	16 (64%)	0.04
Induction to delivery/min	676.1 (411)	874.9 (406)	0.09
Increase in Bishop score over 6 hours*	3.3 (2.06) # (N=22)	2.0 (2.02) (N=22)	0.038
Number delivered within 6 hours	5 (20%)	3 (12%)	0.35
Number delivered within 12 hours*	18 (72%)	7 (28%)	0.047
Oxytocin used	5 (20%)	8 (32%)	0.52
Pethidine used	16 (64%)	21 (84%)	0.20
Undissolved PG	6 (24%)	7 (28%)	1.00
Second PG used	10 (40%)	17 (68%)	0.09

NB: # 3 patients in each group delivered in less than 6 hours
* Significant difference at p=0.05

Induction outcome

Patients who received misoprostol achieved a significantly higher established labour rate (92%) as compared to dinoprostone (64%, p=0.04). The induction to delivery interval was shorter with a mean of 11.3 hours and the mean increase in modified Bishop score was significantly higher. The need for oxytocin drip and pethidine injection was lesser although this is not statistically significant.

In the misoprostol group, more women (72%) delivered within 12 hours of induction. Sixty percent of the women delivered after only one dose of misoprostol whereas 68% of the women in the dinoprostone group required a second dose before delivery.

One in 4 women however, had incomplete absorption of the PG (irrespective of the type of PG administered). Most of them required a second dose of the PG. All were noted to have thick and viscid cervical mucus on swabbing of the vagina. Labour ensued in all of them following the second dose of PG except for 1 who needed a Caesarean section.

Mode of delivery

Majority of the women delivered vaginally. Four women in the dinoprostone group had Caesarean section done; 2 for failed induction, one had hyperstimulation syndrome and another had fetal distress with thick meconium. The 2 Caesarean sections done (from the misoprostol group) were due to fetal distress.

Maternal and neonatal outcome

Four women in the dinoprostone group had maternal complication; one patient had hyperstimulation syndrome, another had precipitate labour with second degree tear and 2 others had post-partum haemorrhage (PPH) following Caesarean section for failed induction. The cause of PPH was uterine atony. In the misoprostol group, one patient had manual removal of placenta due to a snapped cord.

The estimated blood loss was higher in the dinoprostone group which was attributed to PPH. As a result, the maternal hospitalisation was also slightly longer.

There was no significant difference in terms of Apgar score at both 1 and 5 minutes between the 2 treatment groups. Their mean hospital stay was also comparable. There were 3 moderate meconium aspirations, 2 in the misoprostol group and one in the dinoprostone group. One 3.8 kg baby had shoulder dystocia and another had scalp abrasion following a ventouse, both were from the misoprostol group. All the babies were discharged well except for one with right brachial plexus injury due to shoulder dystocia.

Polysystole (ie more than 5 contractions in 10 minutes) was the main side effect noted. Others included: giddiness in one patient and vomiting in another, both patients received dinoprostone. The incidence of polysystole was higher with the use of misoprostol. However, it was not associated with any fetal distress. The only woman with hyperstimulation syndrome (polysystole plus fetal distress) belonged

Table III - Mode of delivery

Mode of delivery Frequency (%)	Misoprostol N=25	Dinoprostone N=25	p value
Spontaneous vaginal	20 (80)	19 (76)	1.00
Ventouse	3 (12)	0	0.12
Forceps	0	2 (8)	0.24
Caesarean	2 (8)	4 (16)	0.33

No significant difference

Table IV - Maternal and neonatal outcome

Attributes Freq (%)/Mean (SD)	Misoprostol N=25	Dinoprostone N=25	p value
Maternal complication	1 (4%)	4 (16%)	0.35
Estimated blood loss (mL)	180 (48)	246 (336)	0.18
Maternal hosp. stay (day)	2.2 (0.6)	2.6 (1.0)	0.08
AS 1 min	7.7 (0.7)	7.6 (1.3)	0.69
AS 5 min	8.9 (0.4)	8.7 (1.1)	0.39
Neonatal complication	4 (16%)	1 (4%)	0.17
Neonatal hosp. stay (days)	2.9 (2.3)	2.7 (1.0)	0.69
Polysystole	7 (28%)	3 (12%)	0.28
Other side effects	0 (0%)	2 (8%)	0.24

No significant difference
AS – Apgar score

to the dinoprostone group and she delivered via emergency Caesarean section.

Pre- and post-treatment blood pressure, pulse rates and temperature did not change significantly in both treatment groups.

DISCUSSION

There is no doubt that induction of labour confers benefit in prolonged pregnancy[14]. However, this can be a costly affair when the cervix is unfavourable for delivery. Until now, the agent of choice is PG E2[15] and it costs SGD100.35 per 3 mg tablet[7a].

Misoprostol, an analogue of PG E1 appears to be a perfect substitute. It is cheaper compared to PG E2 and does not require refrigeration. A few studies have shown that it is effective and safe[8-10]. A recent study by Fletcher et al using 100 μg of vaginal misoprostol as a single dose, reported an established labour rate of 78%. However, the induction to delivery interval was long, with a mean of 21.8 hours[10].

In this study, we used 200 μg of misoprostol hoping to achieve a less protracted labour induction period. The 6-hour interval and a maximum of 2 doses used were stipulated to coincide with our dinoprostone protocol.

Our results showed that intravaginal misoprostol was a more effective agent for cervical ripening and labour induction. It gave a significantly higher established labour rate and increase in modified Bishop score over 6 hours. The induction to delivery period was reasonably shorter with a mean of 11.3 hours.

The main side effects observed with the use of misoprostol was polysystole. The incidence was relatively high (28%) compared to 9.4% reported by Fletcher[10] and 17% by Margulies[16]. Sanchez-Ramos reported an even higher incidence of polystole (38%)[8]. Interestingly, there was no fetal distress associated with it, as was found in this study. On the other hand, dinoprostone, which showed less frequent polysystole, had 1 in 3 cases associated with fetal distress.

There was lesser maternal complication in the misoprostol group, probably due to its higher efficacy. No systemic effects were noted with respect to blood pressure, pulse rates or temperature.

Neonatal complications were slightly higher but the difference was not significant. Furthermore, a shoulder dystocia and scalp abrasion could not be attributed to the drug itself. Admittingly, the number of subjects was too small and Apgar scores might not be the best measures.

In conclusion, misoprostol was more effective than dinoprostone in ripening the cervix and inducing labour for prolonged pregnancy. It had no serious side effects to both mother and baby. However, the higher incidence of polysystole unrelated to fetal distress needs further study.

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