COMPARISON OF DINOPROSTONE PLUS OXYTOCIN AND OXYTOCIN ALONE FOR INDUCTION OF LABOR

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Abstract- Role of labor induction has increased in the last decade due to the early detection of fetal jeopardy. Although very useful, oxytocin alone is not always successful for induction of labor. In a randomized clinical trial we compared vaginal dinoprostone plus oxytocin with oxytocin alone for induction of labor in 91 pregnant women at 40 weeks or greater gestation with Bishop scores ≤ 4. Forty six patients assigned to the dinoprostone group received 3 mg intravaginal dinoprostone. Six hours later the Bishop score was evaluated and if the patient had not at least 3 contractions in 10 minutes lasting for more than 40 seconds, intravenous oxytocin was started at a dose of 6 mu/min and increased by 6 mu/min at 40 minute intervals until adequate uterine activity. Forty five patients assigned to the oxytocin group underwent oxytocin induction from the start of labor induction. Although the Bishop score change after 6 hours of receiving vaginal dinoprostone from 2.54 to 4.97 was statistically significant, the oxytocin only group had a much better response with a change from 2.60 to 6.28. Median time between induction to the start of active labor was significantly shorter in the oxytocin alone group ($P = 0.04$). Median time between induction to delivery and the rate of cesarean did not differ significantly in these groups ($P > 0.05$). It was concluded that single dose of dinoprostone is effective for initiating labor in patients with an unfavorable cervix and appears safe but it is not as effective as oxytocin.
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INTRODUCTION

The role of labor induction has been gradually increased in the last decade due to the early detection of fetal jeopardy, improvement of neonatal therapy and availability of cervical ripening agents (1). Induction of labor in the presence of an unfavorable cervix is now performed in approximately 10% of all pregnancies (2). However, the choice of agent for induction of labor is still an unresolved problem in

obstetrics. Clinicians have used numerous agents, both mechanical and pharmacologic, for cervical ripening and to decrease the duration of labor and the risk of failed induction and operative delivery (3). Oxytocin alone is very useful for induction of labor but is not always successful, especially in patients with low Bishop scores.

Use of dinoprostone (PGE2) for ripening of the cervix in near term pregnancies that need to be delivered has been suggested (4, 5). More than 70 studies on the pharmacologic methods of labor induction have centered on preparations of PGE2 delivered by a variety of vehicles, concentrations, dosing schedules and routes of administration (6). Recently, the use of 10 mg vaginal prostaglandin E2 for cervical ripening has been approved. With this

dose the rate of drug release is less than the gel and its efficiency is the same. However, it can be removed if there is uterine hyperstimulation (4). There are numerous treatment modalities and different doses have been administrated but it is believed that a single dose of intravaginal PGE2 can induce labor faster (7). Also, a low dose of prostaglandin (2-5 mg) can be as effective as the higher doses (8).

With respect to the ease of use of a single dose of dinoprostone for medical personal and patients, we sought to determine whether either method of single dose of dinoprostone with oxytocin or oxytocin alone would result in a shorter time to delivery.

MATEIRALS AND METHODS

The study sample consisted of 91 women referred to Mirza Kouchak Khan Hospital from May 2001 to March 2003. These women were divided into two groups by stratified randomization technique, 45 women in oxytocin alone group and 46 in dinoprostone plus oxytocin group. The informed consent was obtained from all of these patients.

The inclusion criteria included being 16 to 45 years old and post date based on their last menstrual period or sonography in the first half of gestation and having singleton pregnancy with the fetus in the cephalic presentation, unfavorable cervix defined as a bishop score of ≤ 4, intact membranes, a reassuring fetal heart rate tracing and no more than two painful contractions in a 10 minute period. Women were excluded from this study if they had a prior cesarean delivery or a uterine scar, severe unstable preeclampsia, fetal heart rate abnormality, placenta previa or vaginal bleeding, ruptured membranes, suspected chorioamnionitis, any contraindication to vaginal delivery, or a contraindication to receiving prostaglandins (history of glaucoma, liver or renal or lung or preexisting cardiac disease).

After enrollment, baseline data, including maternal age, gestational age, gravidity, parity, cervical Bishop score and indications for induction were recorded. Those assigned to the dinoprostone group received a 3 mg dinoprostone tablet intravaginally. Before administration of each dose, the patient was evaluated and a cervical exam was performed. Afterward the patient was evaluated every

one hour for vital signs, every 10 minutes for fetal heart rate and every 15 minutes for uterine contractions in the labor ward. Six hours later, the Bishop score was evaluated again and if the patient had not at least 3 contractions in 10 minutes lasting for more than 40 seconds, intravenous oxytocin was started with a dose of 6 mu/min and increased by 6 mu/min at 40 minute intervals until adequate uterine activity (3 contractions in 10 minutes). The maximum dose of oxytocin allowed was 42 mu/min. Those assigned to the oxytocin group underwent oxytocin induction with the same dose from the start of labor induction. In both groups artificial rupture of membranes was performed as soon as clinically feasible, generally when cervical dilatation was 3 to 4 cm. There were no cases of failed induction, defined as failure to enter the active phase (inability to dilate the cervix beyond 4 cm) of labor within 24 hours after start of induction.

Uterine tachysystole was defined as ≥ 12 contractions in 20 minutes. Uterine hyper stimulation syndrome was defined as uterine tachysystole or hyper tonus (single uterine contraction lasting 3 minutes) associated with nonreassuring fetal heart pattern (repetitive severe variable decelerations, late decelerations, or bradycardia lasting ≥ 3 minutes). In these cases oxytocin was discontinued in conjunction with change of maternal position and oxygen administration through a face mask.

The primary outcome was delivery within 24 hours from the start of induction. Secondary outcomes were: time between induction to 4 cm dilatation (time to active labor), time between induction to delivery, cesarean delivery, indications for cesarean delivery, uterine hyperstimulation, time to regular contractions and neonatal outcomes.

The statistical analysis was undertaken using parametric and non-parametric tests including Student t test, Chi square test and Fisher exact test. P value less than 0.05 was considered as significant. SAS version 8.00 software was used for data analysis.

RESULTS

A total of 91 patients were enrolled in the study. The study groups did not differ demographically or in the indication for induction of labor, or primary Bishop score (Table 1).

Table 1. Comparison of primary characteristic of dinoprostone plus oxytocin (group 1) and oxytocin alone groups (group 2).

Variable	Group 1 (n = 46)	Group 2 (n = 45)	P value
Age (year)	25.6 ± 4.9	25.3 ± 3.9	0.75
Gestational age (week)	40.85 ± 0.153	40.81 ± 0.162	0.80
First Bishop score	2.5 ± 1.3	2.6 ± 1.3	0.84

* Data are given as mean±SD.

There were 46 patients in the dinoprostone plus oxytocin group and 45 patients in the oxytocin alone group. The minimum time to the beginning of regular significant uterine contractions in the first and second group was 1 and half hour, respectively. The maximum interval was 19 and 16.2 hours in the first and second group, respectively. The minimum and maximum induction to active phase interval was 3 and 24 hours in the PGE2 group and 1.5 and 34 hours in the oxytocin alone group, respectively. Minimum and maximum of induction to delivery time was 1 and 28 hours in the first and 2 and 37.5 hours in the second group. The least neonatal Apgar score in the first group was 4, and 8 in the 2nd group. The least 5 minute Apgar score in both groups was 8 and the maximum 5 minute Apgar score was 9 and 10 in the first and second group, respectively. Neonatal intensive care unit admission was not evaluated. Median time between induction to delivery did not differ significantly in two groups. Median time between induction to the start of active labor was significantly shorter in the oxytocin alone group (6.8 ± 6.3 vs. 9.7 ± 5.2, P = 0.04) (table 2). Hyperstimulation syndrome rate was not different in two groups.

The rates of cesarean delivery in parturient were not significantly different between the dinoprostone plus oxytocin and the oxytocin alone group (30% vs. 36%; P = 0.21). Side effects mainly constituting fetal distress and hyperstimulation (28% vs. 13%; P = 0.12) and the difference between two groups was not statistically significant (Table 3). The most frequent indication for cesarean delivery was fetal heart rate deceleration and bradycardia with a frequency of 85% in the first and 65% in the second group.

DISCUSSION

Our study was a clinical trial of 22 months duration to evaluate and compare the efficacy of induction of labor with vaginal dinoprostone and oxytocin. The outcome was measured by comparing the change in cervical ripening and induction to active phase interval between two groups. Three mg of vaginal dinoprostone was significantly less effective in induction of labor than oxytocin. Although the Bishop score change after 6 hours of receiving vaginal dinoprostone from 2.54 to 4.97 was a statistically significant elevation, the oxytocin only group had a much better response from 2.60 to 6.28. The explanation of this finding may lie in the 3 mg dosage of dinoprostone, which may not be enough to induce labor and the fact that in another group we used oxytocin 6 hours earlier. However, other studies have confirmed that one 2-5 mg dose of PGE2 intravaginally significantly reduces delivery time in patients with unfavorable cervixes (7, 8), a point that we could not confirm in our study.

Table 2. Comparison of different outcomes between two groups*

Outcome	Dinoprostone + oxytocin (n = 46)	Oxytocin alone (n = 45)	P value
Second Bishop score	4.97 ± 1.7	6.23 ± 1.98	0.001
Difference between two Bishop scores	2.51 ± 1.59	3.87 ± 1.63	0.001
Intervention to good contractions interval, h	6 ± 3.7	3.63 ± 3.34	0.001
Intervention to active phase interval, h	9.7 ± 5.2	6.8 ± 6.3	0.04
Intervention to delivery interval, h	11.63 ± 6.4	9.6 ± 6.8	0.15
Apgar score in first minute	8.59 ± 1	8.87 ± 0.3	0.09
Apgar score in fifth minute	9.85 ± 0.4	9.93 ± 13	0.28
Birth weight, kg	3259 ± 290.5	3500 ± 431.5	0.001

* Data are given as mean ± SD

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Table 3. Comparison of complications and cesarean delivery rates in dinoprostone plus oxytocin (group 1) and oxytocin alone groups (group 2).

Variable	Group 1 (n= 46)	Group 2 (n=45)	*P* value
Complications	13 (28%)	6 (13%)	0.12
Cesarean delivery	14 (30%)	16 (36%)	0.21

* Data are given as number (percent).

In a study in 1999 on 42 patients with postterm pregnancies and unfavorable cervices, PGE2 was efficacious in induction of labor (3). In another study 3 mg PGE2 applied in 2 doses was compared to continues oxytocin infusion. Sixty patients were randomly divided into two groups and PGE2 was found to be more effective in the induction of labor (9). In another study 46 patients who required only a single dose of dinoprostone had a reduced time to delivery with intracervical compared with intravaginal placement (10). In our study we used dinoprostone intravaginally and less effectiveness of it may be due to this point.

Some studies have shown that use of prostaglandins results in a reduced cesarean rate but most have not confirmed a significant reduction. The risk of emergency cesarean section was high in women who required more than two doses of vaginal prostaglandin (11). In our study cesarean delivery rate was not statistically different in two groups. Maternal side effects and uterine hyperstimulation was not significantly different in two groups.

Vaginal dinoprostone has all the properties that constitute available technique for labor induction. It is efficacious, inexpensive, easily administered and well tolerated by mother and fetus. In contrast to oxytocin dinoprostone does not have to be mixed and tubing and effusion pumps do not have to be used, reducing the possibility of drug errors. A formal cost analysis was not done in this study because it should have included the number of hours that the patient spent in the labor and delivery unit, days in the post partum unit, and neonatal hospital stays. We should caution that this powerful uterotonic drug should be used in a hospital setting with continues monitoring and under the supervision of trained personnel. We conclude that higher doses may be used in clinical trials before final conclusions about the safety and efficacy of this induction technique can be made; further randomized controlled trials are warranted.

REFERENCES

1. Csorba R, Aranyosi J, Juhasz G, Zatik J, Major T. [Current practice and results of labor induction]. Orv Hetil. 2003 Oct 5; 144(40):1977-1980.

2. Bolnick JM, Velazquez MD, Gonzalez JL, Rappaport VJ, McIlwain-Dunivan G, Rayburn WF. Randomized trial between two active labor management protocols in the presence of an unfavorable cervix. Am J Obstet Gynecol. 2004 Jan; 190(1):124-128.

3. Milchev N, Pehlivanov B, Paskaleva V, Velchev G, Gurova A. Prostaglandin E2 in preinduction cervical ripening in postdate pregnancy. Folia Med (Plovdiv). 1999; 41(3):81-85.

4. Cunningham F, Gant N, Leveno K, Gilstrap L, Hauth J. Induction and augmentation of labor. In: Seils A, Noujaim S,Davis K, editors. Williams obstetrics, 21nd ed. USA: the McGraw-Hill; 2001. p. 471-2.

5. Bernstein EP. Therapeutic considerations for preinduction cervical ripening with intracervical prostaglandin E2 gel. J Reprod Med. 1993 Jan; 38(1 Suppl):73-77.

6. McKenna DS, Costa SW, Samuels P. Prostaglandin E2 cervical ripening without subsequent induction of labor. Obstet Gynecol. 1999 Jul;94(1):11-14.

7. Zuspan F,Quilligan E. Current therapy in obstetrics and gynecology. 5nd ed. USA: W. B .Sanders publisher; 2000.

8.Mackenzie I.Z. Labor induction including pregnancy termination for fetal anomaly. In: James D, Steer P, Weiner C, Gonik B,editors. High risk pregnancy management options 2nd ed.London:W.B. Saunders; 1999. p.1087.

9. Atad J, Hallak M, Auslender R, Porat-Packer T, Zarfati D, Abramovici H. A randomized comparison of prostaglandin E2, oxytocin, and the double-balloon device in inducing labor. Obstet Gynecol. 1996 Feb; 87(2):223-227.

10. Perry MY, Leaphart WL. Randomized trial of intracervical versus posterior fornix dinoprostone for induction of labor. Obstet Gynecol. 2004 Jan; 103(1):13-17.

11. Chan LY, Fu L, Leung TN, Wong SF, Lau TK. Obstetric outcomes after cervical ripening by multiple doses of vaginal prostaglandin E2. Acta Obstet Gynecol Scand. 2004 Jan; 83(1):70-74.