Obstetrics; *Maternal-Fetal Medicine and Perinatology*

Oxytocin Versus Dinoprostone For Labor Induction in Multiparous Women with Unfavorable Cervix

Gul Nihal BUYUK[1], Umit Yasemin SERT[1], Zeynep Aslı OSKOVI KAPLAN[1], Serkan KAHYAOGLU[1]

Ankara, Turkey

ABSTRACT

OBJECTIVE: Dinoprostone is a drug of choice in our daily practice for the induction of labor. The aim of our study; to compare the use of oxytocin with dinoprostone (PGE2- Propess©) used in term multiparous pregnant women to ripen the cervix.

STUDY DESIGN: A total of 507 patients were included in the study. Group A, consisted of 262 women with term multiparous pregnancy Bishop score ≤6 underwent induction of labor with a vaginal insert containing 10-mg timed-release dinoprostone (Propess© -prostaglandin E2). Group B, consisted of 245 cases of pregnancy with Bishop score ≤6 underwent induction of labor with iv oxytocin and was matched for the patient's age and parity. The following data were recorded: age, gestational age, body mass index, the time from the drug administration to the vaginal labor, delivery mode, indications of induction, cesarean indication, birth weight, Apgar score, and need of neonatal intensive care unit.

RESULTS: The primary outcome of the in group B interval from induction to vaginal delivery was similar between the two groups. In group A, 41 patients and in group B, 23 patients had a cesarean section. Cesarean section rate was lower in the oxytocin group (cesarean rate 15.6% versus 9.3%, $p<0.05$).

CONCLUSION: It appears; Dinoprostone ovule increases the cesarean rate in terms, multiparous cases with inappropriate cervical score and does not shorten the duration of delivery. Therefore, the use of oxytocin for cervical ripening in multiparous women may be a more appropriate option.

Keywords: Cesarean rate, Dinoprostone, Labor induction, Oxytocin

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Introduction

The main objective of obstetrics is to provide the birth of a healthy fetus with minimal trauma to the mother. Usually, the birth starts spontaneously and vaginal delivery occurs near term or term. However, it may be necessary to terminate the pregnancy at any time due to maternal or fetal indications (1, 2). Medical or obstetric complications or post-term pregnancies may require labor induction. If Bishop's score is not appropriate, cervical maturation methods are needed first for successful labor-management (3). Mechanical or medical methods have been defined for this purpose. If the Bishop score is less than 6, it is recommended that one of the cervical ripening methods should be used.

Medical methods such as prostaglandin derivatives, misoprostol, mifepristone, relaxin and mechanical methods such as finger enlargement, membrane stripping, hygroscopic dilators, and balloon catheterization are frequently used for providing cervical maturation and induction of labor (2,4-7). All the mechanical modalities use the prostaglandin release effect of local pressure (8). There are mild risks associated with these methods such as infections, bleeding, rupture of membranes, ablatio placenta. The advantages of these methods are no need to follow the fetal heart rate and easy to apply and remove. Hygroscopic dilators result in mechanical pressure by absorbing cervical and local tissue fluids. Trials demonstrate that all the mechanical methods are efficient and have favorable cesarean rates (7,9-12). Membrane stripping causes mechanical pressure which helps to release prostaglandins and dilatation

[1] *Dr. Zekai Tahir Burak Women's Health Application and Research Center, University of Health Sciences, Department of Obstetrics and Gynecology, Ankara, Turkey*

Address of Correspondence: *Umit Yasemin Sert*
Dr. Zekai Tahir Burak Women's Health Application and Research Center, University of Health Sciences, Department of Obstetrics and Gynecology, Talatpasa Bulvari, 06230, Ankara, Turkey
ysmn.sert88@gmail.com

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ORCID IDs of the authors:
GNB:0000-0003-4405-2876 UYS: 0000-0003-0862-4793
ZAOK: 0000-0001-7554-4393 SK: 0000-0001-8964-3552

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via finger lets the cervix ripen. Although stripping is known to reduce the cesarean rate and need of oxytocin, Cochrane reviews do not address a clinically important benefit (13). Amniotomy is known to increase the level of local prostaglandins and is not considered to be beneficial for labor induction alone (14).

Prostaglandin derivatives are generally accepted for lower Bishop scores (<6) to ensure cervical maturation. Prostaglandins enhance the collagenase activity of the cervix by increasing PGE2, elastase, glycosaminoglycan, hyaluronic acid, and dermatan sulfate. These substances not only facilitate the cervical dilatation but also cause myometrial contractions by calcium canal regulation (15). Cochrane reviews compared prostaglandins with the placebo group and concluded that vaginal prostaglandins increase the rate of vaginal delivery without effecting cesarean rate (16-18). The locally administered dinoprostone vaginal insert, Propess© (Ferring Laboratories, United Kingdom), was approved for use in 1995. It is used to initiate cervical ripening in patients with a Bishop score of 6 or less in the absence of fetal and maternal contraindications and the presence of a singleton cephalic condition (6,19,20).

Each Propess© vaginal release system contains 10 mg of dinoprostone (prostaglandin E2- PGE2), which is dispersed in a hydrogel polymer and releases about 0.3 mg per hour for 24 hours. After administration, uterine contractions and cervical changes should be carefully evaluated. In particular, multigravida patients may exhibit regular painful contractions without a significant cervical change. Softening and dilatation of the cervix may not be seen until uterine activity begins. Therefore, to avoid the risk of uterine hyperstimulation when regular painful uterine activity due to dinoprostone starts, the ovule should be removed without regard to the cervical condition (21,22).

This study aimed to compare the efficacy of oxytocin and dinoprostone vaginal insert (Propess©) for cervical ripening in term multiparous pregnant women.

Material and Method

In this retrospective cohort study, medical records of term multiparous pregnant women who were admitted to the labor unit of a tertiary referral center for labor induction between April 2015 and December 2017 were reviewed.

Ethical approval

The study was approved by the local institutional ethics committee (22/26.02.2018*). The informed consent for using data was taken from the ethical committee and obstetric department of our hospital. The work was undertaken and it conformed to the provisions of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013).

A total of 507 patients were included in the study after verbal and written informed consent was obtained. Group A consisted of 262 term multiparous pregnant women whose Bishop score was ≤6 and who underwent induction of labor with a vaginal insert containing 10 mg dinoprostone, prostaglandin E2 (Propess©). The control group, Group B, consisted of 245 multiparous pregnant women, matched for age and parity, with a Bishop score ≤6 who underwent induction of labor with iv oxytocin time from induction to delivery was calculated for 443 patients who in the end had a vaginal delivery. Inclusion criteria were: multiparous women with the unfavorable condition between 37 and 42 weeks of gestation with a singleton pregnancy, occipital presentation, Bishop score ≤6, no contraindication for vaginal delivery. Patients with multiple gestations, preterm gestations, ruptured membranes at the time of admission, prior cesarean section, maternal or fetal contraindications for vaginal delivery or use of another primary induction agent (Foley catheter, cervical balloon catheter, hygroscopic dilators, and oral misoprostol) were excluded. The dinoprostone insert was left in place until the onset of active labor or for a maximum of 12 hours. Active labor was considered to begin when cervical dilatation was 4 cm. All cases were followed by continuous electronic fetal monitoring. A partograph was drawn to follow the progress of labor. A low dose oxytocin protocol (less than 100 mU oxytocin in the first 40 minutes, and increments delivering less than 600 mU total in the first two hours) was used for induction of labor in group B. Gestational age was established by the last menstrual period and confirmed with first-trimester ultrasound measurements. Demographic and antenatal data were collected from the delivery chart, computerized data and patient files. The following data were recorded: age, gestational age, body mass index, the time from drug administration to vaginal labor, delivery mode, indications of induction, the reason for cesarean indication, birth weight, Apgar scores and admission to the neonatal intensive care unit.

Statistical analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) for Windows 22 (SPSS Inc., Chicago, IL). Oxytocin was administrated by using an infusion pump. 10 IU oxytocin was added to one lire of 0.9 % normal saline with a starting rate of 1-5 Mu/min until the effective contractions were found. Results are given as mean±SD or percentage, time intervals were analyzed with ANOVA test, other data were analyzed with Chi-square test for qualitative and Mann-Whitney U test for quantitative variables. Logistic regression analysis was performed for risk factors affecting delivery time. All tests were two-sided and $p<0.05$ was considered statistically significant.

Results

A total of 507 patients were included in the study. Two hundred and sixty-two women were in the dinoprostone vaginal insert group named group A, and 245 women were in the

oxytocin group named group B. In group A, 41 pregnant women had a cesarean section and in group B, 23 patients had a cesarean section.

There was no statistically significant difference between the two groups in terms of age, gestational week, gravidity, parity, body mass index, cervical length and initial bishop scores (Table I). The mean gestational age was 39.9±1.1 weeks in the oxytocin group and 40.1±1.1 weeks in Dinoprostone vaginal insert group. There was no difference in terms of 1st and 5th minute APGAR scores (Table I).

Subgroup analysis was performed with a consideration that the duration of delivery could be affected by the indication of labor induction. The most common indications for induction were post-term pregnancies (40.9%), followed by oligohydramnios (36.8%) and non-reassuring fetal heart rate (17.1%) in both groups. The indications for induction were similar in both groups (Table II).

The primary outcome, the interval from induction to vaginal delivery, was similar in the two groups. The duration from the administration of the drug to vaginal delivery was 17.0±3.4 hours in group A and 16.8±3.3 hours in group B. There was no difference between the two groups (p=0.425).

Meconium-stained amniotic fluid was found in 5.3% (14/262) of women in the Propess© group and 2.4% (6/245) of women in the oxytocin group (p<0.05).

In group A, 41 pregnant women had a cesarean section and in group B, 23 patients had cesarean section; the cesarean rate in group A and group B was 15.6% and 9.3% respectively (p<0.05). The most common indications for cesarean section were fetal distress and labor arrest. There was no difference between the two groups in terms of cesarean indications and also neonatal outcomes (Table I). Neonatal birth weights and the need for neonatal intensive care unit admission were similar between the two groups (p=0.156 vs. p=0.032).

Discussion

In this retrospective study, the use of oxytocin in multiparous term pregnant women as a primary induction agent was compared with the cervical maturation agent dinoprostone vaginal insert. There was no statistically significant difference between the two groups in terms of the time from drug administration to delivery, admission to the neonatal intensive care unit or 5th min APGAR score <7 (Table I). But the rate of cesarean section was higher in the dinoprostone vaginal in-

Table I: *Comparison of demographic and clinical characteristics of the patients*

Variables	Group A_propess (n=262)	Group B_oxytocin (n=245)	*p* value
BMI (kg/m²)	27.5±2.5	27.8±2.7	0.346*
Age (year)	33.8±5.6	32.9±5.5	0.376*
Birth weight (gram)	3442±509	3545±581	0.156*
Gestational age (week)	40.1±1.1	39.9±1.2	0.175*
Delivery time (hour)	17.0±3.4	16.8±3.3	0.425*
Apgar 1.	7.68±0.75	7.66±0.77	0.965¶
Apgar 2.	9.71±0.57	9.72±0.58	0.945¶
Parity	1.7±0.9	1.3±1.0	0.614¶
NICU admission	10(3.81%)	13(5.30%)	0.032¶
Meconium presence	14(5.3%)	6(2.4%)	<0.05¶
Cesarean rate	41(15,6%)	23(9.3%)	<0.05¶

*BMI: Body mass index, NICU: Neonatal intensive care unit, Mean ±standard deviation and number (percentage). *Mann Whitney-U test, ¶ :Chi-square test, A p value<0.05 is considered statistically significant.*

Table II: The *subgroup analysis for the indications of labor induction.*

Indication of induction	BMI	Age	Birth weight	Gestational age	Delivery time
Oligohydramnios Group A	27.8±3.0	34.1±6.1	3328±534	38.9±1.1	16.4±3.3
Oligohydramnios Group B	27.4±2.5	33.0±5.6	3314±429	39.4±1.2	17.6±3.8
P value	0.775	0.933	0.930	0.087	0.116
Postdates Group A	27.7±2.7	32.5±5.2	3666±559	40.5±0.6	16.9±3.4
Postdates Group B	27.5±2.6	33.9±5.5	3533±386	40.4±0.8	17.0±3.1
P value	0.485	0.864	0.274	0.505	0.671
Nonreassuring NST Group A	28.3±2.5	32.9±5.8	3400±623	38.9±0.8	17.0±2.9
Nonreassuring NST Group B	27.9±2.2	34.7±6.1	3348±343	39.7±1.3	16.6±4.0
p value	0.501	0.062	0.540	0.606	0.430

sert group than the oxytocin group (15.6% versus 9.3%; $p<0.05$) (Table I). In a study by Wei et al., dinoprostone was compared to oxytocin in late-term pregnancies and with different Bishop scores. The study demonstrated that dinoprostone is more effective if Bishop's score is less than 3, with lower cesarean rate, while the outcome is similar in terms of cesarean rate, with Bishop's score of 4-6 (23).

Induction of labor is an iatrogenic stimulation of uterine contractions to perform vaginal delivery if spontaneous delivery has not begun. In general, the decision for induction of labor should be given if the benefit of immediate delivery for the mother or fetus is greater than the risks of continuation of pregnancy (24). Recently, the use of labor induction in the world, in particular, the induction of elective labor, has significantly increased and in fact, itself brings a serious risk of morbidity. Less than two-thirds of pregnant women undergoing labor induction give birth without requiring further intervention. However, labor induction may increase the likelihood of using uterotonic agents, operative delivery and cesarean section, risk of postpartum bleeding, need for blood transfusion and postpartum hysterectomy (25,26). The physiology of induction with oxytocin is similar to normal birth. According to the wait-and-see approach of oxytocin induction, it has been reported that it decreases the possibility of non-birth within 24 hours and increases the need for epidural analgesia and cesarean section (27). According to a Cochrane analysis, which included sixty-nine studies and more than 10,000 pregnant women, vaginal PGE2 improved vaginal delivery rates and cervical maturation without decreasing operative deliveries and reduced the need for oxytocin supplementation (28). However, it is important to determine which patients will benefit from vaginal PGE2 to reduce costs and prevent complications.

Prostaglandin preparations should be administered under conditions where the fetal heartbeat and uterine activity can be closely monitored. Uterine contractions occur within the first hour following the administration and show maximum activity for four hours. Monitoring should be continued as long as regular uterine contractions persist (29). For this reason, it is important to predict whether the induction of labor will be successful, the factors affecting a successful labor induction and the knowledge of methods of labor induction to minimize morbidity.

In this study, the meconium-stained amniotic fluid rate was higher in the dinoprostone vaginal insert group than the oxytocin group (Table I), similar to the results of the study by Mahendru et al. (30).

The success of labor induction is affected by gestational week (31). We examined the indications of induction separately and no significant difference was found between oligohydramnios and post-term pregnancy (Table II).

However, Canda et al. demonstrated that oxytocin plus dinoprostone is more effective than oxytocin alone (7), this study suggests that intravenous oxytocin is more effective than the dinoprostone insert for the induction of multiparous women at term, especially for women with an unfavorable cervix. We did not evaluate a group with both oxytocin and Propess©, and this could be thought of as the weak point of our study. The patient selection with similar age, gestational week, bishop score and indication for labor induction is the strong point of the study.

Conclusion

Dinoprostone ovule increases the cesarean rate in term pregnancies with lower Bishop scores and does not shorten the duration of delivery. Therefore, the use of oxytocin for cervical ripening in multiparous women may be a more appropriate option when the higher cost of dinoprostone vaginal insert is taken into consideration.

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