

Comparison of Dinoprostone Vaginal Tablet and Vaginal Insert in Primigravid Women for Induction of Labor

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Abstract

Background: Labor of induction by use of different drugs is generally preferred for avoiding complications with prolonged pregnancy. Dinoprostone vaginal gel or insert tablets are commonly used for inducing contractions similar to normal delivery contractions. The current study compares the effectiveness of dinoprostone vaginal tablet and dinoprostone vaginal insert in induction of labor for primigravid women.

Methods: The participants of the prospective cohort observational study were primigravid women. BISHOP score was used as a tool for predicting patient who required labor induction. All the participants with BISHOP score less than 6 were given either dinoprostone vaginal tablet or dinoprostone vaginal insert for induction of labor. Chi-square statistical analysis was performed using SPSS, version 17.0.

Results: A total of 135 patients were studied. Post-term pregnancy was found to be most common indication among studied patients. Labor induction was executed by using dinoprostone vaginal tablet and insert in 61% and 31% patients, respectively. Statistically, no significant differences were found in the rate of cesarean section among two treatment regimens on applying Chi-square analysis. On average, two dinoprostone tablets per patient as compared to one vaginal insert were used for labor induction.

Conclusion: Dinoprostone vaginal tablet and vaginal insert both have similar efficacy in induction of labor to be used in primigravid women.

Keywords: Dinoprostone; Vaginal insert; Labor induction

Manuscript submitted December 10, 2017, accepted February 28, 2018

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doi: <https://doi.org/10.14740/jcgo471w>

Introduction

Labor induction is procedure of initiation of labor in artificial way by stimulating uterus to induce uterine contractions. Induction of labor is usually done in third trimester to achieve delivery before the date of spontaneous labor [1, 2]. The overall frequency of labor induction has been raised from 9.5% to 23% from year 1990 to 2012 in United States [3]. Out of four, every one delivery in developed countries is by means of labor induction [4-6]. Labor induction is recommended when the risk of waiting for delivery by spontaneous labor is expected to be associated with worst outcomes as compared to the early induction of labor [6].

Labor induction is preferred under following circumstances: 1) To avoid the risks associated prolonged pregnancy usually between 41st and 42nd week; 2) Pre-labor rupture of membranes at pre-term which requires use of vaginal PGE₂ for labor induction at least after 34 weeks unless under special circumstances like high fetal risks; 3) Pre-labor rupture of membranes at term which requires induction of labor after 24 h by using vaginal PGE₂ at or after 37 weeks; 4) To avoid risk of uterine rupture and emergency cesarean section in women with history of previous cesarean section [7].

Medications which are used for labor induction include: 1) prostaglandin gel or inert which is usually administered via vaginal route; 2) misoprostol which is administered orally or through vaginal route; 3) oxytocin which is usually used via intravenous route [7].

Dinoprostone, naturally occurring prostaglandin E₂, stimulates contraction of uterine gravid myometrium similar to contractions as seen during natural term labor. These contractions are sufficient enough to accomplish the delivery of fetus in majority of cases. The exact mode of contraction induced by dinoprostone remains unknown. It is also responsible to elicit gastrointestinal smooth muscle contraction resulting in vomiting and/or diarrhea [8]. Other indications of dinoprostone include: termination of pregnancy from the 12th to 20th gestational week, evacuation of the uterine contents in the management of missed abortion or intrauterine fetal death up to 28 weeks of gestational age, and the management of non-metastatic gestational trophoblastic disease [9].

Oxytocin is not as effective as dinoprostone for inducing labor in women with unripe cervixes or premature rupture of membranes. Most studies have indicated intravaginal dino-

prostone gel or suppository (3 to 4 mg) and intracervical dinoprostone gel (0.4 mg) are more effective than IV oxytocin for inducing labor when the cervix is not ripe [10-12]. One study, however, reported similar length of labor and cesarean delivery rate with dinoprostone suppository versus oxytocin [13].

BISHOP score, also commonly called as cervix score or pelvic score, is usually used for predicting the likelihood of vaginal delivery. BISHOP score is usually calculated by combining points for five measurements after cervical examination. These measurements include dilation in centimeter, fetus station, position of cervix and consistency of cervix. BISHOP score with less than 6 points indicates that the cervix is unfavorable for induction and probability for vaginal delivery is very low [14].

The purpose of current study was to determine the effectiveness and efficacy of dinoprostone vaginal tablet (brand: PROSTIN) in induction of labor compared to dinoprostone vaginal insert delivery system (brand: PROGRESS) which contains 10 mg of dinoprostone spread on a non-biodegradable polymeric drug matrix.

Materials and Methods

The prospective cohort study was carried out in a tertiary care public sector 300 bedded King Abdulaziz Hospital, Alahsa, Saudi Arabia. Study period was 2 years from January 2015 to December 2016. The study was confined to patients who were admitted in the Obstetrics and Gynecology ward of the hospital which usually caters 2,500 delivery cases per year. The retrospective data of last 5 years showed that around 18% of the cases delivered through cesarean section surgical method in hospital.

The study included all those primigravid patients who were admitted to the Gynecology Department during the study period. Sample size was based considering $P = 0.05$, study power = 80%, effect size = 0.3. Only those patients were included in the study whose induction of labor was carried out by using dinoprostone vaginal tablet 0.5 mg (PROSTIN) or vaginal insert 10 mg (PROGRESS). The use of PROSTIN or PROGRESS was solely the decision of on-duty consultant present at the duty at the time of initiation of induction of labor. The choice of drug also depends on patient compliance during vaginal examination.

For all the patients who received either dinoprostone vaginal tablet or vaginal insert, the BISHOP score was documented just before the commencement of induction of labor. The BISHOP score was used to assist in predicting the response to induction of labor. All the selected patients who were given dinoprostone vaginal tablet or vaginal insert had a BISHOP score of less than 6 at the time of initiation.

For patients who were given dinoprostone vaginal tablet for induction of labor, the tablet was inserted into posterior vaginal fornix and was reexamined after every 6 h. If the response of cervix as calculated by BISHOP score was found to be less than 6, another dose of tablet was given to the patient. The process was repeated until the initiation of normal contractions keeping in mind that a maximum of three tablets could be given to a single patient.

Table 1. Characteristics of Studied Primigravid Women

| Characteristics | Mean \pm SD (range) |
|--------------------------------------|--------------------------|
| Age (years) | 23 \pm 4.4 (19 - 35) |
| Body mass index (kg/m ²) | 27.8 \pm 2.1 (24 - 31) |
| Weight (kg) | 52 \pm 7.9 (44 - 63) |
| Gestational week | 36 \pm 3 (31 - 41) |

For all those patients who were given dinoprostone vaginal insert, the insert was placed *in situ* for 24 h initially but was removed if patients started to experience painful contractions or if the patient passed into labor or 30 min before initiation of oxytocin intravenous infusion.

All those patients with multiple gestations, intrauterine fetal death or who received medications other than PROGRESS/PROSTIN for induction of labor were excluded from study.

Results

During the study period of 2 years, a total of 135 patients were enrolled whose induction of labor was carried out by given either dinoprostone vaginal tablet or vaginal insert. Out of 135 enrolled patients, 82 (60.8%) patients were given dinoprostone vaginal tablet for induction of labor while induced labor was carried out by using dinoprostone vaginal insert in 53 (39.2%) patients.

The average age of the enrolled patients was found to be 23 \pm 5.4 (19 - 35) years with an average weight of 52 \pm 7.9 (44 - 63) kg. The patient's characteristics such as age, body mass index and average gestational age of patients given dinoprostone vaginal tablet or vaginal insert are mentioned in Table 1.

The patients with indication of post-term pregnancy was found to be highest in number, i.e. 51 (37.8%) in which patients who received dinoprostone vaginal tablet or vaginal insert were 29 (56.8%) and 22 (43.2%) patients, respectively. The patients with indication of antepartum hemorrhage were found to be at least in number with a total of three (2.2%) patients. The indication of patients for which they were opted for induction labor is summarized in Table 2.

The spontaneous vaginal delivery was found to be most prominent as an outcome of induction of labor which accounts for 59 (43.8%) of the enrolled patients. The other two outcomes were cesarean section surgery and instrumental delivery method as 48 (35.6%) and 28 (20.7%), respectively. The comparisons of induction of labor among these three methods of delivery by dinoprostone vaginal tablet or vaginal insert are summarized in Table 3.

No significant differences were found in any of the three outcomes when dinoprostone vaginal tablets were compared with dinoprostone vaginal insert. For all three outcomes of induction of labor, Chi-square analysis does not reveal significant differences as P-value of comparison was found greater than level of significance, i.e. 0.05. An average of two tablets of dinoprostone 0.5 mg vaginal tablet with a range of 1 - 4 (0.5 - 2 mg) tablets were used in enrolled patients who were given tablet for induction of labor. The average lengths of labor after

Table 2. Indications for Use of Dinoprostone Vaginal Tablet and Vaginal Insert

| Indications | Overall (n = 135) | Vaginal tablet (n = 82) | Vaginal insert (n = 53) |
|--------------------------------------|-------------------|-------------------------|-------------------------|
| Post-term pregnancy | 51 (37.8%) | 29 (35.4%) | 22 (41.5%) |
| Premature rupture of membrane (PROM) | 29 (21.5%) | 26 (31.7%) | 3 (5.7%) |
| Gestational diabetes mellitus | 24 (17.8%) | 10 (12.2%) | 14 (26.4%) |
| Intrauterine growth restriction | 10 (7.4%) | 5 (6.1%) | 5 (9.4%) |
| Preeclampsia | 6 (4.4%) | 4 (4.9%) | 2 (3.8%) |
| Pregnancy induced hypertension | 4 (3.0%) | 2 (2.4%) | 2 (3.8%) |
| Cholestasis | 5 (3.7%) | 3 (3.7%) | 2 (3.8%) |
| Oligohydramnios | 3 (2.2%) | 2 (2.4%) | 1 (1.9%) |
| Sickle cell + antepartum hemorrhage | 3 (2.2%) | 1 (1.2%) | 2 (3.8%) |

The number in parentheses represents the percentage of patients in particular group.

giving dinoprostone vaginal tablet and vaginal insert were 7 and 6 h, respectively.

Discussion

Prostaglandins have been used for induction of labor via cervical ripening for decades [15]. Prostaglandin E2 insert is approved by Food and Drug Administration and is considered to be more effective than oxytocin infusion for successful induction of labor [16].

Current study suggests that there is no significant difference ($P = 0.756$) in the outcome of cesarean section when dinoprostone tablet was compared with dinoprostone insert with the values of 36% and 34%, respectively. Similar results have been reported by Ziad et al while comparing efficiency of dinoprostone vaginal insert with vaginal gel and there was no significant difference when two were used for induction of labor [17]. Sara et al stated misoprostol more effective than dinoprostone for cervical ripening [18]. Dinoprostone insert was found superior to dinoprostone gel in a meta-analysis study performed by Xeng et al which showed that dinoprostone insert was associated with shorter hospital stay but is associated with decreased cesarean section when compared to dinoprostone gel [19].

Successful induction of labor not requiring cesarean section was achieved in 63.4% patients with dinoprostone vaginal tablet while 66.1% patients with dinoprostone insert and statistically no significant difference ($P > 0.05$) was found between two dinoprostone formulations in the successful outcome. In 2008, Kalat et al also reported similar outcomes of

successful vaginal delivery through dinoprostone tablet and gel with results of 6.6% and 63.3% patients, respectively [20]. A randomized control trial comparing two vaginal preparations of dinoprostone suggested that the two induction procedures (controlled-release vaginal dinoprostone pessary or dinoprostone gel) should be considered equivalent as far as ripening the cervix and initiating labor. In view of this finding, the low BISHOP score should be considered an indication to prefer the controlled-release device, since it reduces pain thereby improving the physical and emotional wellbeing of the parturient [21].

In 2014, Hassan et al conducted a study to compare the success rate of vaginal birth after cesarean section between two vaginal forms (dinoprostone vaginal tablet and dinoprostone vaginal pessary) of dinoprostone for labor induction in women with prior cesarean section. And the results of the study were consistent with our research, i.e. both forms of dinoprostone were effective methods for labor induction in women with prior cesarean section. However, the patient satisfaction with the birth process was in favor of the dinoprostone sustained release vaginal pessary [22].

In 2002, Mukhopahyay et al reported that 72% patients with successful vaginal delivery required only a single dose of dinoprostone vaginal tablet for induction [23]. Our study also reports similar results with 77% patients who delivered with single tablet while 23% patients required more than one tablet with a maximum of three tablets required by some patients.

Study limitation

The limitation of our study was small number of patients in-

Table 3. Comparison of Outcomes of Labor Induction Between Dinoprostone Vaginal Tablet and Vaginal Insert

| Outcomes | Vaginal tablet (n = 82) | Vaginal insert (n = 53) | P-value |
|------------------------------|-------------------------|-------------------------|---------|
| Cesarean | 30 (36.6%) | 18 (34.0%) | 0.756 |
| Spontaneous vaginal delivery | 35 (42.7%) | 24 (45.3%) | 0.766 |
| Instrumental delivery | 17 (20.7%) | 11 (20.8%) | 0.997 |
| Length of labor (h) | 7 (2 - 13) | 6 (3 - 12) | 0.616 |
| Number of tablets | 1 (1 - 3) | - | NA |

cluded.

Conclusion

In modern obstetric, judicious and timely induction of labor has an important and vital role. No significant difference was found in the rate of cesarean section, neonatal and maternal morbidity and hyper-stimulation when dinoprostone vaginal tablets were compared with dinoprostone vaginal insert. Further studies are essential for superior effective results.

Conflict of Interest

None.

Financial Disclosure

None.

Ethics Approval

This study was approved by the Local Ethics Committee of King Abdullah International Medical Research Center, King Abdulaziz Hospital.

Grant Support

None.

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