Comparison of Two Forms of Dinoprostone: Propess and Prostin for Induction of Labor

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Background: Induction of labor (IOL) aims to achieve a successful vaginal delivery. Dinoprostone is a synthetic prostaglandin (PGE2) which works on the connective tissue stroma of the cervix and makes it favorable for normal labor.

Objective: To compare the two variants of PGE2: intra-vaginal dinoprostone vaginal suppository (Prostin E2) and 24 hours controlled-release vaginal dinoprostone pessary (Propess) for successful normal vaginal delivery.

Setting: Obstetrics and Gynecology Department, Bahrain Defence Force Hospital, Bahrain.

Design: A Retrospective Study.

Method: This study included all pregnant women who had induction of labor from January 2018 to June 2018. A total of 322 women with a singleton pregnancy, fetal cephalic presentation and bishop score ≤4 were admitted for induction of labor. Fifty-eight (18%) patients received 24-hours 10 mg controlled-release Propess and 264 (81.9%) received repeated doses of 2 mg Prostin E2 vaginal tablets.

Result: A high incidence of cesarean delivery in the Propess group 20/58 (34.5%) compared to 45/264 (17%) in the Prostin group was found, P-value of 0.002. There was no difference in the incidence of hyperstimulation, need for oxytocin or fetal distress in labor. Shorter induction-to-delivery interval was obtained with Propess, 19 hours compared to 23.5 hours for Prostin E2, but the difference was not statistically significant. Data was analyzed using StatsDirect software, P-value of less than 0.05 was considered statistically significant.

Conclusion: IOL with slow release dinoprostone is associated with increased cesarean section rate compared to Prostin.

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Induction of labor (IOL) is one of the most common obstetric procedures. It is estimated that up to 20% of all full-term pregnancies might need IOL[1]. IOL is the initiation of contractions in a pregnant woman who is not in labor to help her achieve a vaginal birth within 24 to 48 hours[2]. IOL is usually done for both fetal and maternal indications. Most common indications are postdated pregnancy, preeclampsia, intrauterine growth restriction and rupture of the membranes without the onset of spontaneous contractions within the next 24 hours[3].

The success of induction of labor is highly dependent upon the cervix score; it is well-known that a favorable cervix is associated with successful induction, decreased operative vaginal delivery and cesarean section rates[4]. Assessment of cervical status is fundamental for the clinician to estimate the likelihood of successful vaginal delivery. The most important factor in the bishop score criterion to predict successful induction is cervical dilatation, effacement, head station, cervical position, and cervical consistency[5]. During the last two decades, research has focused on the role of prostaglandin in labor induction. Dinoprostone is a Prostaglandin (PGE 2) which acts on the cervical tissue preparation for parturition. It can be used in different forms, such as tablets, suppositories, gel or as slow-release vaginal tablets (Propess)[6].

The slow-released vaginal insertion has many advantages compared to other forms. It is applied as a single application. The insertion is easy and the termination of drug effect can be achieved by removing the Propess in cases of uterine hyperstimulation or fetal distress. It reduces the number of pelvic examinations and thus reduces the risk of pelvic

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infections; it is extremely safe during pregnancy, also it reduces maternal anxiety associated with pelvic examination[7].

Many studies compared the efficacy of Propess against other prostaglandin formulations (Prostin E2) revealed diverse results. These findings could be due to the heterogeneity in the characteristic of inclusion groups, indications for induction of labor and pre-induction bishop score[8]. Many studies had been done to establish existing difference between Propess and Prostin regarding the rate of vaginal delivery (VD) within 24 hours. Furthermore, the studies looked at alteration in the rates of VD, CS, or artificial assisted vaginal delivery, as well as the reasons for CS[9]. The length of hospitalization with different type of dinoprostone formulas was also reported in many studies[10,11]. Further studies were performed to compare between IOL drugs with regard to the incidence of postpartum hemorrhage[10,12]. Oxytocin was utilized during the process of induction of labor[13].

The aim of this study was to compare the efficacy of two forms of dinoprostone (Propess and Prostin E2) for induction of labor.

METHOD

All pregnant women for induction of labor from January 2018 to June 2018 were included in the study. A total number of 322 women with a singleton pregnancy, fetal cephalic presentation and bishop score ≤4 were admitted for induction of labor. The choice of prostaglandin form for IOL was randomly allocated based on the resident's choice. The two types of prostaglandin for induction of labor included 24-hour 10mg controlled-release Propess given to 58 patients and a repeat dose of 2mg Prostin E2 vaginal tablet given to 264 patients.

The inclusion criteria were full-term pregnancy together with one or more indication for induction of labor, including post-term pregnancy, pregnancy-induced hypertension, polyhydramnios, oligohydramnios, premature rupture of membranes, diabetes mellitus and intrahepatic cholestasis. In addition, an absence of spontaneous labor and a bishop score of ≤4 were required. Patients with contraindication for (IOL), such as breech presentation, abnormal CTG at admission, signs of infection and the necessity for immediate delivery as severe intra-uterine growth restriction with high Doppler indices were excluded from the study. All the patients were informed about the induction protocol and a written informed consent was taken. Patients assigned to the Prostin E2 group, received a maximum of six doses of vaginal suppository, each containing 2 mg in their posterior fornix once every 12 hours. The women in the Propess group received one pessary vaginally in the posterior fornix once over 24 hours for total of two doses.

Cardiotocography (CTG) 30 minutes prior and 45 minutes after administration of prostaglandin was performed. During active labor, fetal monitoring was performed by continuous auscultation employing external CTG or a scalp electrode. Amniotomy was reserved for women with a favorable cervix. Special care was taken in cases of unengaged head to avoid the risk of cord prolapse. After amniotomy, oxytocin commenced early in order to establish labor. Oxytocin started 30 minutes after removal of Propess and 6 hours after the last Prostin insertion. Patients infected with group B Streptococcus were immediately started on Syntocinon after rupturing of the membranes in order to achieve delivery within 24 hours. Fetal distress is defined when there is an abnormal CTG pattern or the presence of meconium in the amniotic fluids. A pathological CTG was considered to be present in cases where changes in CTG pattern required immediate delivery. Uterine hyperstimulation was defined as more than five contractions occurring within 10 minutes.

Data were analyzed using StatsDirect statistical package (version: 3.0.141 2015). A two-sided unpaired T-test was used to assess the difference in mean minutes taken to fully dilated and birth weight. The Chi-square test was used. The Fisher-Freeman-Halton exact test was used in crosstabs. A P-value of less than 0.05 was considered statistically significant.

RESULT

Two hundred sixty-four (81.9%) patients were in the Prostin group and 58 (18%) were in the Propess group. Maternal age revealed a high incidence of older patients in the Prostin group, P<0.0001. No significant difference in maternal BMI between the two groups, P=0.99. Patients who received Prostin had obvious previous delivery, P<0.0001; in addition**,** they had more miscarriages 82 (25.5%) versus 8 (2.5%), P=0.008. No significant difference in comorbidity was found between the groups, P=0.7. High incidence of fertility treatment was found with Propess group (12.1%) compared to Prostin (4.6%); the difference was not statistically significant, P=0.05, see table 1.

Table 1: Patient's Characteristics

	Prostin N=264	Propess N=58	P-value
Maternal age median (range)	30 (48-17)	26 (40-17)	0.0001**
Maternal BMI median (range)	32 (57-21)	31.5 (50-19)	0.99**
Previous delivery median (range)	3 (13-1)	1 (4-1)	<0.0001**
Previous miscarriage	82 (25.5%)	8 (2.5%)	0.008***
Co-morbidity	62 (19.3%)	15 (4.7%)	0.7***
Fertility treatment	12 (3.7%)	7 (2.2%)	0.05****

** two-sided Mann-Whitney *** Chi-square
****Fisher-Freeman-Halton exact

There was no significant difference between Prostin and Propess groups regarding gestational age or postdate status, P=0.17 and 0.6, respectively. There was no difference between the two groups in the presence of PROM, macrosomia, IUGR, gestational diabetes and PIH. Oligohydramnios was seen more in the Propess group, 9 (2.8%), compared to Prostin, 6 (1.9%), P=0.04. There was high incidence of obstetric cholestasis in the Propess group, 2 (0.6%) compared to 3 (0.9%), P-value=0.04, see table 2.

We found a high incidence of cesarean delivery in the Propess group 20/58 (34.5%) compared to 45/264 (17%) in the Prostin group, P-value of 0.002. There was no difference between the groups regarding hyperstimulation, the need for oxytocin, fetal distress or the presence of meconium. No difference in the instrumental delivery rate and delivery within 12 or 24 hours from IOL was found. The two groups had no difference in the incidence of postpartum hemorrhage and the need for blood transfusion, see table 3.

Table 2: Current Pregnancy Characteristics

	Prostin N= 264	Propess N= 58	P-value
More than 37 weeks	228 (70.8%)	46 (14.3%)	0.17***
Post date	96 (29.8%)	19 (5.9%)	0.6***
PROM	29 (9%)	3 (0.9%)	0.18***
Oligohydramnios	9 (2.8%)	6 (1.9%)	0.04****
Polyhydramnios	6 (1.9%)	0 (0%)	0.6****
Macrosomia	7 (2.2%)	2 (0.6%)	0.67****
IUGR	19 (5.9%)	3 (0.9%)	0.78****
GDM	74 (22.9%)	18 (5.6%)	0.65***
Obstetric cholestasis	2 (0.6%)	3 (0.9%)	0.04****
PIH	13 (4%)	5 (1.6%)	0.34****
***Chi-square ****Fisher-Freeman-Halton exact			

Table 3: Labor Outcome

	Prostin N= 264	Propess N= 58	P-value
Hyperstimulation	5 (1.6%)	3 (0.9%)	0.16****
Need for oxytocin	86 (26.7%)	19 (5.9%)	0.98***
Fetal distress in labor	105 (32.6%)	35 (10.9%)	0.33***
Meconium	35 (10.9%)	7 (2.2%)	0.81***
Time to fully dilated Minutes mean±SD	23.5±31	19.8±26.3	0.39*
Cesarean delivery	45 (13.9%)	20 (6.2%)	0.002***
Instrumental delivery	5 (1.6%)	2 (0.6%)	0.61****
Delivery within 12 hours	48 (14.9%)	14 (4.3%)	0.3***
Delivery within 24 hours	104 (32.3%)	22 (6.8%)	0.84***
Postpartum hemorrhage	3 (0.9%)	1 (0.3%)	0.55****
Birth weight mean ± SD	3.17 ±0.6	3.07±0.6	0.26*
Blood transfusion	2 (0.6%)	1 (0.3%)	0.45****
* two-sided Unpaired t-test ***Chi-square ****Fisher-Freeman-Halton exact			

DISCUSSION

Induction of labor is a very commonly performed intervention in obstetrics. Proper selection of the cases and the methods for induction of labor is very important. Meta-analysis showed that the risk of cesarean delivery following induction of labor was significantly lower than the risk associated with expectant management[1]. Several meta-analyses and systematic reviews evaluated the use of PGE2 and suggested that it is effective for cervical ripening and labor induction, without differentiating between Propess and Prostin. A study by Laxman et al found that Propess is a highly effective method of induction of labor for a full-term pregnancy. It consistently reduces the number of pelvic examinations and the risk of genital infections[8]. Another study found that Propess is highly effective in the induction of labor with an average induction-delivery interval of 18 hours. In our study, the rate of spontaneous vaginal delivery with Propess was 72% compared to 65.5%, which is similar to other studies[14].

A randomized controlled trial of 133 women with singleton pregnancy compared between Propess and Prostin for induction of labor and found no difference between the two groups with regards to the number of women delivering within 24 hours, mode of delivery, induction-to-delivery interval, and neonatal outcome[14]. On the other hand, the number of pelvic examinations was statistically less in the Propess group. Propess was found to be less costly compared to Prostin in view of single dose usage and less midwife working hours[7].

A meta-analysis concluded that Propess is equally effective as other prostaglandin routes of administration in terms of delivery by 24 hours, the rate of uterine hyperstimulation with fetal heart rate changes and cesarean delivery rate[15]. Zeng et al compared between Propess and Prostin insertion found that Propess insert does yield a distinct superiority in terms of VD within 24 hours and has the advantage of shorter hospital stay and less Postpartum hemorrhage compared to Prostin E2[16]. However, the insert does not perform much better than Prostin in decreasing rates of CS and promotion of VD in women at term with intact membrane and an unfavorable cervix. There is a consideration that the insert may have a higher rate of uterine hyperstimulation, despite the low rate. Even so, the superior benefit of vaginal insert compared to Prostin can be easily seen. A study looking at the mode of delivery even demonstrated that Propess achieved a significantly higher rate of spontaneous vaginal delivery compared to Prostin[3].

In our study, no difference in induction to delivery interval and complications associated with IOL between the two groups was found; but there was a significant increase in cesarean section rate in the Propess group. The causes for these different results could be the heterogeneity of the patients included in our study.

One major limitation to our findings is the trend of our junior staff to use Propess for induction of labor in primigravidas mainly. Our induction of labor protocol advises the use of Propess for patients with previous vaginal delivery with a maximum of 4 previous birth. The higher prevalence of primigravida in the Propess group would automatically increase the cesarean section rate. Various studies compared the two methods while confirming that parity remains the most predictive factor. Induction of women with an unfavorable cervix is associated with higher failure rate in nulliparous patients and a higher cesarean section rate in nulliparous and parous patients. This study was conducted immediately after introducing Propess for IOL in our hospital. The level of experience in the appropriate technique of application among the clinical team was inconstant.

The inappropriate application of Propess is associated with hyperstimulation, fetal distress or premature expulsion of the pessary. Bishop score assessment was not recorded in all cases which limit the ability to utilize it in our data collection. This is a very vital factor in assessing the visibility of successful vaginal delivery.

CONCLUSION

Induction of labor with Propess is associated with increased cesarean section rate compared to Prostin.

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