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Evaluation of Propess outcomes for cervical ripening and induction of labour in full-term pregnancy

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This study was to investigate the efficiency and safety of vaginal Propess as a methodology for cervical ripening and labour induction in full-term pregnant patients. Women at term with a Bishop's score of <6 and without any contraindications, to vaginal delivery, or the use of prostaglandin or oxytocin in induction of labour, were divided into three groups: oxytocin group ($n=59$), intact membranes (Propess I group; $n=58$) and natural rupture (Propess R group; $n=52$) groups. The main outcome measures, including change in Bishop's score, induction to delivery interval, total delivery time, rate of vaginal delivery, fetal outcome and maternal complications during induction, were recorded. In the Propess groups, the Bishop's score and rate of vaginal delivery were significantly higher while the induction to delivery interval and total delivery time were much shorter, as compared with oxytocin patients ($p<0.01$). There were no significant differences in fetal and maternal outcome during induction between the Propess groups and oxytocin group ($p>0.05$). In addition, there were no significant differences of Bishop's score, rate of vaginal delivery, induction to delivery interval and total delivery time between the Propess I group and Propess R group ($p>0.05$). Propess is an effective and safe approach to promote cervical ripening and be successfully used in induction of labour.

Keywords: Cervical ripening, induction of labour, oxytocin, Propess

Introduction

The achievement of delivery preceding the onset of spontaneous labour is defined as induction of labour. Induction of labour can be preferred instead of operational intervention in situations such as post-term pregnancies, eclampsia/pre-eclampsia, diabetes, intrauterine growth retardation or fetal distress (Sifakis et al. 2007). About 20–30% of all pregnant women have labour induction and labour induction is becoming a frequent practice (Beebe et al. 2000; Christensen et al. 2002; Coonrod et al. 2000). However, induction of labour may lead to uterine rupture, tachysystole and hyperstimulation of pregnant women (Ozkan et al. 2009; Sifakis et al. 2007). The purpose of promoting cervical ripening and induction of labour is to achieve vaginal delivery and to avoid operative delivery by caesarean section. Success of labour induction depends largely on the degree of cervical ripening at the onset of labour. When the cervix is unfavourable, induction attempts may fail, resulting in prolonged labour and caesarean delivery.

At present, oxytocin is the agent most frequently used for induction of labour (Benrubi 2000; Speert 1980). However, oxytocin for labour induction requires intravenous infusion, and it has many shortcomings such as long induction to delivery interval, high caesarean section rate and high induction failure rate. Propess, a controlled-release hydrogel pessary containing 10 mg prostaglandin E2, is also used for preinduction cervical ripening (Alfirevic et al. 2009; Hadi 2000; Leszczynska-Gorzelak et al. 2001). The major safety concern for Propess use is uterine hyperstimulation and fetal tachysystole. This can be rapidly reversed by terbutaline administration or by removal of the vaginal insert (Calder and MacKenzie 1997; Witter 2000). The pessary has a special retrieval tape that allows it to be removed quickly and easily once labour has started, or if there are any problems during the induction (Mukhopadhyay et al. 2002). The side-effects associated with this medicine are all events that can happen when the body goes into labour naturally, such as nausea and vomiting, diarrhoea or abnormally strong contractions of the womb (Mazouni et al. 2006). In Europe and the USA, Propess has been widely used in clinical settings, but in China, the clinical application is still in the exploratory stage.

The aim of this study is to compare the efficacy and safety of vaginal Propess with intravenous oxytocin administration for cervical ripening and induction of labor. The clinical investigation and the usefulness of Propess were investigated, which indicated its clinical diagnosis value for cervical ripening and induction of labour in full-term pregnancy.

Materials and methods

Patient selection

A total of 169 women were recruited, from December 2010 to December 2012, from the Department of Obstetrics, Shanghai Changning Maternity and Infant Health Hospital, into this study. Inclusion criteria: age between 22–35 years; singleton live pregnancies; primipara; 37–41 weeks' gestation; cervical Bishop's score ≤ 6; no contraindication for vaginal delivery and no contraindication for labour induction with prostaglandin or oxytocin.

Women who participated in the study were assessed by vaginal examination (assessment of the cervix included an assessment of consistency, length, dilatation, position and station of the fetal presenting part, as described by Bishop's and modified by Calder) for Bishop scoring. Bishop's score evaluation was made by a gynaecological specialist. The study was approved

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by the Local Ethics Committee of the hospital and performed in accordance with the ethical standards for human research established by the Declaration of Helsinki. All participants were informed and provided written consent before participation in the study.

Women at term with a Bishop's score ≤ 6 and intact amniotic membranes were randomised into two groups to undergo induction of labour with either low-dose oxytocin administered intravenously (oxytocin group; $n = 59$) or Propess vaginal pessary (Propess I group; $n = 58$). Women at term with a Bishop's score ≤ 6 and ruptured membrane were recruited into the third group to undergo induction of labour with Propess vaginally (Propess R group; $n = 52$).

Methods

The oxytocin group received oxytocin application (2.5 IU in 500 ml of 5% dextrose injection). The dosing regimen of oxytocin used a low-dose protocol (initial dose 8 drops/min, with increases of 4 drops/min until regular uterine contractions (3–4 contractions in ten minutes) had been achieved; 30 drops/min was the maximum limit). If the regular uterine contractions did not arrive after eight hours, the oxytocin was stopped and was continued the next day. Oxytocin should not be used in more than 3 days. In cases of uterine hyperstimulation, the oxytocin was stopped; the left-lying position, nasal oxygen and intravenous hydration were provided. If hyperstimulation continued, tocolytic therapy was administered.

The Propess groups (Propess I group and Propess R group) received a Propess application (containing 10 mg dinoprostone; CTS, UK), which was inserted high into the vaginal fornix. The pessary was removed when labour began (cervical dilatation of ≥ 0.5–1 cm, in the presence of uterine contractions, can be taken to reliably represent the threshold for active labour), uterine hyperstimulation syndrome, and twenty-four hours elapsed.

Observations

In this study, we evaluated Bishop's score changes, induction to delivery interval, total delivery time, rate of vaginal delivery, fetal outcome and maternal complications during induction for each study group.

Cervical ripening was defined as: (1) obvious: increased Bishop's score ≥ 3 at the end of 12 h; (2) effective: increased Bishop's score ≥ 2 at the end of 12 h; (3) invalid: increased Bishop's score < 2 at the end of 12 h or no change.

Labour effect was defined as: (1) success: labour started by 12 h; (2) effective: labour started by 24 h; (3) invalid: labour did not start within 24 h.

Table I. Demographic and baseline characteristics.

	Oxytocin ($n = 59$)	Propess I ($n = 58$)	Propess R ($n = 52$)	p value
Age (years)	27.8 ± 2.3	28.6 ± 1.9	28.9 ± 1.4	> 0.05
Gestational age (weeks)	37.4 ± 3.6	38.3 ± 2.7	39.3 ± 2.9	> 0.05
Bishop's score	3.6 ± 1.6	3.5 ± 1.4	3.8 ± 1.9	> 0.05
Estimated fetal weight (kg)	3.4 ± 0.6	3.5 ± 0.4	3.5 ± 0.8	> 0.05

Data are presented as mean $\pm$ SD. Each p value is two-tailed and significance level is 0.05.

Statistical analysis

Results were expressed as means $\pm$ SD or n (%). Statistical analyses were performed with Student's t-test, one-way ANOVA and χ^2-test. Statistical differences were examined using SPSS software. Each p value was two-tailed, and the significance level was set at $p = 0.05$.

Results

Demographic and baseline characteristics

A total of 169 patients were assigned into three groups: oxytocin group (low-dose oxytocin infusion), Propess I group (sustained-release 10 mg dinoprostone vaginal pessary) and Propess R group (sustained-release 10 mg dinoprostone vaginal pessary). The demographic and baseline characteristics of the participants among the groups are summarised in Table I. There were no significant differences among the three groups in age, gestational age, the initial Bishop's score and estimated fetal weight. Therefore, the indications for induction of labour were comparable among the three studied groups.

Bishop score

As we see in Table II, the Bishop's score gradually increased with the extension of the drug treatment. The Bishop's score was significantly higher in the Propess groups than in the oxytocin group after drug treatment for 6 h and 12 h ($p < 0.01$; Table II). In addition, the Bishop's score was higher in Propess R group than in the Propess I group, though there was no statistical significance. The cervical ripening after 12 h in the Propess groups was also much greater than that in the oxytocin group ($p < 0.01$; Table II).

Delivery outcomes

Both the induction to delivery interval and total delivery time were significantly shorter in the Propess groups ($p < 0.01$;

Table II. Bishop's score.

	Oxytocin ($n = 59$)		Propess I ($n = 58$)		Propess R ($n = 52$)		
	n	(%)	n	(%)	n	(%)	p value
Bishop's score							
Before treatment	3.6 ± 1.6		3.5 ± 1.4		3.8 ± 1.9		> 0.05
Treated for 6 h	4.1 ± 1.3		5.1 ± 1.7		5.8 ± 0.9		< 0.01
Treated for 12 h	4.4 ± 0.9		7.2 ± 1.8		7.9 ± 1.2		< 0.01
Cervical ripening after 12 h							< 0.01
Obvious	9	15.3	35	60.3	33	63.5	
Effective	17	28.8	19	32.8	16	30.8	
Invalid	33	55.9	4	6.9	2	3.8	

Data are presented as mean $\pm$ SD or n, (%). Each p value is two-tailed and significance level is 0.05.

Table III. Delivery effects.

	Oxytocin ($n = 59$)		Propess I ($n = 58$)		Propess R ($n = 52$)		
	n	(%)	*n*	(%)	*n*	(%)	*p* value
Induction to delivery interval (h)	31.4 ± 7.1		15.8 ± 6.4		10.5 ± 3.2		< 0.01
Total delivery time (h)	14.5 ± 2.0		11.7 ± 3.2		9.1 ± 1.1		< 0.01
Labour effect							< 0.01
Success	4	6.8	31	53.4	32	61.5	
Effective	17	28.8	24	41.4	19	36.5	
Invalid	38	64.4%	3	5.1	1	1.9	

Data are presented as mean ± SD or *n*, (%). Each *p* value is two-tailed and significance level is 0.05.

Table III). The labour effect was also better in the Propess groups than in oxytocin group ($p < 0.01$; Table III). The induction to delivery interval and total delivery time were shorter in the Propess R group than in Propess I group. This might be because the amnion had already ruptured in the Propess R group. Meanwhile, there was no significant difference in the labour effects between the Propess I group and Propess R group.

Mode of delivery

In the Propess groups, 90 (81.8%) women had their baby through the vagina versus only 21 (35.6%) women in the oxytocin group ($p < 0.01$; Table IV). The vaginal delivery rate in the Propess I group was slightly lower than that in Propess R group, though there was no statistical significance ($p > 0.05$; Table V). The reasons for caesarean delivery between the oxytocin group and the Propess groups were significantly different ($p < 0.05$; Table IV).

Delivery outcomes

No significant difference was detected in fetal tachycardia, amniotic fluid embolism, fetal weight and postpartum haemorrhage among the three groups ($p > 0.05$; Table VI).

Side-effects and complications of treatments

There were two cases of hyperstimulation, two cases of nausea and vomiting and nine cases of fetal distress in the Propess groups and one case of hyperstimulation, six cases of nausea and vomiting, 12 cases of fetal distress and one case of neonatal asphyxia in the oxytocin group (Table VII).

Discussion

Our study was designed to compare the two protocols: oxytocin and Propess. Propess, approved by the FDA for cervical ripening in women in 1999, is a controlled-release prostaglandin E2 suppository. It has important effects in labour (softens the cervix and causes uterine contractions) (Mukhopadhyay et al. 2002). It is widely welcomed by medical workers and puerperas because its application neither limits movement nor increases the spirit burden of puerperas. Low-dose oxytocin is also used for labour induction and supporting labour in cases of difficult parturition. Oxytocin promotes contractions of the uterine smooth muscle. It is destroyed in the gastrointestinal tract, so must be administered by injection. Excessive dosage of oxytocin administration has been known to result in tetanic uterine contractions, uterine rupture and postpartum hemorrhage. Oxytocin should therefore be started at a low-dose with appropriate dose adjustment. Special management is also needed to avoid potential adverse reactions. Because intravenous oxytocin application limits the freedom of movement, it increases the spirit burden of puerperas and the rate of caesarean sections. Therefore, the effects of oxytocin for cervical ripening and labour induction is not satisfactory.

In this study, the Bishop's score was three scores higher in the Propess groups than that in the oxytocin group ($p < 0.01$) when drugs were treated for 12 h. It indicated that Propess can significantly promote cervical ripening compared with oxytocin. This is consistent with Hawkins' discovery that dinoprostone was superior to oxytocin alone for cervical ripening (Hawkins and Wing 2012). Both the induction to delivery interval and total delivery time were shortened in the Propess groups compared with the oxytocin group ($p < 0.01$), which revealed the effectiveness of Propess in labour induction. Silfeler and colleagues (2011) reported a higher vaginal birth rate in the oxytocin group than in the dinoprostone group. In this study, the vaginal delivery rate was significantly higher in the Propess groups (81.8%) than in the oxytocin group (35.6%). This is consistent with the conclusion of a meta-analysis that oxytocin is less effective than vaginal prostaglandin E2 (PGE2) in bringing about vaginal delivery within 24 h (Alfirevic et al. 2009). Bezircioglu and coworkers (2012) also reported that dinoprostone reduced both the latent phase of labour and total delivery time without increasing the rate of caesarean section. These data proved the efficiency of Propess used in promoting cervical ripening and labour induction. Moreover,

Table IV. Comparison of delivery mode between the oxytocin group and the Propess groups.

	Oxytocin		Propess		
	n	(%)	*n*	(%)	*p* value
Delivery mode					< 0.01
Vaginal	21	35.6	90	81.8	
Caesarean	38	64.4	20	18.2	
Reasons for caesarean					< 0.05
Fetal tachycardia	12		9		
Labour induction failure	18		6		
Social factors	5		5		
Meconium painted amnion	3		0		

Each *p* value is two-tailed and significance level is 0.05.

Table V. Comparison of delivery mode between the natural rupture Propess group (R) and the intact membranes Propess group (I).

	Propess I ($n = 58$)		Propess R ($n = 52$)		
	n	(%)	*n*	(%)	*p* value
Delivery mode					> 0.05
Vaginal	46	78.9	44	84.6	
Caesarean	12	19.2	8	15.4	

Each *p* value is two-tailed and significance level is 0.05.

Table VI. Comparison of delivery outcomes.

	Oxytocin ($n = 59$)		Propess I ($n = 58$)		Propess R ($n = 52$)		
Characteristic	*n*	(%)	*n*	(%)	*n*	(%)	*p* value
Fetal tachycardia	5	8.5	2	3.4	3	5.8	>0.05
Amniotic fluid embolism	4	3.4	2	3.4	1	1.9	>0.05
Fetal weight (kg)	3.4 ± 0.9		3.5 ± 0.5		3.5 ± 0.2		>0.05
Postpartum haemorrhage (ml)	155 ± 21		142 ± 25		151 ± 18		>0.05

Data are presented as mean $\pm$ SD or *n*, (%). Each *p* value is two-tailed and significance level is 0.05.

Table VII. Side-effects and complications of treatments.

	Oxytocin ($n = 59$)		Propess ($n = 110$)	
	n	(%)	*n*	(%)
Hyperstimulation	1	1.7	2	1.8
Nausea and vomiting	6	10.2	2	1.8
Fetal distress	12	20.3	9	8.2
Neonatal asphyxia	1	1.7	0	

there were no significant differences in fetal tachycardia, amniotic fluid embolism, fetal weight and postpartum hemorrhage between the Propess groups and oxytocin group, which indicated the security of the clinical application of Propess.

No significant difference was found in this study in Bishop's scores, induction to delivery time, total delivery time or vaginal delivery rate between Propess I group and Propess R group. It has illustrated that both puerpera with intact membranes and puerpera with rupture amniotic could use Propess safely. Increased hyperstimulation cases in labour induction in the oxytocin group have been reported (Seitchik and Castillo 1982). We found Propess could prevent the infection risk caused by long delivery time and increase the confidence of puerpera in vaginal delivery. However, there were also some adverse reactions in Propess groups, such as nausea and vomiting and fetal distress. Therefore, the uterine contraction and fetal heart rate should be monitored when using Propess. If there is something wrong, Propess should be removed immediately, and appropriate measures should be taken. The hospital stay was also consequently shorter in the Propess groups, thus contributing to cost-effectiveness, as compared with the oxytocin group (Vollebregt et al. 2002).

A major limitation of this study was that the patients and doctors were not blind to the allocation of the study groups because the nature of the intervention did not permit blinding of healthcare providers.

In conclusion, results of this randomised trial showed that use of vaginal Propess resulted in a shorter induction to delivery interval, a shorter total delivery time and a higher vaginal delivery rate compared with intravenous oxytocin. These results suggested that Propess might be used to achieve timely and safe delivery in the presence of an unfavourable cervix and could be popularised in domestic clinical application.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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