Original Article

DOI: 10.5582/ddt.2015.01033

Efficiency of dinoprostone insert for cervical ripening and induction of labor in women of full-term pregnancy compared with dinoprostone gel: A meta-analysis

Xianling Zeng[1,*], Yafei Zhang[2,*], Quan Tian[1], Yan Xue[1], Rong Sun[1], Wei Zheng[1], Ruifang An[1,]**

[1] *Department of Obstetrics and Gynecology, the First Affiliated Hospital, Xi'an Jiao Tong University, Xi'an, Shaanxi, China;*
[2] *Department of General Surgery, the Second Affiliated Hospital, Xi'an Jiao Tong University, Xi'an, Shaanxi, China.*

Summary **The aim of this study is to evaluate the efficiency of dinoprostone insert, compared with dinoprostone gel, for cervical ripening and induction of labor in women at term. We searched electronic databases and bibliographies of relevant papers to identify randomized controlled trials (RCTs) reporting dinoprostone insert and gel used for cervical ripening and induction of labor. Fifteen RCTs involving 1779 women were included. Dinoprostone insert could greatly contribute to vaginal delivery (VD) within 24 h compared with dinoprostone gel (OR = 2.35, 95% CI = 1.34, 4.13) and the researchers found obvious statistically significant difference (p = 0.003). Yet a meta-analysis of the rates of VD, artificial assisted vaginal delivery and caesarean section (CS) revealed no margin between dinoprostone insert and gel. Dinoprostone insert showed a distinct superiority in terms of VD within 24 h and had an advantage of a shorter hospital stay and less postpartum hemorrhage in contrast to gel. Even though the insert did not perform much better than gel in decreasing the rate of CS and increasing the rate of VD, yet the superior benefit of the vaginal insert compared to gel was still not difficult to observe.**

Keywords: Cervical ripening, caesarean section, dinoprostone, induction of labor, vaginal delivery

1. Introduction

Induction of labor, a common practice that is used in pregnant women, accounts for 20% of all births (*1*). It is applied for the intentional initiation of labor before spontaneous onset, for the purpose of delivery of the fetoplacental unit (*2*). The rate of induction varies by location and is currently more than 20% in America (*3,4*). When the cervix is unfavorable, in order to increase the likelihood of successful induction, promoting cervical ripening is automatically recommended.

Conventionally, oxytocin is used for augmentation of labor in patients with a favorable cervix. Yet for patients with an unfavorable cervix, a sharply ripening agent may be considered. As is well known to all, prostaglandin works efficiently in cervical ripening and labor induction. So dinoprostone surely performs quite well in promoting cervical ripening and labor induction since its main component is prostaglandin E2 (PGE2).

Dinoprostone gel has been successfully used for many years to achieve cervical ripening and induction of labor in women of full-term pregnancy (not less than 37 weeks of gestation) with an unfavorable cervix (Bishop's score < 7). While dinoprostone insert which has also been proved to be effective for cervical ripening and gradual onset of labor for women of full-term pregnancy with suitable indications as a local application through the consistently controlled release of 0.3mg of dinoprostone per hour (*5*). There have been several meta-analyses and systematic reviews evaluating the use of PGE2 and suggesting that it is effective for cervical ripening and labor induction, without distinguishing between dinoprostone insert and gel (*6-8*). A study reported that slow-release PGE2

*These authors contributed equally to this works.
***Address correspondence to:*
Dr. Ruifang An, Department of Obstetrics and Gynecology, the First Affiliated Hospital, Xi'an Jiao Tong University, Xi'an 710061, China.
E-mail: anruifangxj@163.com

vaginal insert achieved cervical ripening and subsequent delivery over a shorter time period (*9*). Conversely, another study declared PGE2 vaginal gel was superior for the induction of labor (*10*). As mentioned above, when it comes to which formulation is optimal, there is an extremely fierce ongoing debate on the preparations of PGE2.

So we assumed that a meta-analysis of published randomized control trails (RCTs) may be beneficial. Thus our objective was chiefly to evaluate the efficiency of dinoprostone insert, compared with dinoprostone gel, for cervical ripening and induction of labor in women at term with an unfavorable cervix and intact membranes.

2. Materials and Methods

2.1. *Search strategy*

We searched PubMed, Medline, the Cochrane Library and bibliographies of relevant papers for articles in English published up to December 2014, using the keywords and combinations of the following search terms "induction of labour/ labor" or "cervical ripening", "intracervical insert" or "Propess" or "Cervidil" or "vaginal pessary" or "dinoprostone insert", "intracervical gel" or "Prepidil" or "dinoprostone gel".

2.2. *Study selection criteria*

We identified RCTs of women of full term pregnancy (not less than 37 weeks of gestation), with intact membrane and unfavorable cervix. Simultaneously, their Bishop's score was less than 7. Dinoprostone insert and gel were given separately to women in treatment group and matched group.

2.3. *Study exclusion criteria*

Abstracts, reviews and unpublished work were excluded because of the absence of details concerning study methods and results. Studies were surely ineligible if there was no information provided on any of the outcomes of focus, if data were not reported regarding the intention to deal with it or if more than 20% of women in either group were lost to follow up.

2.4. *Data extraction, synthesis and analysis*

If the abstract described a study which did not meet the eligible criteria, the study was not reviewed any further. Eligible articles were reviewed in detail. The review of articles was undertaken independently by two reviewers (Zeng and Zhang) who decided which articles were eligible. Any disagreements were resolved by discussing with a third reviewer (Tian).

The two reviewers extracted data for outcomes independently. The primary outcomes were the rates of vaginal delivery (VD) and caesarean section (CS). While VD within 24 h, artificial assisted vaginal delivery, as well as reasons for CS, such as fetal distress, abnormal labor and failure of induction were considered as the secondary outcomes. A subgroup analysis for nulliparous and multiparous women was also conducted. Usage of oxytocin, hospital stay and uterine hyperstimulation were analyzed if data were provided. Baseline data were depicted explicitly if possible.

Statistical analyses were conducted using the program "Review Manager 5.2". We calculated a summary odds ratio (OR) and 95% confidence interval (CI) for dichotomous variables, using Mantel-Haenszel and fixed/random effects mode (*11*). The OR was calculated as the ratio of the number of events using the vaginal insert over that using gel. If the 95% CI did not encompass 1.0 for OR or if the *p* value was less than 0.05, then the results were considered to be statistically significant. Homogeneity of tests among pooled results were performed using simple chi-square test. Quality assessment of the trials was conducted based on the criteria of the Cochrane Handbook for Systematic Reviews of Interventions by categorizing as adequate, inadequate or unclear with respect to allocation concealment, blinding, completeness of follow-up and whether a study was multicenter (*12*). Available from www.cochrane-handbook.org.roach to examine publication bias (*13*).

3. Results

The research generated 53 pieces of paper totally. However, 24 articles were excluded undoubtedly owing to lack of eligible criteria and the remaining 29 articles were reviewed carefully. Among these, 14 articles were not recruited for the following reasons: 5 studies were in abstract only (*14-18*); 5 studies were reviews (*6,19-22*); 3 studies had unavailable data (*23-25*); 1 study had incomplete data (*26*). Finally, 15 RCTs (*27-41*) involving 1779 women were included (Figure 1).

The demographics of the included studies and the methods used for randomization are exhibited (Table 1). The largest number of objectives was 320, while the number of remaining studies enrolled was fewer than 150. Most studies included a large proportion of nulliparous women who accounted for almost more than 60 percent in 9 studies. The basal Bishop score (BBS) in 13 trials was less than 5, with one untold and another ≤ 7. The gestational age (GA) in 14 trails was more than 38 weeks except one was almost 36 weeks. All trials described randomized assignment, usually using computer-generated random numbers, with one trial using opaque, sealed envelopes and another using pre-packed, identical, sealed envelopes to attempt

allocation concealment.

As to quality assessment (Table 2), quality was quite poor on the whole. Only the follow-up achieved total adequateness. Binding was applied in just three studies. Only one had a multi-center study and allocation concealment was inadequate in almost all studies.

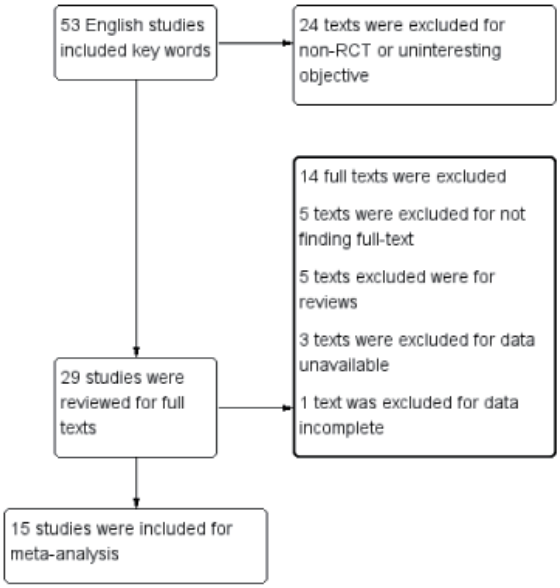

Figure 1. Search algorithm.

Dinoprostone insert could neither increase the odds of VD nor that of artificial assisted vaginal delivery compared with dinoprostone gel (OR = 1.12, 0.96) and there were no statistically significant differences (p = 0.34, 0.87) (Figures 2 and 3). Simultaneously, in contrast to dinoprostone gel, dinoprostone insert cannot decrease the rate of CS (OR = 0.89; 95% CI = 0.71, 1.12) and no statistically significant difference was observed (p = 0.34) (Figure 4). In terms of sub-analysis of reasons for CS, dinoprostone insert could not sharply decrease the rate of CS owing to fetal distress, abnormal labor and failure of induction, compared to dinoprostone gel. Gratefully, dinoprostone insert did much better in contributing to VD within 24 h than dinoprostone gel (OR = 2.35, 95% CI = 1.34, 4.13) and the researchers found an obvious statistically significant difference (p = 0.003) (Figure 5). To evaluate possible exiting publication bias for the outcome, a funnel plot demonstrated no evidence of asymmetry, suggesting that publication bias was not present (Figure 6).

4. Discussion

The findings indicate that dinoprostone insert could increase the rate of VD within 24 h, which was consistent with the conclusion of a current study (*42*). While the

Table 1. Description of populations and methods of randomization of included studies

Study	Country	NP, *n* (%)	MA (years)	BBS	GA (weeks)	Method of randomisation
Vollebregt *et al.*	Netherlands	33 (66)	30.4 ± 4.2	–	40.3 ± 1.8	–
		37 (74)	29.9 ± 4.9	–	40.5 ± 1.9	–
D'Aniellol *et al.*	Italy	54 (82)	29.3 ± 3.2	3.64 ± 1.43	40.5 ± 2.7	Computer-generated
		37 (75)	28.6 ± 3.7	3.5 ± 1.04	40.9 ± 2.7	as assignment
Marconi *et al.*	Italy	109 (66.7)	30.3 ± 5.1	4.0 ± 1.1	39.6 ± 1.4	Computer-generated
		111 (68.9)	31.0 ± 4.7	4.1 ± 1.2	39.6 ± 1.3	as assignment
Facchinetti1 *et al.*	Italy	70 (100)	29.1 ± 4.9	≤ 3	40.7 ± 1.4	Computer-generated
		70 (100)	27.9 ± 5.1	≤ 3	40.9 ± 1.1	as assignment
Ramsey *et al.*	Ireland	22 (57.9)	26.7 ± 3.6	3.0 ± 1.2	39.3 ± 1.3	Computer-generated table
		21 (60.0)	28.0 ± 4.4	3.0 ± 1.2	39.2 ± 1.3	with opaque,sealed envelopes
Grignaffini *et al.*	Italy	36 (71)	30.0 ± 3.6	< 5	40 ± 1.0	Unclear
		40 (77)	31.0 ± 4.9	< 5	40 ± 1.0	
Strobelt *et al.*	Italy	34 (61)	33*	≤ 4	37-41	Single-blind
		30 (59)	33*	≤ 4	37-41	randomisation
Connell *et al.*	UK	–	27.6	3.8	40.4	Computer-generated
		–	28.1	3.6	40.4	as assignment
Kalkat *et al.*	UK	13(43)	27.1 ± 5.4	3.5 ± 1.4	38.5 ± 1.9	Pre-packed, identical,
		10(33)	27.1 ± 5.9	3.3 ± 1.6	38.8 ± 1.7	sealed envelopes.
Ottinger *et al.*	America	28(62)	26.0 ± 7.0	2.8 ± 1.6	39.1 ± 3.0	Computer-generated
		27(60)	25.2 ± 6.7	2.9 ± 1.9	39.0 ± 2.8	as assignment
Chyu *et al.*	Chicago	20(54)	29.8 ± 5.7	≤ 7	39.2 ± 2.1	Computer-generated
		18(50)	27.8 ± 6.5	≤ 7	39.0 ± 2.2	as assignment
Stewart *et al.*	Oklahoma, USA	39(53)	24.8 ± 5.8	3.4 ± 1.5	39.9 ± 1.6	Computer-generated
		38(49)	24.1 ± 6.1	3.5 ± 1.4	40.1 ± 1.5	as assignment
Hennessey *et al.*	Oklahoma, USA	15(42)	23.4*	1.6 ± 0.7	36.9 ± 3.4	Computer-generated
		16(47)	24.4*	1.9 ± 0.5	35.9 ± 3.6	as assignment
Facchinetti *et al.*	Italy	58(100)	29.7 ± 4.8	< 4	41.7 ± 0.6	Computer-generated
		58(100)	29.1 ± 5.9	< 4	41.6 ± 0.8	as assignment
Triglia *et al.*	Italy	52(80)	31*	2	41.0 ± 3.0	Computer-generated
		46(71)	32*	3	41.0 ± 3.0	as assignment

BBS, basal Bishop score; MA, maternal age; NP, nulliparous; GA, gestational age; *, mean; —, data unavailable. Values are mean ± S.D.

Table 2. Description of quality assessment of included studies

Study	Treatment	Comparision	Allocation concealment	Blinding	Follow-up	Multicenter
Vollebregt *et al*.2002	Controlled release PgE2 (Propess)PV 10 mg (12h), *n* = 50	PgE2 gel (Prepidil) 0.5 mg IC one dose, *n* = 50	IA	IA	A	IA
D'Aniellol *et al*.2003	PgE2 pessary 10 mg (12 h), *n* = 49	PgE2 gel 0.5 mg IC one dose, *n* = 66	IA	IA	A	IA
Marconi *et al*.2008	Controlled release PgE2 (Propess)PV 10 mg (12 h), *n* = 159	PgE2 gel (Prepidil) 0.5 mg IC or 1 mg IV 6 hours up to three doses, *n* = 161	IA	IA	A	IA
Facchinetti *et al*.2005	Controlled release PgE2 (Propess)PV 10 mg (12 h), *n* = 70	PgE2 gel (Prepidil) 0.5 mg IC Q12 h, *n* = 70	IA	A	A	IA
Ramsey *et al*.2003	Controlled release PgE2 (Cervidil)PV 10 mg (12 h), *n* = 38	PgE2 gel (Prepidil) 0.5 mg, 6 hours up to two doses, *n* = 35	IA	IA	A	IA
Grignaffini *et al*.2004	Slow release PgE2 (Propess) PV 10 mg (12 h), *n* = 51	PgE2 gel (Prepidil) 1.0 mg, 6 hours up to two doses, *n* = 52	U	U	A	IA
Strobelt *et al*.2006	Slow release PgE2 (Propess) PV 10 mg (12 h), *n* = 56	PgE2 gel (Prepidil) 0.5 mg, 6 hours up to two doses, *n* = 51	IA	A	A	A
Connell *et al*.2006	Sustained-release PgE2 (Propess)PV 10 mg (12 h), *n* = 34	PgE2 gel (Prostin) 0.5 mg, 6 hours up to two doses, *n* = 38	IA	IA	A	IA
Kalkat *et al*.2008	Slow release PgE2 (Propess) PV 10 mg (12 h), *n* = 60	PgE2 gel (Prostin), unclear, *n* = 60	A	A	A	IA
Ottinger *et al*.1998	Controlled release PgE2 (Cervidil)PV 10 mg (12 h), *n* = 45	PgE2 gel (Prepidil) 0.5 mg,6 hours up to two doses, *n* = 45	IA	IA	A	IA
Chyu *et al*.1997	Controlled release PgE2 (Cervidil)PV 10 mg (12 h), *n* = 37	PgE2 gel (Prepidil) 0.5 mg, unclear, *n* = 36	IA	IA	A	IA
Stewart *et al*.1998	Controlled release PgE2 (Cervidil)PV 10 mg (12 h), *n* = 37	PgE2 gel (Prepidil) 0.5 mg, unclear, *n* = 36	IA	IA	A	IA
Hennessey *et al*.1998	Controlled release PgE2 (Cervidil)PV 10 mg (12 h), *n* = 36	PgE2 gel (Prepidil) 0.5 mg, unclear, *n* = 34	IA	IA	A	IA
Facchinetti *et al*.2007	Slow release PgE2 PV 10 mg (12 h), *n* = 58	PgE2 gel, unclear, *n* = 58	IA	IA	A	IA
Triglia *et al*.2010	(Pessary)PV 10 mg (24 h), *n* = 65 Controlled release PgE2	PgE2 gel (Prepidil), 2.0 mg up to two doses, *n* = 65	IA	U	A	IA

Mg, microgram; PV, per vaginum; Q, every; h, hour; IC, intracervical; IV, intravaginal; A, adequate; IA, inadequate; U,unclear.

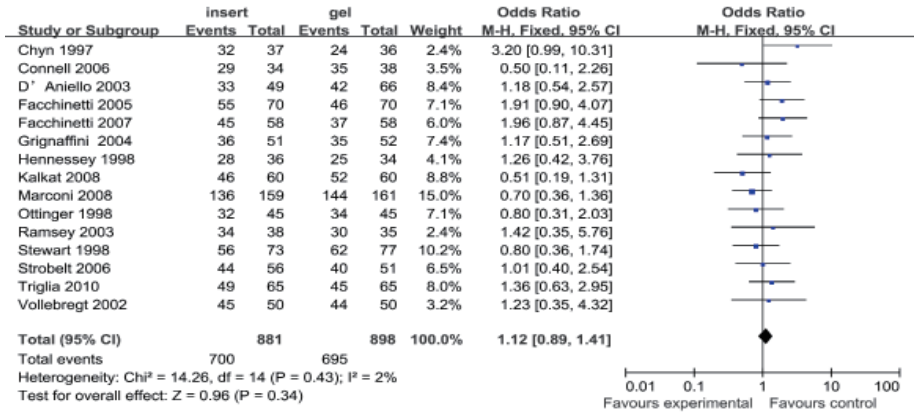

Figure 2. Meta-analysis of data about vaginal delivery (VD) from 15 studies using a fixed-effect model. CI, confidence interval; OR, odds ratio.

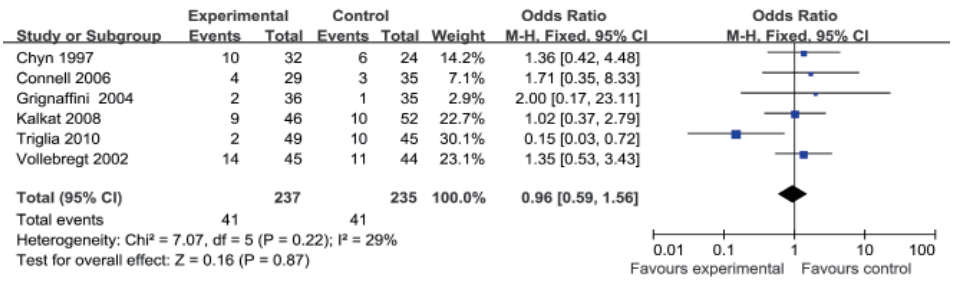

Figure 3. Meta-analysis of data about artificial assisted vaginal delivery from 5 studies using a fixed-effect model. CI, confidence interval; OR, odds ratio.

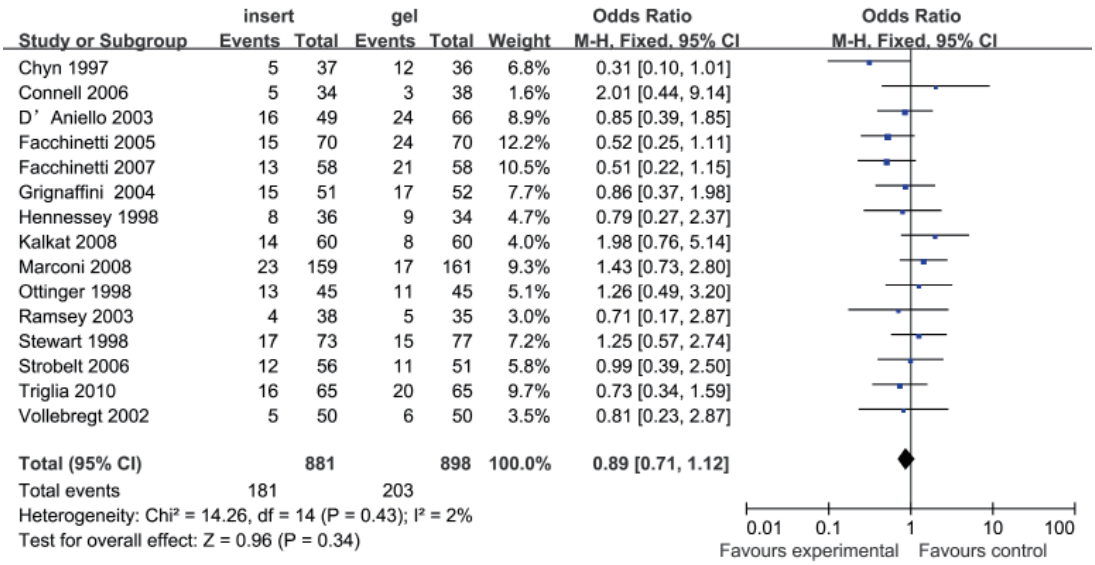

Figure 4. Meta-analysis of data about caesarean section (CS) from 15 studies using a fixed-effect model. CI, confidence interval; OR, odds ratio.

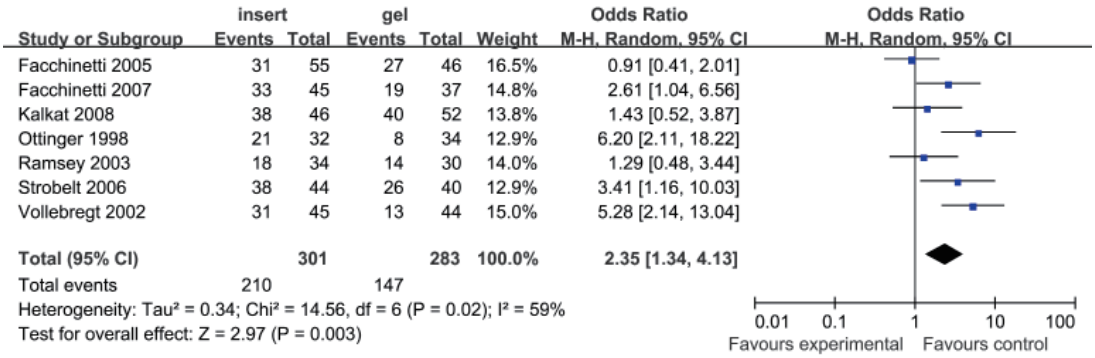

Figure 5. Meta-analysis of data about vaginal delivery within 24 h from 7 studies using a random-effect model. CI, confidence interval; OR, odds ratio.

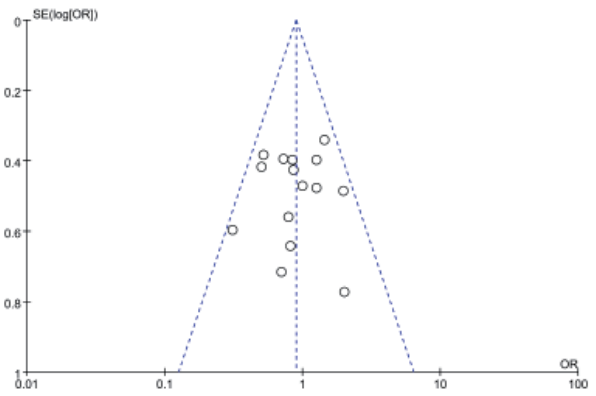

Figure 6. Publication bias is assessed by funnel plot, of which the asymmetry is exhibited by evidence of small studies with higher odds ratio and the paucity of small negative studies in the lower right of the funnel plot.

insert did not appear to be more effective than gel in altering the rates of VD, CS, or artificial assisted vaginal delivery, as well as the reasons for CS. This distinguished with a previous report which showed dinoprostone insert had a better effect than gel (*26*). The inconspicuous advantage may attribute to that the vaginal insert was applied for only 12 h in most cases and we probably speculated that a longer application of insert, such as 24 h, may generate a remarkable difference.

In order to test whether a distinction exists between nullipara and multipara, researchers conducted an analysis of a subgroup of VD and CS for dinoprostone insert and gel in nullipara and multipara cases respectively. Results showed both insert and gel assisted more in promoting VD and decreasing the odds of CS in multipara than nullipara. By comparing the ORs, insert appeared to contribute much more than gel. However, the net effect of dinoprostone was worth further investigation in that the possibilities of successful cervical ripening and induction of labor were intrinsically greater in multipara.

Oxytocin was utilized additionally during the process of induction of labor as well, so researchers also gave a glimpse of situations where it occurred in 5 studies (*28,30,32,33,40*). Concerning its homogeneity,

the fixed model was used to achieve the aim (OR = 0.65, 95% CI = 0.35, 1.20). The OR appeared to convey that the utilization rate of oxytocin in the insert group was lower, but no statistically significant difference was observed (p = 0.17). This was inconsistent with previous reports which assumed less need for oxytocin was necessary in the process with the insert working (*43,44*).

The length of hospitalization was reported in only 2 studies (*32,33*), evaluating 246 women, with 123 receiving dinoprostone insert. The result revealed the rates of hospital stay more than 4 days were 0.41 *vs*. 0.46 with respect to dinoprostone insert and gel. Also, postpartum hemorrhage was reported in 2 studies (*31,32*) showing that the rates were 0.13 versus 0.23 regarding dinoprostone insert and gel separately. There existed a flaw that the definition of postpartum hemorrhage in the two studies were not given clearly. In terms of uterine hyperstimulation, Strobelt and D'Anie demonstrated the rates between the two were 0.034 and 0.020 (*28,31*). To conclude, the insert had an advantage of shorter hospital stay and less postpartum hemorrhage in contrast to the gel. However, the insert may have a higher rate of uterine hyperstimulation, even if the rate is quite low. That still leaves a significant flaw. Since a recent study comparing the efficacy of 24h vaginal insert of PGE2 in comparison to vaginal gel of PGE2, a similar rate of uterine hyperstimulation was found (*41*).

Nevertheless, dinoprostone insert functions through the consistent, controlled release of 0.3 mg dinoprostone to attain the aim of a gradual onset of cervical ripening and labor induction. Hence, the times of vaginal examination using dinoprostone insert decrease sharply in contrast to gel during the process of labor. Namely, it could help to lessen doctors' workload and patients' discomfort arising from vaginal examination. From this point of view, dinoprostone insert is surely superior to gel.

In addition, we failed to appraise the risks of Apgar score less than 7 at 5 minutes, admission to a neonatal intensive care unit (NICU), perinatal mortality, neonatal morbidity (such as birth asphyxia and neonatal encephalopathy), maternal morbidity (such as chorioamnionitis, sepsis, uterine rupture and admission to an intensive care unit), maternal mortality and adverse effects (such as nausea, vomiting, and diarrhea) on account of data unavailable.

Moreover, the absence of adequate data about the related risks, such as length of hospitalization, postpartum hemorrhage and hyperstimulation, leads to an observation that analysis of safety was greatly contracted. Although a study reported that sustained-release of dinoprostone led to spontaneous induction of labor without increasing the obstetrical risks in a majority of patients (*45*) but further investigation about this issue should be conducted in the future.

The limitation of this meta-analysis, from the methodological aspect, is that the included studies are mostly of low-to-medium quality. Although we searched all of the worldwide literature, the 6 included studies came from Italy, the others were Netherlands, Ireland, England and America. Perhaps the lack of multicenter studies leads to a deviation. Despite all of the shortages above, the strength of our survey is stronger than any single study since the included primary studies are quite homogeneous, and it incorporated 15 RCTs involving 1,779 women.

Given the previously mentioned variability in characteristics of the patients, locations, and methodologies, careful interpretation of the results should be taken into consideration. Totally, dinoprostone 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 in contrast to gel. However, the insert does not perform much better than gel 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, even if the rate is quite low. Even so, the superior benefit of vaginal insert compared to gel can be easily seen.

References

1. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S. Births: final data for 2004: National vital statistics reports. Hyattsville, MD: National Center for Health Statistics, 2009.
2. ACOG Committee on Practice Bulletins – Obstetrics. ACOG Practice Bulletin No. 107: induction of labor. Obstet Gynecol. 2009; 114:386-397.
3. Zhang J, Yancey MK, Henderson CE. U.S. national trends in labor induction, 1989-1998. J Reprod Med. 2002; 47:120-124.
4. Rayburn WF, Zhang J. Rising rates of labor induction: present concerns and future strategies. Obstet Gynecol. 2002; 100:164-167.
5. Justus Hofmeyr G. Induction of labour with an unfavourable cervix. Best Pract Res Clin Obstet Gynaecol. 2003; 17:777-794.
6. Crane JM, Butler B, Young DC, Hannah ME. Misoprostol compared with prostaglandin E2 for labour induction in women at term with intact membranes and unfavourable cervix: a systematic review. BJOG. 2006; 113:1366-1376.
7. Sanchez-Ramos L, Kaunitz AM, Delke I, Gaudier FL. Cervical ripening and labor induction with a controlled-release dinoprostone vaginal insert: a meta-analysis. Obstet Gynecol. 1999; 94:878-883.
8. Hughes EG, Kelly AJ, Kavanagh J. Dinoprostone vaginal insert for cervical ripening and labor induction: A meta-analysis. Obstet Gynecol. 2001; 97:847-855.
9. Ashwal E, Hiersch L, Melamed N, Manor Y, Wiznitzer A, Hod M, Yogev Y. Pre-induction cervical ripening: comparing between two vaginal preparations of dinoprostone in women with an unfavorable cervix. J Matern Fetal Neonatal Med. 2014; 27:1874-1879.

10. Taher SE, Inder JW, Soltan SA, Eliahoo J, Edmonds DK, Bennett PR. Prostaglandin E2 vaginal gel or tablets for the induction of labour at term: a randomised controlled trial. BJOG. 2011; 118:719-725.
11. DerSimonian R, Laird N. Meta-analysis in clinical trials. Controlled clinical trials. 1986; 7:177-188.
12. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011.
13. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997; 315:629-634.
14. Nikolov A, Dimitrov A, Krusteva K, Nashar S. Study of the effect of Propess for ripening of the unfavorable cervix for the induction of labor due to medical indications. Akush Ginekol (Sofiia). 2003; 42:5-8.
15. Facchinetti F, Venturini P, Fazzio M, Volpe A. Elective cervical ripening in women beyond the 290th day of pregnancy: a randomized trial comparing 2 dinoprostone preparations. J Reprod Med. 2007; 52:945-949.
16. Arduini M, Giri C, Giannone L, Giannone E. Prepidil versus Propess: pharmacological induction of labour with dinoprostone. Minerva Ginecol. 2008; 60:127-133.
17. Grignaffini A, Soncini E, Anfuso S, Ronzoni E. Dinoprostone: slow release vaginal insert (Propess) and intracervical gel (Prepidil) for the induction of labour with unriped cervix. Minerva Ginecol. 2004; 56:413-418.
18. Hassan AA. A comparison of oral misoprostol tablets and vaginal prostaglandin E2 pessary in induction of labour at term. J Coll Physicians Surg Pak. 2005; 15:284-287.
19. Facchinetti F, Fontanesi F, Giovane CD. Pre-induction of labour: comparing dinoprostone vaginal insert to repeated prostaglandin administration: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2012; 25:1965-1969.
20. Mozurkewich EL, Chilimigras JL, Berman DR, Perni UC, Romero VC, King VJ, Keeton KL. Methods of induction of labour: a systematic review. BMC Pregnancy Childbirth. 2011; 11:84.
21. Calder AA, MacKenzie IZ. Review of Propess − a controlled release dinoprostone (prostaglandin E2) pessary. J Obstet Gynaecol. 1997; 17 (Suppl 2):S53-67.
22. Austin SC, Sanchez-Ramos L, Adair CD. Labor induction with intravaginal misoprostol compared with the dinoprostone vaginal insert: a systematic review and metaanalysis. Am J Obstet Gynecol. 2010; 202:624 e1-9.
23. Chen W, Zhou Y, Pu X, Xiao C. Evaluation of Propess outcomes for cervical ripening and induction of labour in full-term pregnancy. J Obstet Gynaecol. 2014; 34:255-258.
24. Faschingbauer F, Voigt F, Kunzmann U, Dammer U, Heller F, Beckmann MW, Goecke TW. Is Propess a better method to induce labour in nulliparous women with adverse conditions for induction? Geburtsh Frauenheilk. 2011; 71:277-281.
25. Mazouni C, Provensal M, Menard JP, Heckenroth H, Guidicelli B, Gamerre M. Evaluation of controlled-release dinoprostone Propess® for labor induction. Gynecol Obstet Fertil. 2006; 34:489-492.
26. Mukhopadhyay M, Lim KJ, Fairlie FM. Is propess a better method of induction of labour in nulliparous women. J Obstet Gynaecol. 2002; 22:294-295.
27. Grignaffini A, Soncini E, Anfuso S, Ronzoni Ei. Dinoprostone slow release vaginal insert (Propess) and intracervical gel (Prepidil) for the induction of labour with unriped cervix. Minerva Ginecol. 2004; 56:413-418.
28. D'Aniello G, Bocchi C, Florio P, Ignacchiti E, Guidoni CG, Centini G. Cervical ripening and induction of labor by prostaglandin E2: a comparison between intracervical gel and vaginal pessary. J Matern Fetal Neonatal Med. 2003; 14:158-162.
29. Vollebregt A, van't Hof DB, Exalto N. Prepidil compared to Propess for cervical ripening. Eur J Obstet Gynecol Reprod Biol. 2002; 104:116-119.
30. Ramsey PS, Harris DY, Ogburn PL Jr, Heise RH, Magtibay PM, Ramin KD. Comparative efficacy and cost of the prostaglandin analogs dinoprostone and misoprostol as labor preinduction agents. Am J Obstet Gynecol. 2003; 188:562-565.
31. Strobelt N, Meregalli V, Ratti M, Mariani S, Zani G, Morana S. Randomized study on removable PGE2 vaginal insert versus PGE2 cervical gel for cervical priming and labor induction in low-Bishop-score pregnancy. Acta Obstet Gynecol Scand. 2006; 85:302-305.
32. Marconi AM, Bozzetti P, Morabito A, Pardi G. Comparing two dinoprostone agents for cervical ripening and induction of labor: A randomized trial. Eur J Obstet Gynecol Reprod Biol. 2008; 138:135-140.
33. Facchinetti F, Venturini P, Verocchi G, Volpe A. Comparison of two preparations of dinoprostone for pre-induction of labour in nulliparous women with very unfavourable cervical condition: a randomised clinical trial. Eur J Obstet Gynecol Reprod Biol. 2005; 119:189-193.
34. Connell RJ, El-Shawarby SA. Induction of labour at term with vaginal prostaglandins preparations: A randomised controlled trial of Prostin vs Propess. J Obstet Gynaecol. 2006; 26:627-630.
35. Kalkat RK, Mcmillan E,Cooper H, Palmer K. Comparison of dinoprostone slow release pessary (Propess) with gel (Prostin) for induction of labour at term – a randomised trial. J Obstet Gynaecol. 2008; 28:695-699.
36. Hennessey MH, Rayburn WF, Stewart JD, Liles EC. Pre-eclampsia and induction of labor: A randomized comparison of prostaglandin E2 as an intracervical gel, with oxytocin immediately, or as a sustained-release vaginal insert. Am J Obstet Gynecol. 1998; 179:1204-1209.
37. Stewart JD, Rayburn WF, Farmer KC, Liles EM, Schipul AH Jr, Stanley JR. Effectiveness of prostaglandin E2 intracervical gel (Prepidil), with immediate oxytocin, versus vaginal insert (Cervidil) for induction of labor. Am J Obstet Gynecol. 1998; 179:1175-1780.
38. Ottinger WS, Menard MK, Brost BC. A randomized clinical trial of prostaglandin E2 intracervical gel and a slow release vaginal pessary for preinduction cervical ripening. Am J Obstet Gynecol. 1998; 179:349-353.
39. Chyu JK, Strassner HT. Prostaglandin E2 for cervical ripening: A randomized comparison of cervidil versus Prepidil. Am J Obstet Gynecol. 1997; 117:606-611.
40. Facchinetti F, Venturini P, Fazzio M, Volpe A. Elective cervical ripening in women beyond the 290th day of pregnancy. J Reprod Med. 2007; 52:945-949.
41. Triglia MT, Palamara F, Lojacono A, Prefumo F, Frusca T. A randomized controlled trial of 24-hour vaginal dinoprostone pessary compared to gel for induction of labor in term pregnancies with a Bishop score < or = 4. Acta Obstet Gynecol Scand. 2010; 89:651-657.
42. Ashwal E, Hiersch L, Melamed N, Manor Y, Wiznitzer

A, Hod M, Yogev Y. Pre-induction cervical ripening: comparing between two vaginal preparations of dinoprostone in women with an unfavorable cervix.J Matern Fetal Neonatal Med. 2014; 27:1874-1879.
43. Miller AM, Rayburn WF, Smith CV. Patterns of uterine activity after intravaginal prostaglandin E2 during preinduction cervical ripening. Am J Obstet Gynecol. 1991; 165:1006-1009.
44. Smith CV, Rayburn WF, Miller AM. Intravaginal prostaglandin E2 for cervical ripening and initiation of labor. Comparison of a multidose gel and single, controlled-release pessary. J Reprod Med. 1994; 39:381-384.
45. Denoual-Ziad C, Aicardi-Nicolas S, Creveuil C, Gaillard C, Dreyfus M, Benoist G. Impact of prolonged dinoprostone cervical ripening on the rate of artificial induction of labor: A prospective study of 330 patients. J Obstet Gynaecol Res. 2015; 41:370-376.

(Received May 26, 2015; Revised June 19, 2015; Accepted June 20, 2015)