Dinoprostone in Term Premature Rupture of Membranes

Term Erken Membran Rüptürü Olgularında Dinoproston

Oya DEMİRCİ, MD,[a]
Esra BOYBEK, MD,[a]
Elif DEMİRCİ, MD,[a]
Yeşim AKDEMİR, MD,[a]
Hamdullah SÖZEN, MD,[a]
Ayşegül ÜNAL, MD,[a]
Suna SOĞUKTAŞ, MD,[a]
Mehmet ULUDOĞAN, MD[a]

[a]Department of Obstetrics and Gynecology,
Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, İstanbul

Yazışma Adresi/*Correspondence:*
Oya DEMİRCİ, MD
Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, Department of Obstetrics and Gynecology, İstanbul,
TÜRKİYE/TURKEY
demircioya@gmail.com

ABSTRACT Objective: To determine the effect of vaginal slow-release dinoprostone in women with premature rupture of membranes (PROM) and unfavorable cervices. **Material and Methods:** Women included in the study met the following criteria: a live singleton fetus at term (37-41 weeks of gestation) in cephalic presentation, a reactive nonstress test without any contractions, presenting PROM confirmed by demonstration of pooling of amniotic fluid in vaginal vault, a Bishop score of 4 or less before the onset of labor and no uterine contractions for a period of 4 hours after PROM. Participants were compared into 2 groups. In the first group, one dinoprostone vaginal ovule (10 mg) was placed in the posterior fornix. The women in the second group did not receive any cervical maturation medication. Duration of latent labor, duration of active labor, cervical maturation rate and interval from PROM to delivery were evaluated as the primary outcome. **Results:** Women who received the dinoprostone vaginal ovule were found to have significantly higher cervical maturation rate in 12 hours, shorter duration of latent labor, consequently shorter interval from PROM to delivery and smaller proportion of women requiring oxytocin augmentation compared with expectant management. The hyperstimulation rate was significantly higher in the dinoprostone group (p< 0.05). There were no significant differences in the deceleration of fetal heart rate and mode of delivery. **Conclusion:** The controlled released dinoprostone ovule shortened the latent labor duration and the interval time from PROM to delivery without increasing cesarean delivery rates.

Key Words: Dinoprostone; prostaglandins E; fetal membranes, premature rupture

ÖZET Amaç: Uygunsuz bishop skoru olan term erken membran rüptürü olgularında kontrollü salınımlı dinoproston ovulün etkinliği ve güvenilirliğini araştırmak amaçlanmıştır. **Gereç ve Yöntemler:** 37-41 gestasyonel haftalarında sefalik prezentasyonlu, non-stres testti reaktif olup kontraksiyon saptanmayan, vajinal değerlendirme ile doğrulanmış erken membran rüptürü olan, bishop skoru 4 veya altında olan, membran rüptürü sonrası 4 saatlik periyot içerisinde doğum eylemi başlamamış, uterin kontraksiyonu olmayan tekil gebelikler çalışmaya dâhil edilmiştir. Hastalar servikal maturasyon için vajinal dinoproston ovül uygulanan ve herhangi bir uygulama yapılmayan olmak üzere 2 gruba ayrılmıştır. Latent faz, aktif faz süresi, servikal maturasyon oranı ve erken membran rüptüründen doğuma kadar geçen zaman primer olarak değerlendirilmiştir. **Bulgular:** Dinoproston vajinal ovül uygulanan hasta grubunda 12 saat içerisinde servikal maturasyon oranı istatistiksel olarak daha yüksek, latent faz süresi anlamlı olarak daha düşük, erken membran rüptüründen doğuma kadar geçen zaman daha kısa, oksitosin kullanım gerekliliği daha düşük olarak bulunmuştur. Ayrıca hipersitimulasyon oranı istatistiksel olarak daha yüksek bulunmuş, fetal kalp hızında düşme ve doğum şekli yönünden fark saptanmamıştır. **Sonuç:** Kontrollü salınımlı dinoproston ovül sezaryen oranını arttırmadan latent faz süresini ve membran rüptüründen doğuma kadar geçen zamanı azaltmıştır.

Anahtar Kelimeler: Dinoproston; prostoglandin E; fetal membranlar, prematür rüptür

The definition of premature rupture of membranes (PROM) is rupture of membranes before the onset of labor.[1] Incidence of PROM is between 8% and10%, mostly occurring at term.[2-4] Gestational age

has significant implications in the occurrence of PROM. It is also the leading factor that increases perinatal complications. 95% of women with PROM at term will deliver within 28 hours of membrane rupture and latency increases with decreasing gestational age.[5] A prolonged interval from rupture of membrane to delivery is associated with an increase in the incidence of chorioamnionitis and neonatal sepsis.[6,7] Optimum management of PROM is controversial.[8] Management options have included expectant management or induction of labor with oxytocin and prostaglandins. Expectant management is related with increased maternal and perinatal morbidity.[9] However, induction of labor reduces the time interval between PROM and delivery as well as frequencies of chorioamnionitis and postpartum febrile morbidity.[1,5]

Dinoprostone, which is one of the induction methods, for local administration is available in different dosage forms, including vaginal tablets and endocervical or vaginal gel. Sometimes, these forms of administration can cause a very quick initial response in the myometrium, giving rise to uterine hyperactivity, which could jeopardize, to a certain extent, fetal well-being. Therefore, alternative dosage forms have been developed, such as the dinoprostone vaginal device or pessary (Vitalis, Ankara), which allow the controlled and continuous release of PGE2 and an almost immediate suppression of the prostaglandin effect and possible undesirable effects after removing the device.[10,11]

The aim of this study was to determined whether the use of vaginal slow-release dinoprostone in women with PROM and an unfavorable cervix before stimulation of labor with oxytocin improves obstetric out-come compared with the expectant management.

MATERIAL AND METHODS

This prospective study was carried out at the Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, İstanbul, from December 2007 to April 2008. The institution's ethics committee approved the study (No: 55) and informed consent was obtained from the participants. Women with a live singleton fetus at term (37-41 weeks of gestation) in

cephalic presentation, a reactive nonstress test without any contractions , PROM patients confirmed by demonstration of pooling of amniotic fluid in vaginal vault and a Bishop score of 4 or less before the onset of labor were included in the study. Women in active labor or with previous uterine surgery, contraindication to vaginal delivery, contraindication to prostaglandin use (asthma, glaucoma), intrauterine growth restriction, antepartum hemorrhage, grandmultiparity or major fetal anomalies were excluded from the study. A detailed medical history was taken for all patients followed by clinical examination. Amniotic fluid content was assessed clinically. Patients who did not have uterine contractions for a period of 4 hours after PROM were included in the study and sterile digital cervical examination was performed to note Bishop score. When rupture of membranes occurred more than 12 hours earlier, the women were given prophylactic antibiotics to reduce the risk of chorioamnionitis and postpartum endometritis. Before the women were randomized into groups, fetal heart rate and uterine contractions were monitored by continuous electronic fetal monitoring in all patients. One single dose of dinoprostone was used even if cervical maturation did not exist after 12 hours of administration. Participants were randomized into 2 groups. In the first group, one single dinoprostone vaginal ovule (10 mg) was placed in the posterior fornix. If active labor had not been established after 12 hours, an intravenous dose of 2 mLU/min of oxytocin was started; this was increased in increments of 2 mLU every 30 minutes to establish an effective contraction pattern up to maximum of 32 mLU/min. The second group was designed to be the control group. These patients did not have any cervical maturation medication. An infusion of oxytocin was given at 12 hours if labor had still not established. The dose and increments for infusion were the same as in group 1.

A partogram was maintained for all subjects. Onset of labor was determined by either regular uterine contractions or progressive cervical dilatation. Active labor was determined by moderate uterine contractions (3 or more contractions in 10 minutes) or 4 cm or greater cervical dilatation. Continuous cardiotogram monitoring was maintained throug-

hout the induction and labor. The women in group 1 received a single dinoprostone vaginal ovule which was applied for 12 hours at most and removed early in the following situations: nonreassuring cardiotocogram, hyperstimulation (uterine contractions frequent than 1 contraction in 2 minutes) and onset of active labor. Sterile digital cervical examination was carried out in patients with effective contractions on the cardiotocogram to note if there was any change in Bishop score. Bishop score greater than 9 was accepted as cervical maturation at the end of 12 hours.

Duration of latent labor, duration of active labor, cervical maturation rate and interval from PROM to delivery were evaluated as the primary outcome. Mode of the delivery and use of oxytocin for augmentation in active labor were other outcomes.

Data were analyzed using NCSS 2007. Descriptive statistical methods (mean, standard deviation), independent t test comparing two groups, chi-square test comparing qualitative data, one way analysis of variance comparing according to the distribution of latent phase for bishop scores of groups, tukey multiple comparisons test comparing sub-groups were used for evaluation of the data. A

p value of < 0.05 was accepted statistically significant.

RESULTS

During the study period 95 patients were allocated to two groups. There were no significant difference between the groups with respect to maternal age, gravidity, parity, gestational age, history of abortion, educational status, cigarette smoking, previous PROM, body mass index, amniotic fluid index, Bishop score at baseline, birth weight (Table 1).

The median interval time between PROM and admission to the study was 12.07 ± 10.99 hours and median duration of dinoprostone treatment was 5.43 ± 3.33 hours. Characteristics of labor are shown in Table 2. Women in the dinoprostone group had a shorter median duration of latent labor ($p< 0.001$). Consequently the interval from PROM to delivery was also significantly shorter in the dinoprostone group ($p< 0.05$). Duration of active labor of the two groups were not significantly different ($p< 0.01$). In the dinoprostone group, the number of women who required oxytocin augmentation was significantly lower than the number of women who required oxytocin in the control group (60%, 86.2% respecti-

TABLE 1: Baseline characteristics of the patients.				
Characteristics		**Dinoprostone** (n= 30)	**Control** (n= 65)	**p**
Maternal age		25.8 ± 5.82	25.82 ± 4.67	NS
Gravidity		1.9 ± 1.4	1.95 ± 1.23	NS
Parity		2.11 ± 1.05	1.67 ± 0.92	NS
Abortus		1 ± 0.01	1.09 ± 0.3	NS
Educational status	Illiterate	10.00%	4.60%	
	Primary school	63.30%	67.70%	
	Secondary school	13.30%	13.80%	NS
	High school	10.00%	9.20%	
	University	3.30%	4.60%	
Cigarette smoking	No	93.3%	90.80%	
	Yes	6.70%	9.2%	NS
Previous PROM	No	93.3%	90.80%	
	Yes	6.70%	9.2%	NS
BMI		29.47 ± 5.22	28.22 ± 3.63	NS
Gestational age		39.27 ± 0.98	39.05 ± 1.1	NS
AFI		76.5 ± 23.93	84.68 ± 32.55	NS
Bishop score at baseline		1.23 ± 1.1	1.4 ± 1.04	NS
Birth weight, g		3138.33 ± 262.18	3179.23 ± 343.23	NS

a values are given as mean ± SD or percentage.

vely). Cervical maturation in 12 hours rate was significantly higher in dinoprostone group (p< 0.05).

Outcomes of labor are shown in Table 3. The hyperstimulation rate was significantly higher in the dinoprostone group (p< 0.05). None of these patients had a nonreassuring cardiotocogram. In this group, one patient had hyperstimulation one hour after dinoprostone was placed and dinoprostone was not removed because hyperstimulation was eliminated by hydration treatment. Dinoprostone treatment was continued until cervical maturation was achieved and the patient had a normal vaginal delivery. Three patients had cervical maturation when hyperstimulation occurred. Dinoprostone was removed and the patients were treated with hydration. The patients had a normal vaginal delivery. One patient had hyperstimulation 3 hours after dinoprostone was placed; dinoprostone was removed and hyperstimulation eliminated with hydration treatment. This patient had cervical maturation and moderate uterine contractions but labor was arrested for 4 hours after dinoprostone was removed. The patient underwent a cesarean delivery due to arrested labor. In the control group (Group 2), one patient had hyperstimulation, which was treated with hydration and she had a normal vaginal delivery. There were no significant differences in the deceleration of fetal heart rate, mode of delivery and fetal sex between the two groups.

In the dinoprostone group, dinoprostone was removed from 23 of the 30 patients when cervical maturation occurred (76.7%). In 4 patients (13.3%), dinoprostone was removed when moderate uterine contractions began; these patients had cervical maturation in 12 hours and progressed to active labor.

TABLE 2: Characteristics of labor.

		Dinoprostone	Control	p
Latent Labor (h)		5.31 ± 3.56	11.1 ± 8.95	0.001
Active Labor (h)		5.96 ± 3.08	7.24 ± 2.97	NS
Oxytocin Augmentation	Negative	40%	13.8%	
	Positive	60%	86.2%	0.009
Cervical Maturation in 12 hours	Negative	6.7%	41.5%	
	Positive	93.3%	58.5%	0.0014
Interval from prom to delivery(h)		10.88 ± 4.68	17.64 ± 9.87	0.002

a values are given as mean ± SD or percentage.

TABLE 3: Outcomes.

		Dinoprostone		Control		
Hyperstimulation	Negative	25	83.30%	64	98.50%	
	Positive	5	16.70%	1	1.50%	p:0.018
Deceleration of FHR	Negative	26	86.70%	57	87.70%	
	Positive	4	13.30%	8	12.30%	NS
Mode of delivery	NSD	24	80.00%	49	75.40%	
	C/S	6	20.00%	16	24.60%	NS
Fetal sex	Male	16	53.30%	35	53.80%	
	Female	14	46.70%	30	46.20%	NS

In 2 patients (6.7%) dinoprostone was removed when maximum treatment duration (12 hours) ended. One of these patients did not have cervical maturation and uterine contractions at the time of removal. She had no labor induction for a day and then oxytocin was used to induce labor but she had a cesarean delivery due to fetal distress. The other patient had a cesarean delivery too due to prolonged PROM and unfavorable Bishop score.

DISCUSSION

PROM remains as an important issue in obstetrics because of increased maternal and perinatal morbidity and mortality. The benefit of active management in pregnancies with PROM at term has been confirmed.[12] Reports of maternal and perinatal morbidity and mortality in term pregnancy with delayed delivery after PROM confirms that labor should be induced at the time of presentation to reduce the complications.[13-16] Despite a good obstetric outcome achieved by immediate labor induction with oxytocin, such a policy for women with an unfavorable cervix results in increased incidences of fetal distress and cesarean delivery rate.[5,17-25] Preinduction to prepare the uterus for birth in such cases decreases the labor length and increases vaginal delivery rate.[26-29]

Until now, many mechanical or hormonal modalities were used for cervical maturation and many studies on patients compared these between each other and placebo groups. The mechanism of the dinoprostone vaginal ovule was found to be the most similar mechanism of normal spontaneous delivery and was regarded as a safe drug because of FDA (Food and Drug Administration) approval in use for labor induction.[10,30-36]

Our study showed that the use of one single controlled released dinoprostone vaginal ovule for active management of PROM patients at term gestation led to significantly higher cervical maturation rate in 12 hours, shorter duration of latent labor, consequently shorter interval from PROM to delivery and smaller proportion of women requiring oxytocin augmentation compared with the expectant management. Consistent with our results, several placebo controlled studies documented that controlled released dinoprostone had significantly higher rate of cervical maturation, treatment success and lower rates of oxytocin augmentation.[19,23,37] Recently, Larrañaga-Azcárate et al. reported that controlled released dinoprostone applied to 97 women with an unfavorable cervix with PROM at term significantly reduced the time of dilatation and the time until labor compared with 647 women who were subject to expectant management (9.3% vs. 17.6%).[10] But, they reported that the delivery time is shorter in the expectant management group with a difference towards significance. Similarly, Boulvain et al. searched the Cochrane Pregnancy and Childbirth Group's Trials Register (August 2007) and bibliographies of relevant papers. They found that intracervical prostaglandins are effective compared to placebo for induction of labor. On the other hand Tan et al. reported that concurrent treatment with single-dose vaginal dinoprostone and oxytocin infusion for labor induction of term PROM is no better than placebo pessary and similarly oxytocin infusion for inducing labor of term PROM in nulliparas with unfavorable cervices.

At Term PROM, 72% would go to labor spontaneously within 24 hours suggesting PROM alone is an effective pathway for labor onset for many. Hannah et al. showed that immediate induction with oxytocin compared with prostaglandin is associated with significantly shorter time to active labor, duration of active labor and interval of membrane rupture to delivery at TERM PROM study group (5401 patients). On the contrary, Alfirevic et al. reported that comparison of oxytocin with either intravaginal or intracervical PGE2 reveals that the prostaglandin agents probably increase the chances of achieving vaginal birth within 24 hours (Cochrane database-sixty one trials).

In our study, the hyperstimulation rate was significantly higher in women who received the controlled release dinoprostone which is similar to the literature. In the dinoprostone group, 5 of the 30 women had hyperstimulation. In these, the dinoprostone ovule remained in the posterior vaginal fornix in 3 patients when cervical maturation was achieved and active labor had started. There were no fetal heart rate decelerations and hyperstimulation was eliminated by hydration treatment and cesarean delivery rate was not increased due to fetal distress. Due to this information we could criticize that hyperstimulation rate can be decreased with the removal of the dinoprostone ovule at the onset of active labor or at the beginning of the moderate uterine contractions. Similarly, several placebo controlled studies reported that increased hyperstimulation rate was the most common side effect.[19,23,37] In these studies, nonreassuring cardiotocogram and fetal distress were found in 3-10% of cases but this condition resolved after dinoprostone ovule was removed and cesarean delivery rate for the indication of fetal distress did not increase.

We found that there were no statistically significant differences in the rate of cesarean delivery between the dinoprostone and expectant management groups. Similarly, Chua et al. reported that cesarean delivery rates were not different in the prostaglandin group (using a pessary) and the placebo group.[21] Also, Larrañaga-Azcárate et al. reported that controlled released dinoprostone administered to PROM women at term gestation with an unfavorable cervix significantly reduced the cesarean delivery rate compared with the expectant management group.[10] On the other hand results of several studies are controversial.[5,18-23]

One of the clinical advantages of the dinoprostone vaginal ovule is that it is easy to insert and remove and has negligible maternal side effects. Westgate et al. reported that 97% of patients had not felt any discomfort, 88% of patients had not felt the dinoprostone ovule at all and in 97% of patients the dinoprostone ovule was removed without any difficulties.[38] In our study none of our patients had felt any discomfort and the dinoprostone ovule was removed from all patients without any difficulties.

In conclusion, the present study showed that the controlled released dinoprostone ovule shortened the latent labor duration, interval from PROM to delivery without increasing cesarean delivery rates and is also safe and effective to use for induction in PROM women at term gestation as shown in many studies in membrane intact patients. Maternal and fetal infection rates might be lower because of faster cervical maturation and shortened total delivery time. Higher patient comfort and satisfaction were evaluated as secondary gain. Although it can be regarded as a drug that is not cost effective, when it is compared to other cervical maturation drugs, safe induction of labor and shortened hospital stay are the advantages of this drug. Therefore this approach could be advisable in clinical practice. The safety and efficacy profile of using the controlled released dinoprostone ovule in this setting require further study with larger sample sizes.

REFERENCES

1. ACOG Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 80: Premature rupture of membranes. Clinical management guidelines for obstetrician-gynecologists. Obstet Gynecol 2007;109(4): 1007-19.

2. Hannah ME, Hodnett ED, Willan A. Prelabor rupture of the membranes at term: expectant management at home or in a hospital. Obstet Gynecol 2000;96(4):353-8.

3. Mead PB. Management of the patient with premature rupture of the fetal membranes. Clin Perinatol 1980;7(2):243-55.

4. Duff P. Preterm rupture of the membranes in term patients. Semin Perinatology 1996;20(5): 401-8.

5. Hannah ME, Ohlsson A, Farine D, Hewson SA, Hodnett ED, Myhr TL. Induction of labor compared with expectant management for prelabor rupture of the memranes at term. N Engl J Med 1996;334(16):1005-10.

6. Fayez JA, Hasan AA, Jonas HS, Miller GL. Management of premature rupture of the membranes. Obstet Gynecol 1978;52(1):17-21.

7. Guise JM, Duff P, Christian JS. Management of term patients with prelabor rupture of membranes and an unfavorable cervix. Am J Perinatol 1992;9(1):56-60.

8. Mozurkewich E. Prelabor rupture of membranes at term: induction techniques. Clin Obstet Gynecol 2006;49(3): 672-83.

9. Webb GA. Maternal death associated with premature rupture of the membranes An analysis of 54 cases. Am J Obstet Gynecol 1967;98(5):594-601.

10. Larrañaga-Azcárate C, Campo-Molina C, Pérez-Rodríguez AF, Ezcurdia-Gurpegui M. Dinoprostone vaginal slow-release system (Propess) compared to expectant management in the active treatment of prematurerupture of the membranes at term: impacton maternal and fetal outcomes. ActaObstet Gynecol Scand 2008;87(2):195-200.

11. Lyrenas S, Clason I, Ulmsten U. In vivo controlled release of PGE2 from a vaginal insert (0.8mm,10mg) during induction of labour. Br J Obstet Gynaecol 2001;108(2): 169-78.

12. Dare MR, Middleton P, Crowther CA, Flenady VJ, Varatharaju B. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37weeks or more). The Cochrane Library 2006;25(1): CD005302.

13. Fayez JA, Hasan AA, Jonas HS, Miller GL. Management of premature rupture of membranes. Obstet Gynecol 1978;52(1):17-21.

14. Everest NJ, Jacobs SE, Davis PG, Begg L, Rogerson S. Outcomes following prolonged preterm premature rupture of the membranes. Arch Dis Child Fetal Neonatal Ed 2008;93(3): 207-11.

15. Morris JM, Roberts CL, Crowther CA, Buchanan SL, Henderson-Smart DJ, Salkeld G, et al. Protocol for the immediate delivery versus expectant care of women with preterm prelabour rupture of the membranes close to term (PPROMT) Trial. BMC Pregnancy Childbirth 2006;23:6-9.

16. Mercer BM, Crocker LG, Boe NM, Sibai BM. Induction versus expectant management in premature rupture of the membranes with mature amniotic fluid at 32 to 36 weeks. Am J Obstet Gynecol 1993;169(4):775-82.

17. Rydhstrom H, Arulkumaran S, Ingermar-son I, Kumar J, Ratnam SS. Premature ruptureof membranes at term: Obstetric outcome with oxytocin stimulation in relation to parity and cervical dilatation at admission.Acta Obstet Gynecol Scand 1986;65(6):587-91.

18. Marconi AM, Bozzetti P, Morabito A, Pardi G. Comparing two dinoprostone agents for cervical ripening and induction of labor. Eur J Obstet Gynecol Reprod Biol 2008;138(2):135-40.

19. Rayburn WF, Wagner RJ, Barrs VA, Spitzberg E, Molinen RD, Mandsager N, et al. An Intravaginal Controlled-Release prostaglandin E2 pessary for cervical ripening and initiation of labor of term. Obstet Gynecol 1992; 79(3): 374-9.

20. Braems G, Norhausen I. Induction of labor with prostaglandins for medical reasons: Determining explanatory variables of the induction to delivery time interval for vaginal deliveries and caesarean section. Eur J Obstet Gynecol Reprod Biol 2007;135(2):164-9.

21. Chua S, Arulkumaran S, Yap C, Selamat N, Ratnam SS. Premature rupture of membranes in nullipars at term with unfavoral cervices: A double blind randomized trial of prostaglandin and plasebo. Obstet and Gynecol 1995;86(4):550-4.

22. Ben-Haraush A. Yogev Y, Glickman H, Bar J, Kaplan B, Hod M. Mode of delivery in pregnancys with premature rupture of membranes at or before term following induction of labor with vajinal prostaglandin E2. Am J Perinatol 2004;21(5):263-8.

23. Witter FR, Rocco LE, Johnson TR. A randomised trial of prostaglandin E2 in a controlled-release vaginal pessary for cervical ripening at term. Am J Obstet Gynecol 1993; 168(3):1003-4.

24. Dündar Ö, Tütüncü L. Ergür AR, Atasever B, Müngen E. [Comparison of intravaginal misoprostol, oxytosinInfusion and intracervical dinoproston, oxytosin infusion in postterm pregnancies for labor induction]. Turkiye Klinikleri J Gynecol Obst 2008;18(4): 231-6.

25. Yılmaz B, Güngör T, Bilge Ü, Önen Ş, Özakşit G, Süt N, et al. [Randomized comparison of sustained-release dinoprostone vaginal insert versus oxytosin for cervical priming/labor induction in post-term pregnants with unfavorable cervix]. Turkiye Klinikleri J Gynecol Obst 2008;18(4):237-42.

26. Ekman-Ordeberg G, Uldberjg S, Ulsten U. Comparison of intravenous oxytocin and vaginal prostaglandin E2 gelin women with unripe cervicesand premature rupture of the membranes. Obstet Gynecol 1985;66 (3):307-10.

27. Granstrom L, Ekman G, Ulmsten U. Cervical priming and labor induction with vaginal application of 3 mg PGE2 in suppositories in term pregnant women with premature rupture of amniotic membranes and unfavorable cervix. Acta Obstet Gynecol Scand 1987;66 (5):429-31.

28. Mahmood TA, Dick MJ, Smith NC, Templeton AA. Role of prostaglandin in the management of prelabor rupture of the membranes at term. Br J Obstet Gynecol 1992;99(2):112-7.

29. Ray DA, Garite TJ. Prostaglandin E2 for induction of labor in patients with premature rupture of membranes at term. Am J Obstet Gynecol 1992;166(3):836-43.

30. Crane JM, Bennett KA. A meta-analysis of controlled release prostaglandin for cervical ripening and labor induction. J Soc Obstet Gynaecol Canada 2000;22 (9):692-8.

31. Perry MY, Leaphart WL. Randomized trial of intracervical vs. posterior fornix dinoprostone for induction of labor. Obstet Gynecol 2004;103(1):13-7.

32. Chyu JK, Strassner HT. Prostaglandin E2 for cervical ripening: a randomized comparison of Cervidil vs. Prepidil. Am J Obstet Gynecol 1997;177(3):606-11.

33. 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(2):349-53.

34. Fletcher HM, Mitchell S, Simeon D, Frederich S, Brown D. Intravaginal misoprostol as a cervical ripening agent. Br J Obstet. Gynecol 1993;100(7):641-4.

35. Tabowei TO, Oboro VO. Low dose intravaginal misoprostol versus intracervical baloon catheter for pre-induction cervical ripening. East Afr Med J 2003;80(2):91-4.

36. Adeniji OA. Pre-induction cervical ripening: transcervical foley catheter versus intravaginal misoprostol. J Obstet Gynecol 2005;25(2): 134-9.

37. Wing DA, Ortiz-Omphroy G, Paul RH. A comparison of intermittent vaginal administration of misoprostol with continuous dinoprostone for cervical ripening and labor induction. Am J Obstet Gynecol 1997;177(3):612-8.

38. Westgate J, Williams JA. Evaluation of a controlled release vaginal prostaglandin E2 pessary with a retrieval system for the induction of labor. J Obstet Gynaecol 1994;14:146-50.