# Second Trimester Termination of Pregnancy: Comparing Intracervical Prostaglandin E2 (Dinoprostone) to Intravaginal Misoprostol

Özgür Dündar, Ercüment Müngen, Levent Tütüncü, Murat Muhcu, Serkan Bodur, Yusuf Z. Yergök

*Clinics of Gynecology and Obstetrics, Haydarpaşa Educational Hospital, Gülhane Military Medicine Academy of Medicine, Istanbul*

**Abstract**

**Objective:** The purpose of this study was to compare the efficiency and safety of intracervical prostaglandin E2 (dinoprostone) and intravaginal misoprostol in second trimester termination of pregnancy.

**Methods:** Forty cases in which pregnancy were terminated by dinoprostone and 63 cases of pregnancy termination using misoprostol were evaluated retrospectively. The dinoprostone group received 0.5 mg prostaglandin E2 intracervically. Misoprostol was used intravaginally in a dose of 200 µg every 6 h with a maximum of five doses. The success rate, induction to abortion interval and the incidence of side effects were analyzed for both groups. Statistical analysis was performed using independent samples t test, Pearson X2 and Fisher's exact test, where appropriate. A p value <0.05 were considered significant.

**Results:** The pregnancy was terminated within 48 hours in 60 of 63 patients (95.2 %) in the misoprostol group and in 31 of 40 patients (77.5%) in the dinoproston group; the rate of pregnancy termination in the misoprostol group was signifacantly higher than that of the dinoproston group (p=0.01; OR, 5.81; %95 CI, 0.46-2.18). While womitting-nausea rate was significantly higher in the dinoproston group, (p=0.01; OR, 0.09; %95 CI, 0.01-0.79) there were no significant differences in the rates of incomplete abortion, diarrhea, febril morbidity, bleeding, transfusion and cervical laceration between the two groups.

**Conclusion:** Misoprostol is an effective, easy to use, safe and cheap drug then dinoprostone for termination of second trimester pregnancy.

**Keywords:** Second trimester, pregnancy termination, misoprostol, dinoprostone.

### *İkinci trimester gebelik sonlandırılmasında intraservikal prostaglandin E2 (dinoproston) ve intravaginal misoprostolün etkinliğinin araştırılması*

**Amaç:** İkinci trimester gebelik sonlandırılmasında intraservikal prostaglandin E2 (dinoproston) ve intravaginal misoprostolün etkinliğini araştırmak.

**Yöntem:** Çalışmaya 1995-2006 tarihleri arasında, Kliniğimizde 14-28 gebelik haftalarında maternal veya fetal nedenlerle gebelik sonlandırma endikasyonu alıp, intraservikal PGE2 (dinoproston) uygulanan 40 hasta ve intravaginal misoprostol uygulanan 63 hasta dahil edildi. Misoprostol 200 µg, vaginal olarak, 6 saat aralarla maksimum 5 doz uygulandı. Dinoproston (prostaglandin E2) 0.5 mg intraservikal uygulandı. 48 saat içinde gebeliği sonlanmayan olgularda yöntem başarısız kabul edildi. Her iki grubun 48 saatlik süreçte gebelik sonlanmasındaki başarı oranları ile komplikasyon ve yan etkiler karşılaştırıldı. İstatistiksel değerlendirmede student t, Fisher's exact ve X2 testleri kullanıldı. p değerinin 0.05'den küçük olması anlamlı kabul edildi.

**Bulgular:** Misoprostol uygulanan birinci gruptaki 63 hastanın %95.2'inde (60 hasta), intraservikal dinoproston uygulanan 40 hastanın %77.5'inde (31 hasta) gebelik 48 saat içinde sonlandı; misoprostol grubunda gebelik sonlanma oranı, dinoproston grubuna göre anlamlı olarak daha yüksekti (p=0.01; OR, 5.81; %95 CI, 0.46-2.18). Bulantı-kusma, dinoproston grubunda anlamlı olarak daha yüksek oranda gözlenirken ( p=0.01; OR, 0.09; %95 CI, 0.01-0.79), tam olmayan düşük, diyare, febril morbidite, kanama, transfüzyon ve servikal yırtık yönünden gruplar arasında anlamlı farklılık yoktu.

**Sonuç:** İkinci trimester gebeliklerin sonlandırılmasında intravajinal misoprostol kullanımının, dinoproston kullanımına göre daha etkin ve güvenli olduğu sonucuna varıldı.

**Anahtar Sözcükler:** İkinci trimester, sonlandırma, misoprostol, dinoproston.

Correspondence: Dr. Özgür Dündar, GATA Haydarpaşa E. H., Kadın Hastalıkları ve Doğum Kliniği, Tıbbiye Cad. 34668 Üsküdar-İstanbul
e-mail: ozgurdundar72@yahoo.com

## Introduction

In first trimester termination of pregnancy dilatation and curettage (D&C) are used generally. In second trimester termination of pregnancy surgical intervention can be used. However the process is more complicated in second trimester pregnancies since fetal-placental structures are dilated, bleeding is increased and cervix is maturated and a special experience is required in this subject. On account of these reasons prostaglandins (PG) are preferred in second trimester terminations of pregnancy rather than surgical intervention nowadays with the usage of prostaglandins (Prostaglandin E and S).[1] Another frequently used method is oxytocin hormone which is used in different doses intravenously. Misoprostol peptic is a synthetic PGE1 (15-deoksi-16-hidroksi-16-methyl analog) analog used in treatment of ulcer[2]. It is used as per oral (PO), rectal and vaginal methods. It does not require special conditions for to be preserved, and can be preserved for years.[2] It is used in abortion induction, maturation of cervix, postpartum bleeding control and parturition induction due to its effects of uterus contracting and cervix maturating.[2] Misoprostol PO can be determined after two minutes it is taken.[3] and leads to contraction in uterus.[4] It does not lead to hypertension.[5] Prostaglandins are agents which can be used in vaginal and intracervical ways for provision of pre-induction cervical maturation in second trimester termination of pregnancy.[1] Prostaglandin E2 (PGE2, dinoproston) is used as intracervical. PGE2 requires endocervical application and it is so expensive and difficult to preserve since it is easily inactivated in normal room conditions.[6]

## Methods

40 patients in whom PGE2 (dinoproston) had been applied and 63 patients in whom intravaginal misosprostol who had been applied pregnancy termination indications in their 14-28 pregnancy weeks due to maternal or fetal reasons in our Clinic between 1995 and 2006 were included in the study. The group in which misoprostol has been used was evaluated as Group 1 and the other applied dinoproston was evaluated as Group 2. data relating to the patients was obtained by examining patient files in the clinic archive retrospectively. Both groups of patient was passed through a full systemic and gynecologic examination after hospitalized and routine blood analyses and obstetric ultrasonography USG) were applied. In addition, fibrinogen, bleeding time, coagulation time and protrombine time were examined in inutero ex fetuses. Cases with severe lung and kidney disease, decompensate heart failure, placenta previa, hydramnios, myoma, glocom, prostaglandin sensitivity, severe asthma, inflammatory intestinal disease, and those who passed caesarian or operations which may cause uterine scar were not included in the study.

The patients for whom dinoproston was applied was brought in lithotomic position. After vulva and vagina were disinfected, cannula is pushed until internal osmium by putting specially prepared cannula on the injector. While the gel was given to cervical channel slowly cannula was backed out. Special attention was paid in order to prevent gel to extend internal osmium and to be given in vagina. After the process the cases in which discourse was not started were evaluated by touching again. 1% oxytocin infusion was used in those bishop score is above 6 and the repeat of the process was applied in score below 6 and the technique was considered as successful in patients whose pregnancy terminated in 48 hours. In cases bishop score does not extend 6 despite 2 doses of intracervical PGE2 application and in cases whose pregnancy did not terminated in 48 hours, the method was considered as unsuccessful.

In the groups for which misoprostol was applied 200 µg misoprostol (Cytotec tablet 200 µg, Searle®) serum was softened with physiological and located on vagina posterior fornix in lithotomic position and maximum 5 doses were applied in 6 hour intervals. In cases whose pregnancy did not terminated in 48 hours, the method was considered as unsuccessful.

After the process patients were passed from fever, pulse, tension arterial controls in every 15 minutes during the first 2 hours, in every one hour in following 8 hours and in every 4 hour until the pregnancy terminated. After fetus and its supplements were discharged cavity control was applied in patients for whom a suspicion about whether the process was completed. Lactation inhibition was applied in patients whose pregnancy terminated and the patients were followed up. After 24 hours the patients who had no problem were discharged from the hospital and called for a control after 3-6 weeks.

Age, parity, pregnancy week, USG data, reason of pregnancy termination, application hour of the method, amount of the medicine applied, blood count after and before abortus, average duration of termination of the pregnancy and complications were determined and recorded. Diarrhea, vomiting, headache, fatigue, sensitivity in nozzles, fever above 38 °C, febril mobidity were considered as abnormal. Induction-abortion duration was defined as the duration beginning from the first misoprostol and dinoproston application until abortion. Induction-abortion durations, successful abortion rates fulfilled between 12-24 hour, 24-36 hour and 36-48 hour, incidence of adverse effects were compared between the groups. Statistical analyses of the data were performed with SPSS 11.0 (Statistical Package for Social Sciences Chicago, USA) package program which has been prepared for Windows. Statistical calculations were performed with Student's t test, Fisher's exact and X2 tests. p values below 0.05 in were considered as statistically meaningful.

## Results

Ages of 103 patients participated in the study differ between 17 and 41. Average age of two groups was 26.28±5.10. Average age of the patients participated in the first group of the study was determined as 26.73±4.86, and the average age of patients in second group as 25.57±5.41. There is not any meaningful difference between two groups in terms of age, gravida, parity and gestational week. Demographic characteristics of both groups were indicated in Table 1.

Majority of cases were composed of 21-25 age group (43.7%), second frequent age group was 26-30 age group (30.1%), and the third frequent was 31-35 age group (11.6%). The least number of cases are composed of the groups of 36 and above ages (%7.8). This sequence in total number of patients is founded as the same if two groups are evaluated separately.

**Table 1.** Demographic characteristics of the groups.

| | Group 1 | Group 2 | p |
|---|---|---|---|
| **Maternal age** | 26.73±4.86 | 25.57±5.41 | 0.19 |
| **Gravida** | 2.01±0.97 | 1.75±0.97 | 0.11 |
| **Parity** | 1.05±1.02 | 0.75±0.98 | 0.78 |
| **Pregnancy week** | 18.01±3.52 | 18.02±3.02 | 0.99 |

**Note:** Values are stated as average ± standard deviation

All cases were in 14-28 weeks of pregnancy according to examination and ultrasonography results. Average pregnancy week of the patients in the first group was determined as 18.01±3.52, and average pregnancy week of the patients in the first group determined as 18.02±3.02. When distribution of the patients according to pregnancy week, majority of cases was composed of those in 14-16 weeks of their pregnancy (39.8%). Second frequent was composed of those in 17-19 weeks of their pregnancy (34.9%). The least number of cases was determined in 26-28 week pregnancy terminations (3.9%). This sequence in total number of patients is founded as the same if two groups are evaluated separately.

When the patients are evaluated according to their parities, nullipar ones constitute the majority (43.7%), primiparas comes second (29.1%), and multiparas come third (27.2%). This sequence is founded as the same if two groups are evaluated separately.

When indications of termination of pregnancy were investigated in patients inutero exitus comes first (59.2%), cases with fetal anomaly come second (29.1%). Indications of termination of pregnancy in both groups were stated in Table 2.

In 95.2% (60 patients) of 63 patients in the first group for whom misoprostol was applied preg-

**Table 2. Distribution of patients according to indications of termination of pregnancy.**

| | Group 1 | | Group 2 | | Total | |
|---|---|---|---|---|---|---|
| **Indications** | **n** | **%** | **n** | **%** | **n** | **%** |
| İnutero exitus | 32 | 50.8 | 29 | 72.5 | 61 | 59.2 |
| Fetal anomaly | 21 | 33.3 | 9 | 22.5 | 30 | 29.1 |
| Anhidramnios | 10 | 15.9 | – | – | 10 | 9.7 |
| Rubella infection | – | – | 1 | 2.5 | 1 | 1 |
| Severe preeclampsia | – | – | 1 | 2.5 | 1 | 1 |

**n:** Number of cases

nancy terminated in 48 hours. In one of three cases in which this application was considered as unsuccessful pregnancy terminated after 13 dose misoprostol 200 µg given with intervals and in one another pregnancy terminated after 18 doses misoprostol 200 µg. In the third case in which the method was unsuccessful pregnancy terminated after oxytocin infusion. Pregnancy terminated in 48 hour in 77.5% (31 patients) of 40 patients for whom intracervical dinoproston was applied. In nine patients this method was recognized as unsuccessful pregnancy was terminated by applying extraamniotic rivanol. When the success rates of both methods are compared success of misoprostal group has a statistically meaningful difference compare to dinoproston group (p=0.01; OR, 5.81; 95% CI, 0.46-2.18).

In dinoproston group pregnancy of 19 patients terminated in the first 24 hours after a single dose of intracervical dinoproston without any need to another process, pregnancy of 9 patients terminated in 48 hours following a dose of intracervical dinoproston, pregnancy of 3 patients terminated after oxytocin infusion following two doses of intracervical dinoproston. In 4 among 31 patients whose pregnancy terminated cavity control was applied with curette due to the incompletion of discharge. In the group which used misoprostol, pregnancy of 60 patients among 63 terminated in 24 hours with no necessity to another process, oxytocin infusion was applied for 3 patients as additional process.

Cavity control was applied with curette due to the incompletion of discharge for 6 patients in the first group. Minimum 1 and maxium 18 tablets were used in the patients for whom misoprostol was applied. Misoprostol dose applied was found in average as 3.14±2.70 tablet (628±540 mg). Misoprostol dose used in the first 12 hour duration when misoprostol was found statistically meaningful compare to dinoprostol was determined as 1.5±0.51 tablet (300±102 mg).

When the rates of termination of pregnancy in the first 24 hour are compared between two groups there was a statistically meaningful difference in misoprostol group (p=0.01; OR, 4.25; 95% CI, 1.78-10.15). Success rates of groups in 24 hour durations are stated in Table 3.

Any severe complication did not appear in the patients of both groups. Minor complications appeared are indicated in Table 4. In our study minor complication appeared in 8 (12.7%) among 63 patients used minoprostol and 15 (37.5%) among 40 patents used dinoproston. There was determined a statistically meaningful difference in complication arte appeared in dinoproston group compare to misoprostol group (p=0.03; OR, 0.242; 95% CI, 0.091-0.646). While nausea/vomiting appeared in only one patient among those in the

**Table 3.** Distribution of patients according to termination of pregnancy indications

| | Group 1 | | Group 2 | | | | |
|---|---|---|---|---|---|---|---|
| **Duration** | **n** | **%** | **n** | **%** | **p** | **OR** | **95% CI** |
| 0-24 | 50 | 79.4 | 19 | 47.5 | 0.01 | 4.25 | 1.78-10.15 |
| 0-48 | 60 | 95.2 | 31 | 77.5 | 0.01 | 5.81 | 0.46-2.18 |

**n:** Number of cases

**Table 4.** Distribution of complications according to the groups

| | Group 1 | | Group 2 | | | | |
|---|---|---|---|---|---|---|---|
| **Complications** | **n** | **%** | **n** | **%** | **p** | **95% CI** | **OR** |
| Nausea/Vomiting | 1 | 1.6 | 6 | 15 | 0.01 | 0.01-0.79 | 0.09 |
| Incomplete abortion | 6 | 9.5 | 4 | 7.5 | 1.0 | 0.25-3.59 | 0.95 |
| Diarrhea | – | – | 2 | 2.5 | 0.15 | 0.98-1.13 | 1.05 |
| Fever > 38° | – | – | 1 | 2.5 | 0.39 | 0.98-1.08 | 1.03 |
| Bleeding | 1 | 1.6 | 1 | 2.5 | 1.0 | 0.04-10.35 | 0.63 |
| Transfusion | 1 | 1.6 | 1 | 2.5 | 1.0 | 0.04-10.35 | 0.63 |
| Cervical rupture | – | – | 1 | 2.5 | 0.39 | 0.98-1.08 | 1.03 |

**n:** Number of cases

first group, nausea/vomiting appeared in six among patients in the second group. When the complaint of nausea/vomiting is evaluated between both groups the rate of appearance in dinoproston groups was determined as a statistically meaningful difference (p=0.01; OR, 0.091; 95% CI, 0.011-0.791). Antiemetic was given to all patients who complain about nausea/vomiting. These complaints of the patients remained in tolerable levels with symptomatic treatment. The complaint of diarrhea appeared in a patient in dinoproston group which started after two hours from the process and continued for 24 hours. A similar complication did not appear in any patient in the misoprostol group.

500 cc bleeding happened in one patent from each group after discharge. When the patients complained about bleeding after discharge were examined again, retention was determined in placental tissues and cavity was cleaned with curette, blood transfusion was applied in these patients. In one of the patients included in the second group fever above 38 °C appeared, a similar complication did not occur in any of the patients in the first group. Antipyretic treatment was applied in the patient suffered from high fever and the fever did not continue in this patient.

Cervical injury appeared in one of the patients applied intracervical dinoproston. This process was applied to this patient who is 17 week nullipara due to inutero exitus. Cervical laceration and rupture were determined in the patient who suffered from bleeding after discharge. Cervical rupture was sutured duly.

## Discussion

In parallel with improvements in diagnosis of fetal anomaly there appears an increase in second trimester terminations of pregnancy. There is not already a consensus opinion concerning the most ideal method for termination of second trimester pregnancies. Advantages and disadvantages are declared in methods compare to each other used in the studies about this issue.[1,4,6] While determining the most appropriate method, cheapness, easiness of application, efficiency, shortness of duration pregnancy termination, lowness of number and tolerability of its complications are important desired criteria. In addition to them special conditions and counter indications, and experiences and preferences of doctors who will apply the method should also be taken into consideration.

Extraamniotic rivanol, prostaglandin F2 alpha or saline infusion, laminaria and mifeptriston, gemeprost, dinoproston, misoprostol were used in second trimester termination of pregnancy processes until now.[7-10]

In the study we obtained 77% success in 40 patients we used intracervical dinoproston. This rate was meaningfully low compare to success rate in patients for whom misoprostol was used. Failure rate of our study in dinoproston group was found higher than the studies which had been published in the literature before. Mungen et al. has reported 5.45% failure in patients with second and third primester pregnancies with the combination of intracervical dinoproston and oxytocin infusion.[11] Karaman et al. has declared 5.5% failure in 20-36 week pregnant women with the same method.[12] Gedikoglu et al. has reported that the process was failed only in one patient among 30 postterm patients (3.33%) on whom they applied the same procedure, and they determined 8.8% failure in 45 inutero exitus cases with second trimester pregnancy with this method.[13] Yilmaz et al has declared failure only in one case among 13 term pregnant women.[14] Some studies were published which were applied by combining with some other abortive methods than oxytocin infusion in order to increase the efficiency of intracervical dinaproston. Rath and Kunt reported that they obtained 97.5% success in 42 patients by combining intracervical dinaproston with extraamniotic PGF2-alpha and oxytocin.[15]

The usage of misoprostol for the first time was declared by Lehair et al who has used it as intravaginal in termination of second trimester death fetuses. As a result of these studies; it was reported that misoprostol is in high efficiency, minor adverse effect was determined and it did not lead to any complication.[16]

Bugalho et al declared that average termination duration as 14.3 hour and success rate in termination of pregnancies as 88.6% in their study held in 132 pregnant women with legal abortion by using 800-1600 µgr intravaginal misoprostol.[17] In another study about second trimester termination of pregnancy which was held by using misoprostol due to intrauterine death 157.4 µgr misopostol intravaginal was used in average, average termination duration was reported as 13.2 hour and success rate as 77.8%.[18] Contrarily in the study held by Yapar et al by using five different methods in second trimester termination of pregnancy; it was found that

exraamniotic ethacridin, intravenous oxytocin and balloon insertion are more efficient than intracervical PGE2 gel and vaginal misoprostol. In this study, success rate of misoprostol group was reported as 77.5%.[19] In our study on the other hand, pregnancy was terminated in 48 hours in 95.2% (60 patients) among 63 patients in the first group for whom misoprostol was applied and 77.5% (31 patients) among 40 patients in the second group for whom intracervical dinoproston was applied and success rate between pregnancy termination of two groups showed a statistically meaningful difference.

Misoprostol is used as oral, vaginal, sublingual, buccal and rectal methods. Absorption becomes more effective in sublingual usage of misoprostol and it reaches to high concentrations in blood in a short time. Vaginal solubility and vaginal absorption happen slowly in vaginal usage of misoprostol, and so misoprostol effect takes longer. Tang et al reported that termination rate in the first 24 hour is higher in vaginal usage of misoprostol compare to oral and sublingual usage and termination rates in 48 hours are the same in their study on second trimester termination of pregnancy.[20] In another study it was indicated that vaginal usage of misoprostol is more effective in parturition induction compare to its oral and sublingual usage.[21] Any severe complication did not observed in any of the patients we included in the study. We calculated observed minor complications as 12.7% in the first group we have applied misoprostol and as 37.5% in the second group we have applied intracervical dinoproston. The most frequently observed complication in the patients who use misoprostol was rest placenta (9.5%), and the second two minor complications observed only in one patient were nausea/vomiting and bleeding, on the other hand the most frequently observed complication in the group which used dinoproston was nausea/vomiting (15%). In addition some other complications observed rest placenta 7.5%, diarrhea 2.5%, fever above 38°C 2.5%, bleeding 2.5% and cervical rupture 2.5% also occurred.

Complications and rates exhibited in some studies held with intracervical dinoproston before are similar with our study. Karaman has reported infection and bleeding happened with this method.[12] Gedikoglu has reported nausea/vomiting.[13] Rath and Khun reported uterine in addition to them.[15] The complications observed in the group we have used misoprostol are similar with the complications observed the studies held with misoprostol before.[7,16,17] Usage of misoprostol which can be easily provided as a method to terminate undesired pregnancies without control of a gynecologist is found so dangerous. For this reason some measures required to prevent usage of misoprostol out of control of a gynecologist should be taken.

## Conclusion

Findings in our study and the results of researches conducted before indicate that misoprostol is a method required to be preferred firstly as a cheap, easily applicable, efficient and safe in case second trimester pregnancies need to terminated. Intracervical dinoproston is considered as a method which should not be consulted in the first plan in termination of second trimester pregnancies since its success rate is low, it is expensive, required to be combined with oxytocin despite its advantages like being noninvasive and easily applicable.

**References**


1. Ramsey PS RK. Misoprostol, a prostaglandin E1 analog, for prelabor ripening of the unfavorable uterine cervix. Fetal *Mat Med Rev* 1996: 217-27.
2. Collins PW. Misoprostol: discovery, development and clinical applications. *Med Res Rev* 1990; 10:149-72.
3. El-Rafaey H,Hinshaw K, Templeton A. The abortifacient effect of misoprostol in the second trimester. *Hum Reprod* 1993; 8: 1744-6.
4. Norman JE, Thong KJ, Baird DT. Uterine contractility and induction of abortion in early pregnancy by misoprostol and mifepristone. *Lancet* l99l; 338: l233-6.
5. Pregnancy and childbirth Module. In: Keirse MJNC, Renfrew MJ, Neilson JP, Crowther C, editors. Cochrane Database of systematic Reviews. The Cochrane Collaboration, Issue 2. Oxford: Update software, 1995: Review Nos 2974, 2999, 5352.
6. Miller AM, Rayburn WF, Smith CV. Patterns of uterine activity after intravaginal prostaglandine E2 during preinduction cervical ripening. *Am J Obstet Gynecol* 1991; 165:1006-9.
7. Mohamed Nabil MG, Bassam A el H. Second-trimester termination of pregnancy by extra-amnioic prostaglandin F2 alfa or endocervical misoprostol. *Acta Obstet Gynecol Scand* 1998; 77: 429-32.
8. Daskalakis GJ, Mesogitis SA, Papantoniou NE, Moulopoulos GG, Papapanagiotou AA, Antsaklisa AJ. Misoprostol for second trimester pregnancy termination in women with prior caesarean section. *BJOG* 2005; 112: 97-9.
9. Yongyoth H, Boonsri C, Piyaporn P. A randomised controlled trial of 6 and 12 hourly administration of vaginal misop-

rostol for second trimester pregnancy termination. *BJOG* 2005; 112: 1297-1301.

10. Chung YP, Hwa HL, Ko TM. Laminaria and sulprostone in second trimester pregnancy termination of fetal abnormalities. *Int J Obstet Gynaecol* 1999; 65: 47-52.
11. Müngen E, Yergök YZ, Ertekin AA, Bilgin H, Ülgenalp İ. İntraservikal dinoproston (PGE2) jel ile 2. ve 3. trimester gebeliklerde serviksin olgunlaşması ve/veya eylem indüksiyonu. *Jinekoloji Obstetrik Dergisi* 1994; 4: 173-7.
12. Karaman AŞ, Uran B, Erler A, Vural AH. Gebeliğin sonlandırılmasında İntraservikal dinoproston (PGE2) jeli ve intraamniyotik hipertonik NaCl solüsyonu ile yapılan karşılştırmalı bir çalışma. *Jinekoloji ve Obstetrik Dergisi* 1992; 6: 148-53.
13. Gedikoğlu V, İnan A, Bulgur M, Yücesoy İ, Baysal C, Karaosmanoğlu S. İntraservikal PGE2 jel aplikasyonu ile servikal olgunlaşma ve travay indüksiyonu. *Jinekoloji ve Obstetrik Dergisi* 1994; 8: 46-50.
14. Yılmaz H, Çapanoğlu R. Doğum indüksiyonu için prostaglandin jel uygulaması. *Jinekoloji ve Obstetrik Dergisi* 1992; 6: 174-6.
15. Rath W, Khun W. Cervical ripening and induction of labor by intracervical and extra-amniotic prostaglandin gel application in cases of intrauterin fetal death. *Int J Gynaecol Obstet* 1985; 23: 387-94.
16. Lehair J, Lemarie P, Helleringer M, Manini P. Expulsion of arrested pregnancy product in the second trimester using a prostaglandin E1 analog administered intravaginally. Apropos of 12 cases. *Rev Fr Gynecol Obstet* 1989; 84: 19-23.
17. Bugalho A, Bique C, Almedia L, Bergstrom S. Pregnancy interruption by vaginal misoprostol. *Gynecol Obstet Invest* 1993; 34: 226-9.
18. Merrell DA, Koch MA. Induction of labour with intravaginal misoprostol in the second trimesters of pregnancy. *S Afr Med J* 1995; 85: 1088-90.
19. Yapar EG, Senöz S, Ürkütür M, Batıoğlu S, Gömen O. Second trimester pregnancy termination including Fetal death: comparison of five different methods. *Eur J Obstet Gynecol Reprod Biol* 1996; 69: 97-102.
20. Tang OS, Lau WNT, Chan CCW, Ho PC. A prospective randomised comparison of sublingual and vaginal misoprostol in second trimester termination of pregnancy. *BJOG* 2004; 111: 1001–05.
21. Bartusevicius A, Barcaite E, Nadisauskiene R. Oral, vaginal and sublingual misoprostol for induction of labor. *Int J Gynecol and Obstet* 2005; 91: 2-9.