# Induction Of Labor With Intravaginal Misorprostol In Hypertensive Pregnancy*

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**SUMMARY**

***INDUCTION OF LABOR WITH INTRAVAGINAL MISOPROSTOL IN HYPERTENSIVE PREGNANCIES***

**Objective:** Our purpose was to compare the safety and efficacy of intravaginal misoprostol versus intravenous oxytocin for induction of labor in hypertensive disorders of pregnancy.

**Methods:** Twenty-one hypertensive pregmant women with indications for induction of labor and unfavorable cervices were randomly assigned to receive either intravaginal misoprostol or intravenous oxytocin. Misoprostol (50-100 meg) was placed in the posterior vaginal formix every 4 hour with the maximum 400 meg doses. It was not given after either spontaneous rupture of membranes or beginning of active labor. Oxytocin infusion followed an established routine. All patient had a medical indication for induction of labor, a single pregnancy, cephalic-vertex presentation,' no previous surgical scars on uterus, no contraindications for vaginal delivery, Bishop score below 5 and gestational age between 24-42 weeks.

**Results:** The average interval from start of induction to vaginal delivery was similar both misoprostol and oxytocin groups. Successful induction of labor was achieved in 54.1% of misoprostol treated women at a dose of 100 meg or less. Only two patients in misoprostol group necessitated labor augmentation with oxytocin.

**Conclusions:** intravaginal administration of misoprostol is safe, efficient and costeffective alternative to intravenous oxytocin infusion for induction of labor in hypertensive pregnancies.

**Key words:** Hypertensive disorder, pregnancy, labor induction, misoprostol, oxytocin

**ÖZET**

***HİPERTANSİF GEBELERDE DOĞUM EYLEMİNİN İNTRAVAGİNAL MISOPROSTOL İLE İNDÜKSİYONU***

**Amaç:** Hipertansif gebelerin doğum eyleminin indüklenmesinde intravaginai misoprostolün etkinlik ve güvenirliğinin intra venöz oksitosin ile karşılaştırılması.

**Metod:** Eylem indüksiyonu endikasyonu olan ve serviksi uygun olmayan 21 hipertansif gebeye intravaginal misoprostol veya intravenöz oksitosin rastgele uygulandı. Misoprostol, 50-100 meg dozunda, maksimum 400 meg olacak şekilde, 4 saat ara ile posterior vaginal fomikse yerleştirildi. Aktif doğum eylemi başlamış ise veya membranlar rüptüre ise misoprostol uygulanmadı. Oksitosin infüzyonu rutin yoldan yapıldı, tüm gebelerde doğum eylemi indüksiyonu endikasyonu olup, tek gebelik, verteks prezentasyonuna sahiptiler ve uterusu ilgilendiren geçirilmiş cerrahiye bağlı skar, vaginal doğum için kontrendikasyon bulunmamaktaydı. Bishop skoru hepsinde 5'in altında olup gebelik haftası 24-42 haftalar arasındaydı.

**Bulgular:** Doğum eylemine başlanılması ile doğum arasında geçen ortalama süre misoprostol ve oksitosin gruplarında benzer bulundu. Misoprostol uygulanan kadınların %54.1'inde 100 meg veya altındaki doz ile başarılı eylem indüksiyonu gerçekleştirildi. Misoprostol grubunda sadece iki hastada oksitosin ile eyleme yardım gerekti.

**Sonuç:** Hipertansif gebelerin doğum eylemi indüksiyonunda intravaginal misoprostol, intravenöz oksitosinin etkili, güvenilir ve ucuz bir alternatifidir.

**Anahtar kelimeler:** Hipertansiyon, gebelik, eylem.indüksiyonu, misoprostol, oksitosin

Misoprostol, a synthetic PGE1 analogue, is a gastric eytoproteetive agent that used for the prevention of gastric ulcers. Recently several investigations have described the use of a misoprostol for perinduction cervical ripening and labor induction (1-3).

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misoprostol is inexpensive and easy to administer, because it is placed in the vagina, not the cervix. Recently, it was reported that vaginal misoprostol may be as effective as oxytocin for inducing labor with a living fetus (1,4).

Preeclampsia and eclampsia are life-threatening disorders of pregnancy and they still remain as an im-

portant cause of maternal and fetal mortality and morbidity (5,6). In cases with severe preeclampsia and eclampsia the definitive treatment is termination of pregnancy after the patient has been stabilized (5). The induction of labor is difficult and risky, because of these patients are often far from term and mostly have unfavorable cervix (7). so, cervical ripening and labor induction are especially important in hypertensive pregnancy. In our clinic trial we have used misoprostol successfully and we decided to publish it.

This study was undertaken to compare the safety and efficacy of misoprostol with oxytocin used for labor induction in hypertensive disorders of pregnancy.

## METHODS

Twenty-one hypertensive pregnant women with intact membrane and unfavorable cervices (Bishop score<5) were included to study, after hospitalization all patients were evaluated by physical and pelvic examination and laboratory evaluation was immediately performed. Treatments were commenced according to usual protocol. All patients except two mild preeclamptic cases were received magnesium-sulfate treatment. Fetal status was determined by ultrasonography and external fetal monitorization.

If the blood pressure was higher than 160/110 mmHg, accompanied by either generalized edema or proteinuria (of at least 3 or more) on dipstick examination, severe preeclampsia was diagnosed. Eclampsia is diagnosed if there is seizure that can not be attributed to other causes in a preeclamptic patient.

Among the 21 hypertensive pregnant women 11 were randomly assigned to receive intravaginal misoprostol and 10 were assigned to receive intravenous oxytocin. After admission and selection for the study half (100 meg) or quarter (50 meg) tablet of misoprostol was introduced into the vaginal posterior fornix. If the patient far from term 100 meg dose was preferred. In contrast if the patient near to term 50 meg dose was preferred. If the patient was not in labor, the dose was repeated every four hour for up to maximum 400 meg doses, until effective uterine contractions and cervical dilatation were obtained. Vital signs, uterine contractions and, side effects were monitored every 30 minutes. All women monitored by external cardiotocography after the application and continued intermittenly to the delivery.

Oxytocin was started at 4 mU/min and was gradually increased in dose increments of 2 mU/mim to a maximum of 40 mU/min at 30 minutes intervals as needed to achieve an adequate contraction pattern. Criteria for enrollment included the following; (1) absence of active labor or fetal distress, (2) no previous cesarean delivery or other type of uterine surgery, (3) singleton pregnancy with vertex presentation, and (4) no contraindication to vaginal delivery.

Bishop score was evaluated before the treatment was started in all women and repeats Bishop scores were assigned before the administration of a subsequent dose of misoprostol. Patients who have no adequate contractile pattern and progress on cervical dilatation received intravenous oxytocin augmentation. Amniotomy was not undertaken until the cervix was dilated >4 cm. Cesarean section was performed in two cases in misoprostol group and one case in oxytocin group and the indications were rapid deterioration of maternal status and arrest of labor. These cases were not included to the study. Labor induction was considered successful if the women delivered within 24 hours of initiating misoprostol.

Statistical analyses were performed with the x2, student t and, Fisher's exact tests where appropriate. The significance level was $p<0.05$.

## RESULTS

Totally 21 patients with preeclampsia and eclampsia were included to the study. Three patients in misoprostol group and, 4 patients in oxytocin group were nullipar and the others were multipar. Gestational age ranged from 24 to 42 weeks in misoprostol group and from 31 to 39 in oxytocin group. Gestational age was below the 32 weeks in 3 patients in misoprostol group and, in 2 patients in oxytocin group.

The distributions of patient's age, gravidity and gestational age were similar in the misoprostol and oxytocin groups (Table 1). Likewise, indications for labor induction were similar in both groups, bishop score was less than 5 in the all patients and there were similar in both groups. Bishop score was less than 5 in the all patients and there were no significant difference between misoprostol group and oxytocin group according to Bishop score (2.0+1.2 versus 2.4±1.1).

**Table 1. Demographic characteristics of patients and indicating for labor induction**

| | Misoprostol group | Oxytocin group | t | p |
|---|---|---|---|---|
| Age | 30.8±8.2 | 27.1±6.4 | 1.15 | >0.05 |
| Gravidity | 4.0±3.0 | 4.1±3.3 | 0.07 | >0.05 |
| Gestational week | 34.3±6.6 | 34.63.2 | 0.14 | >0.05 |
| Diagnosis (x2=0.09, p>0.05) | | | | |
| Mild preeclampsia | 1 (9.1%) | | 1(10.0%) | |
| Severe preeclampsia | 6(54.5%) | | 6(60.0%) | |
| Eclampsia | 4(36.4%) | | 3(30.0%) | |

Two women in misoprostol group had Hellp syndrome while being induced. Also there were 3 intrauterine death in oxytocin group and 2 in misoprostol group. The interval from initiation of induction to vaginal delivery was similar in both groups (6.2±3.9 versus 7.2±3.3, p>0.05). All pati-

**Table 2. Labor and delivery outcomes and Apgar scores**

| | Misoprostol group | Oxytocin group | t | p |
|---|---|---|---|---|
| Treatment interval (hour) | | | | |
| Insertion to delivery | 6.2±3.9 | 7.2±3.3 | 0.61 | >0.05 |
| Active labor to delivery | 5.1±3.9 | 8.0±4.7 | 1.52 | >0.05 |
| Apgar scores (1 min) | 5.7±3.2 | 5.3±2.9 | 0.24 | >0.05 |
| Apgar scores (5 min) | 7.3±3.2 | 6.3±3.6 | 0.61 | >0.05 |
| Initial Bishop score | 2.0±1.2 | 2.4±1.1 | 0.81 | >0.05 |
| Complications | | | | |
| Fetal distress | 2 | 2 | | |
| Partus precipitatus | 1 | - | | |
| Cervical laceration | - | | | |
| Vaginal laceration | 1 | - | | |
| Second degree perineal laceration | - | 2 | | |

ents were delivered within the first 16 hours. The interval from initiation of active labor to delivery was shorter in the misoprostol group but this did not reach statistical significance (5.1±3.9 versus 8.0±4.7, p>0.05). Successful induction of labor was achieved in 54.1% of misoprostol treated women at a dose of 100 meg or less and all these women only a single dose were applied.

The mean 5th minute Apgar score was lower in the oxytocin group than in misoprostol group (6.3±3-6 versus 7.3±3-2) but this difference was not statistically significant. The first minute Apgar score was below 7 in 4 patients in both groups. The distribution of complications in both groups was similar. There were one partus precipitatus (interval from active labor to delivery was shorter than 3 hours) and one vaginal laceration in misoprostol group and one cervical laceration and two second degree perineal lacerations in oxytocin group. Fetal distress was detected as evidenced by the presence of meconium stained amniotic fluid or fetal tachycardia. There were two fetal distress cases in both groups. There were two infant deaths in misoprostol group and one in oxytocin group after delivery.

Oxytocin augmentation was used in two patients in the misoprostol group because of there were not adequate uterine contraction and progress on cervical dilatation. There were no significant changes in maternal vital signs in both groups. There was no serious maternal side effect in both groups, signs of hyperactivity sweating, fever, diarrhea or other gastrointestinal effects were not detected in misoprostol group. No uterine hyperstimulation were seen in both groups.

## DISCUSSION

Prostaglandins have been used for labor induction for over 20 years (8). Misoprostol, a synthetic PGEl analogue, is a gastric cytoprotective agent that used for the prevention of peptic ulcers. It has been shown that PGE2 is succesful in the labor induction of preeclamptic women (5,9). Also it has been reported that misoprostol effectively induces labor while causing few maternal side effects and apparently no adverse effects on the newborn (1-3,10). It was reported that vaginal misoprostol may be as effective as oxytocin for inducing labor with a living fetus (1,4). In this study the administration of misoprostol (50 meg or 100 meg), intravaginally proved to be as effective as oxytocin for inducing labor in hypertensive pregnancies. Misoprostol therapy was associated with less need for oxytocin and only two patients in misoprostol group necessitated labor augmentation with oxytocin.

Successful induction of labor was achieved in 54.1% of misoprostol treated women at a dose of 100 meg or less and, all these women received only one dose. Sanchez-Ramos et al (1), reported that three quarters of the patients in the misoprostol group required only one half tablet (100 meg). They concluded that possible advantages of misoprostol may be its dual role in cervical ripening and labor induction.

Complications were minimal in the misoprostol group and were not significantly different from the oxytocin group. Maternal side effects of misoprostol such as sweating, fever, diarrhea was not detected in misoprostol group. No uterine hypersitumulation were seen. This study was hampered by inconsistent use of cardiotocography. Most patients were monitored by auscultation and palpation. So, subtle change in fetal heart rate and uterine contractions could have gone undetected. Apgar score was below *1 in A* patients in both groups but two of them in each group were diagnosed before delivery. There were 5 stillbirth in study group and two infants died after delivery in misoprostol group and one infant died in oxytocin group after delivery. In our region hypertensive disorders of pregnancy are common and, they generally belong to low socioeconomic level and have no adequate antenatal care. So these patients usually admit to hospital lately. We concluded that the increased complications such as low Apgar score, increased stillbirth and fetal death related to these factors not to type of induction.

Recently Kailasam at al (11), reported that, when misoprostol was given 400 meg by orally, there was a modest decrease in mean arterial pressure 20 minutes after the dose, accompanied by a decrease in systemic vascular resistance and a compensatory rise in cardiac output and heart rate, so, misoprostol may positive effect on blood pressure on hypertensive pregnant and this concern needs further evaluation.

As reported before cost of misoprostol is not expensive, it does not require refrigeration and also it

does not require the continuous supervision demanded by an oxytocin drip (10,12). As previous investigators have indicated these all advantages of misoprostol are especially important in developing countries.

On the basis of this preliminary findings misoprostol appear to as effective as oxytocin for inducing labor in hypertensive pregnancies. Misoprostol is cheap, effective, safe and easy to administer and it may positive effect on blood pressure. These advantages of misoprostol are especially important for places that have insufficient health care, such as our region. In spite of the effectiveness of misoprostol evident in this preliminary report there is need for further evaluation especially connected with safety and more suitable dose of misoprostol.

## REFERENCES


1. Sanchez-ramos L, Kaunitz AM, Del Valle GO, Delke I, Schroeder PA, Briones DK: Labor Induction With the Prostaglandin El Methyl Analogue Misoprostol Versus Oxytocin: A Randomized Trial. Obstet Gynecol, 81: 332-6, 1993.
2. Fletcher HM, Mitchell S, Simeon D, Frederick J, Brown D: Intravaginal misoprostol as a cervical ripening agent. Br J Obstet Gynaecol, 100:641-4, 1993.
3. Fletcher H, Mitchell S, Frederick J, Simeon D, Brown D: uitravaginal Misoprostol Versus Dinoprostone As Cervical Ripening and Labor-Inducing Agents. Obstet Gynecol, 83:244-7, 1994.
4. Margoulies M, Perez CG, Voto LS: Misoprostol to induce labor (Letter). Lancet, 339:64, 1992.
5. Roberts JM: Pregnancy related hypertension. In: Pedersen D, (ed): Maternal fetal Medicine: Principles and Practice. Philadelphia: WB. Saunders Company, 777-823, 1989.
6. Fadigan AB, Sealy DP, Schneider EF: Preeclampsia: progress and puzzle. Am Fam Physician, 49:849-56, 1994.
7. Taner CE, Hakverdi AU: Hygroscopic cervical dilators in eclampsia. Int J Gynecol Obstet, 41:283-4, 1993.
8. Poulsen HK, moUer LK, Westergaard AG, Thomsen SG, Giersson RT, Arngrimsson R: Open randomized comparison of prostaglandin E2 given by intracervical gel or vagitory for preinduction cervical ripening and induction of labor. Acta obstet Gynecol Scand, 70:549-53, 1991.
9. danışman N, Vicdan K, Ozmen Ş, Yapar EG, Gökmen O: Prostaglandin E2 Gel in Patients With Severe Preeclampsia and Eclampsia. Gynecol Obstet Reprod Med, 1:102-105, 1995.
10. Bugalho A, Bique C, Machungo F, Faundes A: Induction of labor with intravaginal misoprostol in intrauterine fetal death. Am J Obstet Gynecol, 171:538-41, 1994.
11. KailasamMT, Lin MC, Cervenka JH et al: Effects of an oral prostaglandin El agonist on blood pressure and its determinants in essential hypertension. J Hum Hypertens, 8:515-20, 1994.
12. Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH: A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labor induction. Am J Obstet Gynecol, 172:1804-10, 1995.