

Induction of Labor Using One Dose versus Multiple Doses of Misoprostol: RCT

HISHAM M.M. HARB, M.D.*; DINA Y. MANSOUR, M.D.* and NAHED Sh. MOHAMMED, M.Sc.**

The Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University* and Aswan Insurance Hospital**

Abstract

Background: Situations arise in obstetrics where it becomes necessary to end a pregnancy in the interest of the mother or baby or both. There is a growing interest in the use of misoprostol, a prostaglandin E1 analogue for labour induction. Induction of labour is a common obstetric intervention and the use of misoprostol as an induction agent is important due to its low cost and stability at room temperature. These additional advantages make it a suitable agent, particularly in under-resourced settings and tropical countries.

Aim of Study: This study was conducted to compare the rate of vaginal delivery within 24 hour among patients who undergo induction of labor between those who receive vaginal single dose of misoprostol with those receive up to 5 doses of this medication.

Patients and Methods: The study was a randomized controlled open labeled clinical trial, study setting was Obstetrics and Gynecology Department of Ain Shams Maternity University Hospital (Emergency Department), the study timing was 6 months from March to September 2019, this study was conducted on 206 women who came to Emergency Department of Obstetrics and Gynecology Department of Ain Shams Maternity University Hospital.

Results: The majority (70.87%) had V D in 24 hours in one dose group versus 75.73% in multiple doses without significant difference between both groups. Time from induction to delivery in one dose group ranged from 10-32 with mean value of 17.990 ± 5.579 while in multi-dose group was 10-33 (with mean value 18.204 ± 5.206) without significant difference between groups. Latent period in one dose group ranged from 3-11 with mean value of 5.918 ± 2.077 while in multi-dose group was 3-12 (with mean value 6.500 ± 2.173) without significant difference between groups. There was non-significant difference between one dose and multiple doses in incidence of fetal distress as the majority in one dose group 92.23% than 90.29% in multi-dose group.

Conclusion: The single-dose misoprostol appears to be an acceptable alternative to a multiple dose regimen for cervical ripening before the induction of labor. Our data indicates that there was no difference regarding the clinical

efficacy between two labour induction regimens of vaginal misoprostol.

Key Words: Labor – Multiple doses – Misoprostol – RCT.

Introduction

LABOR induction is an intervention that artificially initiates uterine contractions leading to progressive dilatation and effacement of the cervix and birth of the baby, and is to be considered when the risks of continuing pregnancy are outweighed the risks of terminating it. Labor induction is a procedure used for a broad range of common conditions: Post-term pregnancy, pregnancy induced hypertension, pre-eclampsia, eclampsia, maternal diabetes, premature rupture of membranes, intrauterine fetal growth restriction, chorioamnionitis, fetal death, A prompt delivery reduces maternal or neonatal morbidity and mortality [1].

Methods of preparing uterine cervix and inducing labor include administration of oxytocin, prostaglandins, prostaglandin analogues, mifepristone, or mechanical procedures (amniotomy, intracervical Foley catheter, and sweeping of the membranes). There is a great concern about their effectiveness and safety [2].

Misoprostol is a synthetic analogue of prostaglandin E1 with a plasma half-life of <1 hour when given vaginally [3]. The dose mostly recommended is 25 or 50 μ g of misoprostol vaginally. However, there are few studies that address the repeat dosing and frequency of dosing of misoprostol. Although 3 hours might be the most appropriate interval based on the half-life, it is not known how well serum level correlates with clinical effect. Also, it is unknown whether repeat doses result in a cumulative effect or whether there is a latency period between the application of the drug and biochemical

Correspondence to: Dr. Hisham M.M. Harb,
The Department of Obstetrics and Gynecology,
Faculty of Medicine, Ain Shams University

changes in the cervix. One study suggested a single dose is most effective if it is given 12 hours before oxytocin is initiated [4].

Repeat dosing may extend the latent phase of labor. A longer latent phase of labor is associated with an increased rate of cesarean delivery, chorioamnionitis, endometritis, and uterine atony [5].

A previous study hypothesized that repeating the dose of misoprostol extends the cervical ripening time and thus decreases the proportion of women who deliver vaginally within 24 hour after the administration of the first dose of misoprostol. Therefore they compared the rate of vaginal delivery within 24 hour among patients who undergo induction of labor between those who receive a single dose of misoprostol with those receive multiple doses and they found that 50% of women in the multiple dose group would deliver vaginally in 24 hours. A sample size of 220 patients was needed to detect a 20% increase in vaginal delivery rate within 24 hours in the 1 dose misoprostol group [6].

Aim of the work:

This study was conducted to compare the rate of vaginal delivery within 24 hour among patients who undergo induction of labor between those who receive a single dose of misoprostol with those receive up to 5 doses of this medication.

Patients and Methods

Type of study: Randomized controlled open labeled clinical trial.

Study setting: Obstetrics and Gynecology Department of Ain Shams Maternity University Hospital (Emergency Department).

Study timing: 6 months from March to September 2019.

Randomization: Was done using computer generated randomization sheet using Medcalc version 13.

Allocation and concealment: 206 opaque envelopes were numbered serially and in each envelope, the corresponding letter which denotes the allocated group was put according to randomization table. Then all envelopes were closed and put in one box. When each patient arrived, a random envelope was opened and the patient was allocated according to the mode of induction written in the envelope.

Study population: This study was conducted on 206 women who came to Emergency Depart-

ment of Obstetrics and Gynecology Department of Ain Shams Maternity University Hospital.

Inclusion criteria:

- 1- Primigravid women.
- 2- Age: 20-35.
- 3- Singleton term pregnancies (40-42 weeks of gestation).
- 4- Normal laboratory investigations.
- 5- AFI: 10-20cm.
- 6- Normal placental location.
- 7- Estimated fetal weight (2.5-3.5kg).
- 8- Fetal monitoring was category I by CTG.

Exclusion criteria:

- 1- Previous C.S.
- 2- Contraindication to misoprostol.
- 3- Contraindication to vaginal delivery.
- 4- Fetal death, major fetal anomaly, or fetal growth restriction.
- 5- Premature rupture of membranes.
- 6- Associated medical conditions like D.M, HTN, PET.

• Sample size:

Group 1: Include 103 women who received 25 µg of misoprostol as a single dose Vaginally (Vagiprost).

Group 2: Include 103 women who received up to 5 doses of misoprostol starting with 25 µg in the form of one tablet of vagiprost vaginally repeated every 6 hours.

• Process of delivery:

In the multiple dose misoprostol group, misoprostol 25 µg (vagiprost 25 µg) was administered vaginally every 4-6 hours for a maximum of 5 doses. Before insertion of each repeated dose, the patient condition was evaluated. If the patient had regular efficient uterine contractions, or fetal monitoring wasn't category I, no further misoprostol would be given. Alert and action lines were drawn when the women was in the active phase of labour.

- Maternal assessment included (BP, pulse, Temperature).
- Fetal assessment included (amniotic fluid color and volume monitoring and fetal heart rate monitoring).

- Vaginal examination was performed 4 hours after the initial one or earlier if showed dilatation between Alert and action line, subsequent examination was carried out in 2 hours.
- If there were no cervical changes, no contractions in both groups within 24 hour of first dose, failed induction was considered.
- If there were fetal complications (fetal monitoring wasn't category I), maternal complications or failed induction, cesarean section was considered.

Study procedure:

All the patients were subjected to the following:

- **Informed consent was taken:**
 - 1- Complete history was taken.
 - 2- General examination.
 - 3- Abdominal examination.
 - 4- Abdominal ultrasound.
 - 5- Investigations: CBC, urine analysis for albumin and sugar, blood group, RH type.
 - 6- CTG.

Results

Table (1): V D in 24 hours.

V D in 24 hours	Groups						Chi-square	
	Ond dose		Multi-dose		Total		χ^2	p-value
	N	%	N	%	N	%		
No	30	29.13	25	24.27	55	26.70	0.620	0.431
Yes	73	70.87	78	75.73	151	73.30		
Total	103	100.00	103	100.00	206	100.00		

The majority (70.87%) had V D in 24 hours in one dose group versus 75.73% in multiple doses without significant difference between both groups ($p=0.431$).

Table (2): Incidence of neonatal morbidities.

Neonatal morbidities	Groups						Chi-square	
	Ond dose		Multi-dose		Total		χ^2	P-value
	N	%	N	%	N	%		
• No	70	67.96	83	80.58	153	74.27	5.247	0.155
• Supplemental oxygen	18	17.48	9	8.74	27	13.11		
• NICU admission	6	5.83	6	5.83	12	5.83		
• Low APGAR score	9	8.74	5	4.85	14	6.80		
Total	103	100.00	103	100.00	206	100.00		

The majority (67.96%) of cases in one dose group had no neonatal morbidities versus 80.58% in multi-dose group while supplemental oxygen, NICU admission and low APGAR score was 17.48%, 5.83% and 8.74% respectively in single dose group versus 8.74%, 5.83% and 4.85% respectively in multi-dose group without significant difference between both groups ($p=0.155$).

Table (3): Time from induction to delivery (hours).

Time from induction to delivery (hours)	Groups		t-test	
	Ond dose	Multi-dose	t	p-value
Range	10-32	10-33	-0.284	0.777
Mean ± SD	17.990±5.579	10.204±5.206		

Time from induction to delivery in one dose group ranged from 10-32 with mean value of 17.990 ±5.579 while in multi-dose group was 10-33 (with mean value 18.204±5.206) without significant difference between groups as $p=0.777$.

Table (4): Latent period (hours).

Latent period (hours)	Groups		t-test	
	Ond dose	Multi-dose	t	p-value
Range	3-11	3-12	-1.791	0.075
Mean ± SD	5.918±2.077	6.500±2.173		

Latent period in one dose group ranged from 3-11 with mean value of 5.918±2.077 while in multi-dose group was 3-12 (with mean value 6.500 ± 2.173) without significant difference between groups as $p=0.075$.

Table (5): Indication of C.S (hours).

Indication of C.S	Groups						Chi-square	
	Ond dose		Multi-dose		Total		χ^2	P-value
	N	%	N	%	N	%		
• Failed Induction	18	60.00	17	68.00	35	63.64	0.377	0.828
• Non reassuring NST	6	20.00	4	16.00	10	18.18		
• Obstructed labour	6	10.00	4	16.00	10	18.18		
Total	30	100.00	25	100.00	55	100.00		

The majority (60%) of cases in one dose group delivered by CS due to failed induction while 20% due to either non reassuring NST or obstructed labour. And in multi-dose group, the majority (63.64%) of cases in multi-dose group delivered by CS due to failed induction while 18.18% due to either non reassuring NST or obstructed labour without significant difference between both groups ($p=0.828$).

Table (6): Fetal complications.

Fetal complications	Groups						Chi-square	
	Ond dose		Multi-dose		Total		χ^2	P-value
	N	%	N	%	N	%		
No	95	92.23	93	90.29	188	91.26	0.243	0.622
Fetal distress	8	7.77	10	9.71	18	8.74		
Total	103	100.00	103	100.00	206	100.00		

There was non-significant difference between one dose and multiple doses in incidence of fetal distress ($p=0.622$) as the majority in one dose group 92.23% and 90.29% in multi dose group had no fetal distress.

Table (7): Maternal complications.

Maternal complications	Groups						Chi-square	
	Ond dose		Multi-dose		Total		χ^2	P-value
	N	%	N	%	N	%		
No	95	92.23	91	88.35	186	90.29	0.886	0.347
Yes	8	7.77	12	11.65	20	9.71		
Total	103	100.00	103	100.00	206	100.00		

The majority (92.23% and 88.35%) in one dose and multiple doses had no maternal complications without significant difference between both groups in the incidence of maternal complication ($p=0.347$).

Table (8): Maternal complications.

Maternal complications	Groups						Chi-square	
	Ond dose		Multi-dose		Total		χ^2	P-value
	N	%	N	%	N	%		
• No	95	92.23	91	88.35	186	90.29	6.419	0.492
• Hyperthermia	4	3.88	4	3.88	8	3.88		
• Nausea	1	0.97	0	0.00	1	0.49		
• Postpartum-hemorrhage	1	0.97	3	2.91	4	1.94		
• Vomiting	1	0.97	0	0.00	1	0.49		
• Shivering	1	0.97	2	1.94	3	1.46		
• Exhaustion	0	0.00	2	1.94	2	0.97		
• Hypersystole	0	0.00	1	0.97	1	0.49		
Total	103	100.00	103	100.00	206	100.00		

There was non-significant difference between one dose and multiple doses in incidence of Hyperthermia, nausea, post-partum hemorrhage, vomiting, shivering, exhaustion and hypersystole as $p=0.492$.

Age in one dose group ranged from 20-30 with mean value of 24.184 ± 3.386 while n multi-dose group was 20-30 (with mean value 24.738 ± 3.290) without significant difference between groups as

$p=0.236$. Weight in one dose group ranged from 65-90 with mean value of 75.835 ± 6.691 while n multi-dose group was 64-90 (with mean value 75.718 ± 6.450) without significant difference between groups as $p=0.899$. Height in one dose group ranged from 157-170 with mean value of 162.777 ± 3.958 while n multi-dose group was 157-170 (with mean value 162.398 ± 3.989) without significant difference between groups as $p=0.495$ BMI in one dose group ranged from 23.88-35.16 with mean value of 28.657 ± 2.738 while n multi-dose group was 23.03-35.25 (with mean value 28.778 ± 2.986) without significant difference between groups as $p=0.762$. GA in one dose group ranged from 40-42 with mean value of 40.534 ± 0.639 while n multi-dose group was 40-42 (with mean value 40.398 ± 0.566) without significant difference between groups as $p=0.108$. Bishop score in one dose group ranged from 3-5 with mean value of 3.932 ± 0.675 while n multi-dose group was 3-5 (with mean value 3.835 ± 0.658) without significant difference between groups as $p=0.297$.

Table (9): Demographic data of both groups.

	Groups		t-test	
	Ond dose	Multi-dose	t	p-value
Age:				
Range	20-30	20-30	-1.190	0.236
Mean \pm SD	24.184 ± 3.386	24.738 ± 3.290		
Weight:				
Range	65-90	64-90	0.127	0.899
Mean \pm SD	75.835 ± 6.691	75.718 ± 6.450		
Height:				
Range	157-170	157-170	0.684	0.495
Mean \pm SD	162.777 ± 3.958	162.398 ± 3.989		
BMI:				
Range	23.88-35.16	23.03-35.25	-0.304	0.762
Mean \pm SD	28.657 ± 2.738	28.778 ± 2.986		
GA:				
Range	40-42	40-42	1.616	0.108
Mean \pm SD	40.534 ± 0.639	40.398 ± 0.566		
Bishop score:				
Range	3-5	3-5	1.045	0.297
Mean \pm SD	3.932 ± 0.675	3.835 ± 0.658		

Discussion

We conducted this randomized control study to compare the rate of vaginal delivery within 24 hours among patients who undergo induction of labor between those who receive a single dose of misoprostol (group I) and those who receive up to 5 doses of this medication (group II).

Primary outcome was rate of vaginal delivery within 24 hour while secondary outcome including time from induction to delivery, duration of latent

period, maternal complications (maternal exhaustion, fever, rigors, diarrhea), fetal complications (fetal distress-intra uterine fetal death), neonatal morbidities (low APGAR score-NICU admission).

In the current study, no significant difference between groups in age as $p=0.236$, weight as $p=0.899$, height as $p=0.495$ and BMI as $p=0.762$ as Body Mass Index (BMI) is an important maternal characteristic that can influence the dose response to vaginal misoprostol. Obese women might be expected to require higher doses or more frequent applications, while women with a low BMI may require lower doses.

This was supported by finding of Pimentel et al., on 243 participants. There was no difference in the demographic and clinical characteristics of both treatment groups including body mass index, race/ethnicity and parity [6].

In the current study, GA in one dose group ranged from 40-42 with mean value of 40.534 ± 0.639 while in multi-dose group was 40-42 (with mean value 40.398 ± 0.566) without significant difference between groups as $p=0.108$.

In contrast, among one hundred and four women were randomized to either a single dose of 50 µg of intravaginal misoprostol in 24h, or two consecutive doses of intravaginal 50 µg misoprostol 6h apart included in study by Lokugamage et al., the only significant difference when comparing the maternal demographic data was mean length of gestation [7].

In the current study, Bishop score in one dose group ranged from 3-5 with mean value of 3.932 ± 0.675 while in multi-dose group was 3-5 (with mean value 3.835 ± 0.658) without significant difference between groups as $p=0.297$.

And in harmony with this study's results, Lokugamage found there was no difference in the mean Bishop's score between the groups [7].

Also, among five hundred twenty-two patients with indications for induction of labor and unfavorable cervixes were randomly assigned by Wing and Paul, to one or two dosing regimens of vaginally administered misoprostol. The median Bishop score obtained after administration of the initial dose of medication was 3 in both groups also not significantly different ($p>0.05$) [8].

In the current study, the majority (70.87%) had V D in 24 hours in one dose group versus 75.73% in multiple doses without significant difference between both groups ($p=0.431$).

The current study's results are in harmony with Girija and Manjunath, in the 25 µg group, the vaginal delivery rate with one dose was 34%, two doses 28% and three doses 6%. There was no significant difference between groups ($p=0.3$) [9].

In the current study, time from induction to delivery in one dose group ranged from 10-32 hours with mean value of 17.990 ± 5.579 while in multi-dose group was 10-33 hours (with mean value 18.204 ± 5.206) without significant difference between groups as $p=0.777$.

This was in harmony with Pimentel et al., study showed that, the time to vaginal delivery was 1187 minutes for the 1-misoprostol group and 1321 minutes for the multiple misoprostol group ($p=.202$) [6].

Lokugamage et al., studied the efficacy of a single versus two dose regimen of 50 µg vaginal misoprostol for labour induction. Although the author concluded that the two dose regimen was more effective [7].

In contrast, according to a study by Lokugamage et al., the induction to delivery interval was significantly longer in the single-dose regimen. Although this study was randomized, the results revealed heterogeneity within the maternal demographic and 'reasons for induction' data. There were more postdate pregnancies in the two-dose arm. The other component of heterogeneity that should be discussed is the greater number of suspected large-for-date fetuses in the single-dose group, although there were no eventual differences in birth weight between the groups [7].

In the current study, latent period in one dose group ranged from 3-11 with mean value of 5.918 ± 2.077 while in multi-dose group was 3-12 (with mean value 6.500 ± 2.173) without significant difference between groups as $p=0.075$.

This goes in line with Pimentel et al., showed that, the time lapsed from the last dose of misoprostol to the initiation of oxytocin were similar for both groups [6].

In the current study, the majority (60%) of cases in one dose group delivered by CS due to failed induction while 20% due to either non reassuring NST or obstructed labour. And in multi-dose group, The majority (63.64%) of cases in multi-dose group delivered by CS due to failed induction while 18.18% due to either non reassuring NST or Obstructed labour without significant difference between both groups ($p=0.828$).

Although this results was a contrary to a study conducted by Pimentel et al., which showed that, cesarean delivery rate was greater in the 1-misoprostol group compared with the multiple-misoprostol group ($p=.034$; 35.8% vs. 22.8%). But its results were similar to the finding regarding there were no significant differences in the indication for cesarean delivery between groups [6].

Also, in line with current results, indications for caesarean section were comparable among groups (one dose, two doses and three doses) as reported by Girija and Manjunath [9].

In the current study, there was non-significant difference between one dose and multiple doses in incidence of fetal distress ($p=0.622$) as the majority in one dose group 92.23% and 90.29% in multi dose group had no fetal distress. The majority (67.96%) of cases in one dose group had no neonatal morbidities versus 80.58% in multi-dose group while supplemental oxygen, NICU admission and low APGAR score was 17.48%, 5.83% and 8.74% respectively in single dose group versus 8.74%, 5.83% and 4.85% respectively in multi dose group without significant difference between both groups ($p=0.155$).

Similarly, Pimentel et al., showed that there were no statistically significant differences in the secondary fetal outcomes between the 2 groups. There were no cases of hypoxic-ischemic encephalopathy, intraventricular hemorrhage grade 3 or 4, severe respiratory distress syndrome, necrotizing enterocolitis, or death [6].

Also, the neonatal outcomes were comparable among groups according to Girija and Manjunath [9].

Conflicting results was reported by Lokugamage et al., studied the efficacy of a single versus two dose regimen of 50 μ g vaginal misoprostol for labour induction. When evaluating aspects of intrapartum fetal well being, there was an increased amount of clinician input related to suspicious Cardiotocography (CTG) and an increased amount of intervention in the one-dose group, which approached significance. However there were no other differences detected with other parameters of intrapartum well-being [7].

In the current study, the majority (92.23% and 88.35%) in one dose and multiple doses respectively had no maternal complications without significant difference between both groups ($p=0.347$). There was non-significant difference between one dose and multiple doses in incidence of hyperther-

mia, nausea, post-partum hemorrhage, vomiting, shivering, exhaustion and hypersystole as $p=0.492$.

Similarly, Pimentel et al., showed that there were no statistically significant differences in the secondary maternal outcomes between the 2 groups. There was 1 case of intensive care unit admission (in the 1-misoprostol group) and 1 uterine rupture (in the multiple-misoprostol group). There were no cases of thromboembolism, hysterectomy, or death [6].

Also, Lokugamage et al., found that, nausea, vomiting, and diarrhoea rates were similar in both groups, there were no cases of uterine rupture [7].

Conclusion:

Induction of labour is a common obstetric intervention and the use of misoprostol as an induction agent is important due to its low cost and stability at room temperature. These additional advantages make it a suitable agent, particularly in under-resourced settings and tropical countries. Moreover, the vaginal single-dose misoprostol appears to be an acceptable alternative to a multiple dose regimen for cervical ripening before the induction of labor. Our data indicates that there was no difference regarding the clinical efficacy between two labour induction regimens of vaginal misoprostol.

References

- 1- HOFMEYR G.J., GÜLMEZOGLU A.M. and PILEGGI C.: Vaginal misoprostol for cervical ripening and induction of labour. Cochrane Database of Systematic Reviews, 2010.
- 2- GÜLMEZOGLU A.M., CROWTHER C.A., MIDDLETON P., et al.: Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database of Systematic Reviews, 2012.
- 3- WING D.A. and SHEIBANI L.: Pharmacotherapy options for labor induction. Expert opinion on pharmacotherapy, 16: 1657-68, 2015.
- 4- MEYER M., PFLUM J. and HOWARD D.: Outpatient misoprostol compared with dinoprostone gel for preinduction cervical ripening: A randomized controlled trial. Obstetrics & Gynecology, 105: 466-72, 2005.
- 5- ROUSE D.J., WEINER S.J., BLOOM S.L., et al.: Failed labor induction: Toward an objective diagnosis. Obstetrics and gynecology, 117: 267, 2011.
- 6- PIMENTEL V.M., ARABKHAZAEI M., MOON J.Y., et al.: Induction of labor using one dose vs multiple doses of misoprostol: A randomized controlled trial. American Journal of Obstetrics & Gynecology, 218: 614.e611-614.e618, 2018.
- 7- LOKUGAMAGE A., FORSYTH S., SULLIVAN K., et al.: Randomized trial in multiparous patients: Investigating

- a single vs. two-dose regimen of intravaginal misoprostol for induction of labor. Acta obstetrica et gynecologica Scandinavica, 82: 138-42, 2003.
- 8- WING D.A. and PAUL R.H.: A comparison of differing dosing regimens of vaginally administered misoprostol for preinduction cervical ripening and labor induction. American Journal of Obstetrics and Gynecology, 175: 158-64, 1996.
- 9- GIRIJA S. and MANJUNATH A.P.: Comparison of two dosing regimens of vaginal misoprostol for labour induction: A randomised controlled trial. J. Turk. Ger. Gynecol. Assoc., 10: 220-5, 2009.

دراسة للمقارنة بين تحريض المخاض بواسطة جرعة واحدة من الميزوبروستول أو استخدام جرعات متعددة؛ دراسة عشوائية خاضعة للمراقبة

يتحتم في بعض الأحيان إنهاء الحمل لصالح الأم أو الجنين ويوجد إهتمام متزايد في استخدام الميزوبروستول كنظير إصطناعي للبروستاجلاندين في تحريض المخاض.

يعتبر تحريض المخاض تدخل شائع في علم الولادة والذي بدوره يجعل الميزوبروستول ذو أهمية في هذا المجال حيث أنه غير مكلف ويخزن في درجة حرارة الغرفة وهذا يجعله مناسباً في المناطق الحارة.

في هذه الدراسة كانت نقطة الإهتمام والهدف من البحث هو المقارنة بين معدل الولادة المهبلية خلال ٢٤ ساعة بين السيدات اللاتي خضعن لتحريض المخاض بين اللاتي تلقين جرعة واحدة من الميزوبروستول مع تلقي ٥ جرعات من هذا الدواء.

تم تعيين ٢٠٦ سيدة بكرية في هذه الدراسة. تم تقسيمهن إلى مجموعتين كل مجموعة تتكون من ١٠٣ سيدة.

المجموعة الأولى تم إعطاؤها جرعة واحدة من الميزوبروستول المهبلية والمجموعة الأخرى تم إعطاؤها أكثر من جرعة من نفس الدواء بدءاً بجرعة ٢٥ ميكروجرام مهبلية. كان معدل الولادة خلال ٢٤ ساعة في مجموعة الجرعة الواحدة والمتعددة الجرعات بنسبة ٧٠.٨٧٪ و ٧٥.٧٣٪ على التوالي. وكانت المدة ما بين تحريض الولادة إلى الولادة في مجموعة الجرعة الواحدة تتراوح من ١٠ إلى ٣٢ ساعة بمتوسط $٥.٥٧٩ \pm$ ١٧.٩٩٠. بينما تراوحت المدة في المجموعة متعددة الجرعات من ١٠ إلى ٣٣ ساعة بمتوسط ٥.٢٠٦ ± ١٨.٢٠٤ . ولقد تراوحت الفترة ما بين تحريض الولادة إلى المرحلة النشطة من ٣-١١ ساعة في مجموعة الجرعة الواحدة ومن ٣ إلى ١٢ ساعة في المجموعة متعددة الجرعات بمتوسط ٥.٩١٨ ± ٢.٠٧٧ و ٦.٨٧٢ ± ٢.٣٤٠ . على التوالي بينما لم يكن هناك إختلاف في عدد حالات المضاعفات للأم أو الجنين أو المضاعفات الوليدية بين المجموعتين.

وعليه كان استخدام عقار الميزوبروستول بجرعة واحدة في تحريض المخاض بديلاً مناسباً عن التكرار. حيث أنه كان لا يوجد إختلاف في الفاعلية بين مجموعة الجرعة الواحدة والمتعددة الجرعات في تحريض المخاض.