Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2020;45(3):1144-1151
DOI: 10.17826/cumj.734528

ARAŞTIRMA / RESEARCH

Effects of rectally administered misoprostol on intestinal motility and uterine bleeding after cesarean section

Sezaryen sonrası rektal olarak uygulanan misoprostolün bağırsak motilitesi ve uterus kanaması üzerine etkileri

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Cukurova Medical Journal 2020;45(3):1144-1151

Abstract

Purpose: This study was designed to determine the effectiveness of rectal misoprostol administered in primiparous women after elective cesarean to the motility of the gastrointestinal tract and postpartum hemorrhage.
Materials and Methods: This study was conducted as a retrospective cohort study of 240 patients who were administrated rectal misoprostol (misoprostol group, n=120) or intravenous oxytocin (non-misoprostol group n=120) during the postpartum period in a single institution between April 2018 and March 2019
Results: The median values of the first flatulation and defecation time were statistically significantly earlier in the misoprostol group than in the non-misoprostol group (the first flatulation time was 18 hours and 24 hours respectively, the first defecation time was 29 hours and 36 hours respectively). The comparison of the two groups in terms of postoperative hemoglobin and hematocrit values demonstrated that hemoglobin and hematocrit values measured at the postoperative 24th hour (the hemoglobin was 11 g/dL and 10,2 g/dL respectively, the hematocrit was 33% and 30.6% respectively) were statistically significantly higher in the misoprostol group than were those in the non-misoprostol group. Postoperative fever and shivering, negative effects of misoprostol, were more frequent in the misoprostol group than in the non-misoprostol group.
Conclusions: In the present study, demonstrated that the administration of rectal misoprostol after CS led to the early flatulation and defecation by increasing the motility of the gastrointestinal tract and reduced the amount of postpartum hemorrhage in the women.
Keywords:. Rectal misoprostol, cesarean section, postpartum ileus, postpartum hemorrhage.

Öz

Amaç: Bu çalışma primipar kadınlarında elektif sezaryen sonrası uygulanan rektal misoprostolün gastrointestinal sistem motilitesi ve postpartum kanamaya etkinliğini belirlemek için tasarlanmıştır.
Gereç ve Yöntem: Bu çalışma, 2018 Nisan ve 2019 Mart tarihleri arasında tek bir kurumda sezaryen sonrası dönemde rektal misoprostol (misoprostol grubu, n = 120) veya intravenöz oksitosin (misoprostol olmayan grubu n = 120) uygulanan 240 hastada retrospektif bir kohort çalışması olarak gerçekleştirildi.
Bulgular: İlk gaz ve dışkılama süresinin ortanca değerleri misoprostol grubunda nonmisoprostol grubuna göre istatistiksel olarak anlamlı derecede daha erken idi (ilk gaz süresi sırasıyla 18 saat ve 24 saat, ilk dışkılama süresi sırasıyla 29 saat ve 36 saat idi), iki grubun postoperatif hemoglobin ve hematokrit değerleri açısından postoperatif 24. saatte ölçülen hemoglobin ve hematokrit değerlerinin (hemoglobin sırasıyla 11 g / dL ve 10,2 g / dL olduğunu, hematokritin sırasıyla % 33 ve 30,6) misoprostol grubunda nonmisoprostol grubuna göre istatistiksel olarak anlamlı derecede yüksekti. Postoperatif ateş ve titreme, misoprostolün olumsuz etkileri, misoprostol grubunda nonmisoprostol grubuna göre daha sık olarak tespit edildi.
Sonuç: Bu çalışma, CS sonrası rektal misoprostol uygulamasının, gastrointestinal sistemin motilitesini arttırarak erken gaz çıkımına ve dışkılamaya yol açtığını ve kadınlarda doğum sonu kanama miktarını azalttığını göstermiştir.

Anahtar kelimeler: Rektal misoprostol, sezaryen, doğum sonu ileus, doğum sonu kanama.

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Geliş tarihi/Received: 24.06.2019 Kabul tarihi/Accepted: 31.07.2020 Çevrimiçi yayın/Published online: 31.08.2020

INTRODUCTION

Cesarean section is among the most frequently conducted abdominal surgical procedures all over the world. Two of the major complications after a cesarean delivery are ileus and postpartum hemorrhage[1,2,3].

After cesarean section, postoperative bowel movements decrease due to changes in the autonomic nervous system[4,5,6]. Gastrointestinal dysfunction leads to the accumulation of gas and secretion in the intestines, resulting in abdominal distension, vomiting, pain and, ileus. Delayed first flatus and defecation are the main factors affecting postoperative patient comfort. In addition, oral feeding intolerance, parenteral nutrition requirements, inability to breastfeed and long-term hospitalization lead to a serious economic burden on the national health system[7,8]. Therefore, in the postoperative period, low-cost and uncomplicated methods that increase the intestinal motility of an individual should be preferred.

Postpartum hemorrhage, an important complication requiring blood transfusion, is the blood loss of >500ml after vaginal delivery and >1000ml after cesarean section in which hemoglobin level decreases below 10 g/Dl[9]. According to the World Health Organization (WHO), postpartum hemorrhage which may develop within 4 weeks of birth is the leading cause of maternal deaths in low economic levels countries, and it is the cause of 25% of maternal deaths in the world. However, since most of the mortality from postpartum hemorrhage occurs in the first 24 hours due to uterine atony, the timely and appropriate use of prophylactic utero-tonics such as oxytocin and misoprostol after the placenta has come off can prevent more than half of such deaths[2,3].

Misoprostol, a synthetic 15-deoxy-16-hydroxy-16-methyl analog of prostaglandin E1 (PGE1), ulcer was produced for the treatment of peptic ulcer[10]. It is more often used in obstetrics and gynecology clinics for medical abortion, induction of labor and treatment of postpartum hemorrhage[11,12,13]. Misoprostol, in addition to its uterotonic effect, when drug was administered orally it has many other effects such as gastric acid production on the gastrointestinal tract, protection of the mucosal surface, increase in intestinal motility and colonic activation[14,15]. It is also be preferred to other pharmacological agents because it does not require special storage conditions, can be stored for many years, is resistant to high temperatures and is inexpensive[13]. Although misoprostol can be administered vaginally, rectally, orally, sublingually or buccally[16], in recent years, rectal administration has been preferred because it is easy to use, has longer duration of action in the blood, has fewer side effects such as vomiting, nausea, shivering and metallic taste in the mouth[17,18,19].

When the literature is reviewed, although there are many publications with the use of rectal misoprostol and postpartum bleeding, only two studies on intestinal motility have been identified. The role of rectal misoprostol administration on intestinal motility was effective in one of these studies and ineffective in the other[17,20]. To contribute to the uncertainty in this matter this study was designed to determine the effectiveness of rectal administered misoprostol in inducing the early motility of the gastrointestinal tract and reducing the amount of postpartum uterine bleeding in primiparous women.

MATERIALS AND METHODS

The Clinical Research Ethics Committee of Istanbul Medipol University approved the study. The management of Private Nisa Hospital where the study was to be conducted gave its written permission to conduct the study before the data collection phase. After the participants were informed about the purpose of the study, their written consent was obtained (date: April 19, 2019 and reference number: 108400098-604.01.01-E.14127). All the procedures were performed in accordance with rules regarding studies involving human participants by taking into account the ethical standards of the institutional and/or national research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This retrospective cohort study performed at Medipol University Private Nisa Hospital was designed to evaluate the effect of postoperative administration of rectal misoprostol on postpartum intestinal motility and postpartum hemorrhage in primiparae having undergone cesarean section under spinal anesthesia. Data about the patients were collected from the digital patient registration system between January 2018 and January 2019. Between January 2018 and January 2019, 1000 pregnant women were delivered by cesarean section. 600 pregnant women were multiparous, 400 pregnant women were primiparous. 240 primiparae underwent cesarean section under spinal anesthesia Two

different uterine bleeding protocols were applied in the postoperative period in the hospital. Patients who received rectal misoprostol as a routine hospital protocol were grouped as the misoprostol group (n = 120), and patients who received only oxytocin infusion as another routine hospital protocol without rectal misoprostol were grouped as a non-misoprostol group (n = 120).

Inclusion criteria includes being between the ages of 20 and 40, being at the 37th-41th weeks of gestation, having a singleton pregnancy, and having undergone elective cesarean section (upon the mother's request and decision) under spinal anesthesia. Exclusion criteria were changes in serum electrolyte levels that affect intestinal motility, such as sodium, calcium, and potassium, presence of gross peritonitis, sepsis, having had a previous bowel operation, hypothyroidism or hyperthyroidism, hypertension, diabetes mellitus, cardio vascular problem, inflammatory intestinal disease, or history of constipation (<2 bowel movements per week), having risk factors for postpartum hemorrhage, antepartum hemorrhage, spontaneous onset of labor, pre-eclampsia and eclampsia, placenta previa, history of myomectomy, obesity (body mass index > 30), not being allowed to have prostaglandin treatment due to hypersensitivity or asthma, oxytocin hypersensitivity, intraoperative excessive blood loss (> 1000 mL), contraindication to the administration of spinal anesthesia.

Procedure

Two different uterine bleeding protocols were applied in the postoperative period in the hospital. In accordance with the routine hospital protocol, the primiparae undergoing cesarean section under spinal anesthesia were administered 10 IU of oxytocin as an intravenous bolus just before placental delivery ın both groups. Then, according to the routine hospital primary protocol, 20 IU oxytocin in 1000 mL of 5% dextrose saline was infused to the participants in the non-misoprostol group at 40 drops per minute for 240 minutes after surgery.

According to the routine hospital secondary protocol, the participants in the misoprostol group were administered 600 µg of rectal misoprostol at postoperative 5th min and they were infused 1000 mL of 5% dextrose saline under the same conditions as in the non-misoprostol group. In the misoprostol group, oxytocin was not given in the postoperative period. Infusion and postoperative care were performed in the participants in both groups in a similar way.

Intraoperative blood loss was routinely calculated in all the patients using the formula: (A + B) –C[20], in which A refers to the difference between pre- and post-surgery weights of surgical towels in grams were determined with the precision digital scales, B refers to the volume of the contents of the "suction" bottle (ml), and C refers to the amniotic fluid volume (AFV) (ml).The uterus was divided into four quadrants, by the linea nigra, to the right and left quadrants, and the umbilicus to the lower and upper quadrants. The deepest vertical diameter of the amniotic fluid was measured in centimeters per quadrant[21]. AFI was calculated by summing the four vertical diameters. The estimated AFV was obtained by multiplying AFI (cm) by 30[22].

Data on the participants' age, weight, education status, baby's birth weight, preoperative hemoglobin, hematocrit, temperature, systolic-diastolic blood pressure levels and pulse rate, and postoperative hemoglobin, hematocrit, body temperature, systolic-diastolic blood pressure levels, pulse rate, time of the first flatulation- first defecation, length of bed rest, possible adverse effects of the administration of misoprostol such as nausea, vomiting, shivering were obtained from the routine pre- and post-operative follow-up files of the patients.

The primary outcome was the effect of administration of rectal misoprostol on postoperative ileus and postpartum hemorrhage. Adverse effects such as nausea, vomiting, shivering, and fever were also investigated.

Statistical analysis

The study data were analyzed by using the IBM SPSS V23. It was determined that the groups were suitable for normal distribution. The chi-square test was used to compare categorical data by groups. Mann Whitney U test was used to compare the quantitative data. While the quantitative data were presented as median (min-max), the categorical data were presented as frequency (percent). p-values less than 0.05 were considered statistically significant.

RESULTS

There was a statistically significant difference between the misoprostol and non-misoprostol groups in terms of their median age values (p

<0.001). According to the comparison of the groups in terms of their socio-demographic and descriptive characteristics, there were not statistically significant differences between the misoprostol and non-misoprostol groups in regard to maternal height, weight and baby's birth weight, education status and income status (p> 0.05) (Table 1-1 A).

Misoprostol group, compared with non-misoprostol, had shorter surgery-gas time and less hemorrhage. While the median value of the first flatulation time was 18 hours in the misoprostol group, it was 24 hours in the non-misoprostol group. The median value of the first defecation time was 29 hours in the misoprostol group whereas it was 36 hours in non-misoprostol the group. Preoperative hemoglobin median values of the two groups differed statistically significantly (p = 0.011). While the median value was 11.9 g/dL in the misoprostol group, it was 12.2 g/dL in the non-misoprostol group.

Table 1. Sociodemographic characteristics of the groups

	Misoprostol (n=120)	**Non-misoprostol (n=120)**	**Test statistics**	**p value***
Age (year)	30 (20 - 41)	28 (20 - 40)	4921.5	**<0.001**
Height (cm)	162 (147 - 178)	162 (155 - 180)	7030.5	.750
Weight (kg)	75 (44 - 112)	77.5 (65 - 98)	6305.5	.094
Baby's birth weight (gram)	3400 (2300- 4500)	3400 (2300- 4500)	6984.5	.688

*U: Mann Whitney U test

Table 1A. Sociodemographic characteristics of the groups

Income status	**Misoprostol (n=120)**		**Non-misoprostol (n=120)**		**Total (n=240)**		**Test statistics**	**p value***
	n	%	N	%	n	%		
Income less than expenses	4	3.	4	3.	8	3.	0.000	1.000
Income equal to expenses	87	72.5	87	72.5	174	72.5		
Income more than expenses	29	24.2	29	24.2	58	24.2		
Educational status							0.022	0.999
Primary school	4	3.3	4	3.3	8	3.3		
High school	40	33.3	41	34.2	81	33.8		
University	55	45.8	54	45	109	45.4		
Higher than University	21	17.5	21	17.5	42	17.5		

* χ^2: Chi-square test statistics

Postoperative hemoglobin median values of the two groups differed statistically significantly (p=0.011). The median value was 11 g/dL and 10.2 g/dL in the misoprostol and non-misoprostol groups respectively. There was a statistically significant difference between the two groups in terms of the preoperative hematocrit median values (p=0.023). While the median value was 35.4 % in the misoprostol group, it was 36.1 % in the non-misoprostol group. There was a statistically significant difference between the two groups in terms of the median hematocrit values at the postoperative 24th hour (p<0.001). While the median value was 33 in the misoprostol group, it was 30,6 in the non-misoprostol group. There was no statistically significant difference between the two groups in terms of postoperative length of bed rest, duration of operation and intraoperative estimated blood loss. (p>0.05) (Table2).

There were no statistically differences between the two groups in terms of the preoperative systolic and diastolic blood pressure values, postoperative systolic and diastolic blood pressure values, preoperative pulse rate and duration of preoperative fever (p> 0.05). However, there was a statistical difference between the two groups in terms of the postoperative pulse median values (p=0.018). While the median

value was 78 in the misoprostol group, it was 77.5 in the non-misoprostol group.

While 1 patient in the non-misoprostol group had the postoperative fever (>38°C), one of the negative effects of misoprostol, 7 patients in the misoprostol group had the postoperative fever (p= 0.031). There were statistically differences between the two groups in terms of shivering (p = 0.031).The shivering rate was 7.5% in the misoprostol experimental group and 1.7% in the non-misoprostol group. There were no statistically differences between the two groups in terms of postoperative nausea and vomiting (p= 0.354). While 5.8% of the participants in the misoprostol group had postoperative vomiting, this rate was 3.3% in the participants in the non-misoprostol group (Table 3).

Table 2. Laboratuary and clinical results of groups

	Non-misoprostol (n=120)	**Misoprostol (n=120)**	**Test statistics**	**p value***
Preoperative hemoglobin (g/dl)	12.2 (8.9 - 14.4)	11.9 (8.2 - 14)	5785.5	**0.011**
Postoperative 24th hour hemoglobin (g/dl)	10.2 (7.5 - 12.3)	11 (7.3 - 13.3)	4565.5	**<0.001**
Preoperative hematocrit (%)	36.1 (25.9 - 42)	35.4 (26 - 41)	5976.5	**0.023**
Postoperative24th hour hematocrit (%)	30.6 (23.5 - 36.6)	33 (24 - 38.3)	4840.0	**<0.001**
Preoperative systolic blood pressure	120 (90 - 150)	120 (90 - 150)	7152.5	0.928
Postoperative systolic blood pressure	100 (80 - 140)	100 (80 - 140)	6547.0	0.208
Preoperative diastolic blood pressure	80 (50 - 90)	80 (50 - 90)	6919.5	0.577
Postoperative diastolic blood pressure	60 (50 - 90)	60 (50 - 90)	7064.5	0.780
Preoperative pulse rate	70 (64 - 80)	68 (62 - 80)	6610.0	0.259
Postoperative pulse rate	77.5 (68 - 88)	78 (68 - 88)	5953.0	**0.018**
Postoperative length of bed rest (hours)	6 (5 - 8)	6 (5 - 8)	6334.5	**0.059**
The first flatulation time (hours)	24 (8 - 48)	18 (10 - 36)	4224.0	**<0.001**
The first defecation time (hours)	36 (20 - 52)	29 (12 - 50)	3914.0	**<0.001**
Preoperative temperature (°C)	36.5 (35.9 - 37)	36.4 (35.9 - 37)	6725.5	0.372
Duration of operation (min)	30 (20-45)	30 (25-45)	6315.5	0,520
Intraoperative estimated blood loss (ml) median (Range)	300 (250-800)	290 (250-700)	6815.0	0,683

*U: Mann Whitney U test

Table 3. Sides effects of misoprostol experienced by the groups

	Non-misoprostol (n=120)		Misoprostol (n=120)		Total (n=240)		Test statistics	p value*
	n	%	n	%	n	%		
Shivering	2	1.7	9	7.5	11	4.6	4.669	**0.031**
Fever (>38°C)	1	0.8	7	5.8	8	3.3	4.635	**0.031**
Nausea-vomiting	4	3.3	7	5.8	11	4.6	0.857	0.354

* χ^2: Chi-square test statistics

DISCUSSION

Gastrointestinal tract immotility and uterine bleeding are serious complications that frequently occur after cesarean operations, and prolong hospital stays. One of the basic elements in evaluating the motility of gastrointestinal tract is the occurrence of the first defecation and flatulation[20,23].

Adanikin et al. In their study, they evaluated 218 cesarean women. Administered 600 μg rectal misoprostol to the women in one group and 20 intravenous units of oxytocin to the women in the other group after cesarean section and found that postoperative intestinal motility increased in the women who were administered rectal misoprostol[20]. The results of our study are similar to this study. In our study was detected misoprostol group, compared with non-misoprostol group, had shorter postsurgery flatulation and defecation time. The median value of the first defecation time was 29 hours and 36 hours in the misoprostol and non-misoprostol groups respectively. There was a difference between the two groups in terms of the time of the first flatulation, which was 18 hours in the misoprostol group and 24 hours in the non-misoprostol group. Unlike these two studies Demirci et al. administered 200 μg and 400 μg of misoprostol rectally, and found that misoprostol did not induce intestinal motility after surgery. We think that this difference stemmed from the fact that in their study, rectal misoprostol was administered in lower doses[17].

In our study in terms of hemoglobin and hematocrit values demonstrated the postoperative values were statistically higher in the misoprostol group than in the non-misoprostol group (only oxytocin infused group). In several publications in the literature similar to the present study, it has been emphasized that the preoperative and postoperative administration of rectal misoprostol reduces postpartum blood loss[13,24,25,26]. In their meta-analysis of 17 studies including 3174 women having undergone cesarean section, Conde-Agudelo et al. emphasized that the postoperative administration of misoprostol and oxytocin in combination significantly reduced postpartum hemorrhage compared to the postoperative administration of oxytocin alone[27]. When this meta-analysis and our study are evaluated together, it may be thought that the administration of oxytocin and misoprostol in combination in clinical practices may be an appropriate treatment protocol in the prevention and treatment of postoperative bleeding.

Misoprostol has not only positive effects such as uterotonic effect and increased intestinal motility but also undesirable side effects such as shivering, fever, nausea and vomiting. In the study while 7 patient in the misoprostol group had fever above 38°C, 1 patients in the non-misoprostol group had fever. Fever due to misoprostol is caused by a centrally mediated effect of brain[28]. In their study involving 453 pregnant women, Sweed et al. found that the incidence of fever and shivering was higher in the patients who were administered high dose rectal misoprostol (≥800 mg) [26]. In the present study, while the shivering rate was 7.5% in the misoprostol group, it was 1.7% in the non-misoprostol group. Post-delivery shivering is considered normal[29]. On the other hand, its incidence increases after misoprostol administration, which lowers the threshold for physiological shivering[30]. In the literature, it is reported that not only sublingual and oral administration but also rectal administration of misoprostol increases postoperative shivering, the former being higher[24]. Postoperative median values for the pulse rates of the two groups differed statistically significantly. This difference probably stemmed from the fact that postoperative fever and shivering levels were high in the misoprostol group. In the present study, there were no differences between the twogroups in terms of incidences of postoperative nausea and vomiting. While 5.8% of the participants in the misoprostol group suffered postoperative vomiting, this rate was 3.3% in the non-misoprostol group. In other studies, it is emphasized that the incidence of nausea and vomiting is less in the group who are administered misoprostol rectally than it is in other groups[19,20].

Despite all these side effects, misoprostol treatment can be preferred to other medical treatments because it does not require special storage conditions, is resistant to high temperatures, can be stored for many years and is inexpensive[13].

The study had some limitations. First, the study had a retrospective design. Second, only primiparous pregnant women with low probability of postpartum hemorrhage were included in the study groups. Third, patients undergone general anesthesia, which may adversely affect the gastrointestinal tract motility, were excluded from the study group.

In conclusion, the present study demonstrated those

who were administered rectal misoprostol after delivery experienced flatulation and defecation earlier than did those who were not administered rectal misoprostol. In addition, the amount of postoperative bleeding has decreased significantly due to the uterotonic effect of misoprostol. There is a need for large-scale studies to be conducted to investigate the possible role of rectal misoprostol in the prevention and/or treatment of postoperative ileus and postoperative hemorrhage.

Yazar Katkıları: Çalışma konsepti/Tasarımı: DKG; Veri toplama: DKG; Veri analizi ve yorumlama: DKG; Yazı taslağı: DKG; İçeriğin eleştirel incelenmesi: DKG; Son onay ve sorumluluk: DKG; Teknik ve malzeme desteği: -; Süpervizyon: DKG; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Medipol Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'ndan etik onay alınmıştır. (19.04.2019 tarihi ve 108400098-604.01.01-E.14127 numarası ile).
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : DKG; Data acquisition: DKG; Data analysis and interpretation: DKG; Drafting manuscript: DKG; Critical revision of manuscript: DKG; Final approval and accountability: DKG; Technical or material support: -; Supervision: DKG; Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained from Medipol University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee for this study. (With the date 19.04.2019 and the number 108400098-604.01.01-E.14127).
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

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