Research Article

American Journal of Gynecology & Obstetrics

Evaluation of The Efficacy of Intra Uterine Misoprostol Plus Intra Venous Oxytocin Versus Intra Venous Oxytocin Alone in Prevention of Primary Postpartum Hemorrhage in Elective Cesarean Section

Ahmed M. Hagras[1*] and Nareman Elhamamy[2]

[1]Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Tanta University. Egypt
[2]Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Tanta University. Egypt

Corresponding author Ahmed M. Hagras, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Tanta University. Tanta, Egypt.

Citation: Hagras AM and Elhamamy N (2022) Evaluation of The Efficacy of Intra Uterine Misoprostol Plus Intra Venous Oxytocin Versus Intra Venous Oxytocin Alone in Prevention of Primary Postpartum Hemorrhage in Elective Cesarean Section. American J Gyne Obst: AJGO-101.

Received Date: 14 Aug, 2022; **Accepted Date:** 20 Aug, 2022; **Published Date:** 25 Aug, 2022

Abstract

The misoprostol tablet is very soluble and can be dissolved in 20 minutes when it is put under the tongue a pharmacokinetic study compared the absorption kinetics of oral, vaginal and sublingual routes of administration of misoprostol found that sublingual misoprostol has the shortest time to peak concentration, the highest peak concentration and the greatest bioavailability when compared to other routes.

The aim of this work is to improve the management primary postpartum hemorrhage during and after elective CS. This study was carried out on 138 cases admitted for elective cesarean section at University Hospital. They divided into two groups regarding the protocol of treatment, was given oxytocin, 10 IU in 250 ml of Normal saline solution over 10 minutes was administered directly after opening the uterus. Misoprostol group was given 400 mcg misoprostol plus intra venous Oxytocin administered directly after opening the uterus.

Results: *There was statistical significantly between the two studied groups in hemoglobin and HCT postoperatively with higher level among intra venous oxytocin plus intra uterine misoprostol (Mean+ SD 10.1+0.8) than intra venous oxytocin only group (Mean+SD 9.9+0.7). But regarding preoperative hemoglobin and HCT, there was no statistically significant difference before and after treatment. regarding blood loss with higher blood loss either intraoperative, postoperative and overall blood loss on intra venous oxytocin only group (Mean + SD 85.1+8.6) than intra venous oxytocin plus intra uterine misoprostol (Mean + SD 62.3+9.1).*

There was statistical significantly decrease in both hemoglobin and HCT postoperatively in the two studied groups, but this decrease was more among intra venous oxytocin only group (Mean + SD 9.9+0.7) than intra venous oxytocin plus intra uterine misoprostol (Mean + SD 10.1+0.8).

Conclusion: *Intrauterine misoprostol combined with oxytocin infusion during caesarean section can minimize intraoperative blood loss, avoid postpartum haemorrhage, and reduce any additional uterotonic medication requirements. A mild side effect, such as shivering, was detected and spontaneously subsided.*

Introduction

Prevention of PPH in this group is important to safe maternal life. Oxytocin has been routinely used to prevent uterine atony and excessive uterine bleeding during CS. However, despite its effectiveness, 10-40% of cases need additional uterotonics to ensure good uterine contraction (1,2). Misoprostol is a prostaglandin E1 analogue with good uterotonic properties and few adverse effects at therapeutic dose. It can be used oral, sublingual, buccal, rectal and intrauterine. Besides that, it can be used for termination of pregnancy in cases of missed or incomplete miscarriage (3,4).

In situations of preserved placenta, it can also have a role to play in the treatment of associated bleeding, which is often due to atony. In the field of gynaecology, misoprostol may be used for induction of cervical maturation prior to office gynaecological procedures. This could reduce the related pain caused by the transcervical passage of instruments (5).

Aim of Work

The aim of this work is to improve the management primary postpartum hemorrhage during and after elective CS.

Patients and Methods

The present study was prospective study in that 138 pregnant females were recruited for this study scheduled for elective cesarean section.

The study was performed in the period from October 2018 to April 2020 that carried out in Obstetrics & Gynecology department of University Hospital.

Inclusion criteria
Patients included in the study those:
1- Un-complicated pregnancy, gestational age of 37-40 completed weeks.
2- Had no hypersensitivity or contraindications to prostaglandins.
3- Had no history of coagulopathy. 4- Accepting to participate in the study.

The reasons for exclusion:
1- Women with anemia
2- Placental abnormality (e.g placenta previa, placenta abruption).
3- History of complications at previous pregnancy especially post-partum haemorahge.
4- Maternal hypertension, current or previous history of heart disease, liver and renal disorders.

Eligible participants were randomly allocated into two equal groups.
Group A: (69 patients): patients who receive intravenous infusion of 10 I.U oxytocin (Syntocinon 10 IU/1ml ampoule-Sandoz pharmaceutical-NDC 0078-0060-) diluted to 250ml of normal saline for 30 minutes after delivery of the neonate.
Group B: (69 patients): patients who received 400 µg misoprostol intrauterine plus oxytocin intravenous just after cord clamping and delivery of the placenta (2 cytotec tablets each 200 µg –Pfizer-NDC 0025-1461).

the selected cases were subjected to:
- Full history taking Blood pressure measurement.
- Examination
- Preoperative workup including preoperative hemoglobin and hematocrit level within 24 hours before operation and coagulation profile to exclude any coagulopathy.

During Operation:
In the Oxytocin group:

- 10 IU in 250 ml of Normal saline solution over 10 minutes was administered directly before opening the uterus.

Maximum fluids were 500-1000 ml of isotonic solution.

In the Misoprostol plus oxytocin intravenous group:
- 400 mcg misoprostol was administered directly in opening the uterus.
- Maximum fluids were 500-1000 ml of isotonic solution.

Postoperative:
- Postoperative crystalloids: 500 ml of Normal Saline, 500 ml of 5%Glucose and 500 ml of Ringer's Lactate solution.
- Recording of vital signs
- Observing the amount of bleeding.
- Uterine massage to ensure uterine contractility.

Blood loss was estimated by:
- Preoperative hemoglobin level within 24 hours and 12 hours postoperative hemoglobin level was measured.
- The mathematical calculation in which the lost blood intraoperative was estimated by measuring the hematocrit level immediately after hospital admission and one hour postoperative in recovery room.

The blood loss was calculated according to the following formula:

$$\text{Actual Blood Loss} = \frac{[\text{Blood Volume X (Hct1-Hct2)}]}{\text{Hct1}}.(51)$$

Where: Blood volume = Body weight X 70 ml/Kg.
Hct 1 is the initial pre-operative hematocrit.
Hct 2 is the 1-hour post-operative hematocrit.

The uterine tone and size were assessed postoperatively, by using a hand resting on the fundus and palpating the anterior wall of the uterus.

The side effects of each drug as nausea, vomiting, shivering, pyrexia and headache or others were noted. The main outcome measures for each case in each group were registered in the patient input form.

Study outcomes
Primary outcome measures were assessment of amount of intraoperative and postoperative blood loss. Secondary outcomes measures were the differences between pre and postoperative (24 h after CS) hemoglobin concentration and hematocrit values, the need for additional uterotonic drugs and incidence of side effects.

Statistical analysis

The data were collected and entered onto Microsoft access database to be analyzed using the Statistical Package for Social Science (SPSS Inc., Chicago, version 21).

Results

This study included 138 women underwent caesarean section divided into two groups; group (A) 69 pregnant women who received intra venous oxytocin only and group (B) included the same number (69pregnant women) received intra venous oxytocin plus intra uterine misoprostol for prevention of primary postpartum hemorrhage (PPH). there was no statistically significant difference between the two studied groups in age, BMI, gravidity, parity and gestational age. there was no statistically significant difference between the two studied groups regarding indications of cesarean section. there was statistically significant difference between the two studied groups regarding blood loss with higher blood loss either intraoperative, postoperative and overall blood loss on intra venous oxytocin only group than intra venous oxytocin plus intra uterine misoprostol., there was statistical significantly between the two studied groups in hemoglobin and HCT postoperatively with higher level among intra venous oxytocin plus intra uterine misoprostol than intra venous oxytocin only group. But regarding preoperative hemoglobin and HCT, there was no statistically significant difference before and after treatment.there was statistical significantly decrease in both hemoglobin and HCT postoperatively in the two studied groups but this decrease was more among intra venous oxytocin only group than intra venous oxytocin plus intra uterine misoprostol.there was no statistically significant difference between the two studied groups regarding need for additional ecbolic.there was no statistical significantly differences between the two studied groups regarding pre-operative and 24 hours postoperative pulse rate, systolic and diastolic blood pressure . This table shows that there was no statistically significant difference between the two studied groups regarding need for additional ecbolic. This table shows that there was no statistically significant difference between the two studied groups regarding need for blood transfusion. that there was statistically significant difference between the two studied groups regarding side effects of drugs with higher shivering among intra venous oxytocin plus intra uterine misoprostol than intra venous oxytocin only (47.9% versus 4.3%) while headache and vomiting were more common among intra venous oxytocin only than intra venous oxytocin plus intra uterine misoprostol (26.1% and 17.4% versus 13.1% and 8.6% respectively).

Variable	Group (A) No. (69)	Group (B) No. (69)	t-test	P
Age (years) mean ± SD (range)	 29.7±4.9 (19-38)	 31.3±6.1 (20-41)	0.5	0.6
BMI mean ± SD (range)	 28.4±4.6 (20-34)	 28.6±5.7 (19-36)	0.4	0.7
Gravidity *mean ± SD* *(range)*	 2.8±1.3 (1-4)	 2.6±1.2 (1-5)	0.3	0.6
Parity Nulliparous Multiparous	 9 (39.3%) 14 (60.7%)	 7 (30.4%) 16 (69.6%)	0.7	0.9
Gestational age (weeks) mean ± SD (range)	 38.7±2.2 (37-40)	 38.1±2.1 (37-40)	0.5	0.6

Table 1: Basic data of the studied groups (NO=138).

Indications of cesarean section	Group (A) No. (69) NO. (%)	Group (B) No. (69) NO. (%)	χ^2	P-value
Breech presentation	24 (43.8%)	18 (26.1%)	1.2	0.06
PROM	15 (21.7%)	9 (13.1%)		
Oligohydraminos	9 (13.1%)	12 (17.4%)		
Elderly primigravida	6 (8.7%)	9 (13.1%)		
CPD	6 (13.1%)	12 (17.4%)		
Primary infertility	3 (4.3%)	6 (8.7%)		
Prolonged labor	3 (4.3%)	3 (4.3%)		

Table 2: Comparing indications of cesarean section between the two studied groups.

Blood loss	Group (A) No. (69)	Group (B) No. (69)	t-test	P
Intraoperative blood loss (ml) *mean ± SD (range)*	426.5±6.2 (380-450)	395.1±4.1 (365-415)	16.7	**0.001****
Postoperative blood loss *mean ± SD (range)*	85.4±8.6 (67-100.2)	62.3±9.1 (40-75.8)	12.3	**0.001****
Approximate total blood loss (ml) *mean ± SD (range)*	511.9±23.7 (447-550.5)	457.4±21.5 (405-490.2)	14.9	**0.001****
Preoperative hemoglobin mean ± SD (range)	12.1±2.5 (10-14.5)	11.8±2.1 (9.8-14.6)	1.4	**0.6**
Postoperative hemoglobin mean ± SD (range)	9.9±0.7 (9.2-10.8)	10.1±0.8 (9.4-11.4)	2.5	**0.04***
Preoperative HCT mean ± SD (range)	33.86±2.3 (29.8-36.7)	33.67±2.8 (29.8-35.9)	1.6	**0.5**
Postoperative HCT mean ± SD (range)	30.14±3.7 (26.2-33.8)	31.38±2.8 (28.4-35.4)	2.6	**0.04***
**Statistically highly significant difference (P ≤ 0.001).				

Table 3: Mean and standard deviation of blood loss. hemoglobin and HCT pre- and post-operative in the two studied groups.

Vital signs	Group (A) No. (69)	Group (B) No. (69)	t-test	P
Preoperative Pulse rate *mean ± SD*	76.1±3.6	74.5±4.5	0.9	0.1
Postoperative Pulse rate *mean ± SD*	85.6±5	87.2±8.1	1.1	0.2
Preoperative systolic blood pressure *mean ± SD*	102.3±10.1	99.7±12.6	1.4	0.08
Postoperative Systolic blood pressure *mean ± SD*	133±1.7	134.5±1.6	1.7	0.06
Preoperative diastolic blood pressure *mean ± SD*	74.9±0.7	75.1±0.6	1.1	0.3
Postoperative diastolic blood pressure *mean ± SD*	86.4±0.5	87.1±0.8	1.2	0.07
Need for additional ecbolic	**Group (A) No (69) %**	**Group (B) No (69) %**	**test χ^2**	**P**
No	47 82.6	66 95.6		
Yes	12 17.4	3 4.4	1.7	0.06
Need for blood transfusion	**Group (A) No (69) %**	**Group (B) No (69) %**	**test χ^2**	**P**
No	60 86.9	66 95.6		
Yes	9 13.1	3 4.4	0.6	0.9

Table 4: Mean and standard deviation of vital signs pre and post-operative and Need for additional ecbolic AND Need for blood transfusion in the two studied groups.

Side effects of drugs	Group (A) No (69) %	Group (B) No (69) %	test χ^2	P
No	27 39.1	18 26.1	3.8	**0.03***
Shivering	12 17.4	33 47.9		
Vomiting	12 17.4	6 8.7		
Headache	12 17.4	9 13.1		
Dizziness	6 8.7	3 4.3		
*Statistically significant difference (P ≤ 0.05).				

Table 5: Comparison between the two studied groups as regards side effects of drugs.

Discussion

In this research, we used misoprostol intrauterine route because in the case of a caesarean section, it was easy and easier to do than other routes such as oral, sublingual, buccal, or rectal. In addition, one may use spinal anaesthesia in all cases with less infection compared with the rectal route. By the way, misoprostol pharmacology, a related prostaglandin, binds myometrial cells to It triggers extreme myometrial contractions that occur at the fundus near the corn and spread to the body of the uterus leading to tissue removal and decreases postpartum haemorrhage. We figured that inserting the tablets at uteri cornu was quick and easy to repair. It can aid the myometrial cells in their absorption (6).

In our study the statistical comparison between the two groups shows non-significant differences as regards

maternal age, gravidity, parity, maternal BMI and Gestational age.

There was no statistically significant difference in the indicator of caesarean section between the two groups surveyed. In the current study, there was no statistically significant difference between the two groups as a distinct indication of CS. This was in line with the study by (7,8).

In The current there was statistically significant difference between the two studied groups regarding blood loss with higher blood loss either intraoperative, postoperative and overall blood loss on intra venous oxytocin only group than intra venous oxytocin plus intra uterine misoprostol. The blood loss was estimated by preoperative hemoglobin level within 24 hours postoperative hemoglobin level was measured. The mathematical calculation in which the lost blood intraoperative was estimated by measuring the hematocrit level immediately after hospital admission and one hour postoperative in recovery room.

In our study statistical comparison between both groups, showed high significant differences as regards blood loss; P value is (P ≤ 0.001).

The amount of intraoperative blood loss in oxytocin group was 426.5±6.2 ml, Vs 395.1±4.1ml in misoprostol plus oxytocin group, 2h postoerative blood loss was 85.4±8.6 ml, Vs 62.3±91 ml, respectively.

When combined with 20IU oxytocin drip, (200µg) Sublingual misoprostol was found to be as effective as intravenous oxytocin (20IU) in prevention of postpartum hemorrhage following cesarean delivery with less side effects (9).

Also like (Vimala et al. 2006) the estimated mean blood loss during CS was significantly lower among women receiving sublingual misoprostol 400mg (819± 236ml) than among those receiving 20 i.u oxytocin (974± 285 ml, *p = 0.004*) soon after delivery of the neonate (8).

Unlike In other study Two classes are sublingually issued either misoprostol 400 mg or i.v. Infusion of 20 i.u oxytocin soon after birth of the baby no substantial variations in the expected blood loss during surgery were found in both classes. In the misoprostol group the mean blood loss in the first 4 h after the surgery was slightly smaller than in the o in our research there was a substantial statistical gap (P = 0.05) between the two groups tested postoperatively in haemoglobin and HCT with higher levels of intravenous oxytocin + intrauterine misoprostol than intravenous oxytocin group alone. But there was no statistically meaningful increase in pre-operative haemoglobin and HCT before and after treatment) befor CS between both groups. Hemoglobin level in oxytocin intravenous group befor CS was 12.1±2.5 versus 11.8±21 in misoprostol intrautrin plus oxytocin intravenous group, while after CS was 9.9±0.7 in misoprostol group Versus 10.1±0.8 in misoprostol plus oxytocin (10).

In (Vimala et al. 2006) There was no difference in the pre- and post-delivery haemoglobin levels for the two classes. The mean haemoglobin loss for the misoprostol group was 0.4 gm / dl and for the oxytocin group was 0.6 gm / dl. In the oxytocin community there were more women who needed additional oxytocics who had reported blood loss of more than 1000 ml. This disparity however did not hit statistical significance (8).

In our study there was statistical significantly decrease in both hemoglobin and HCT postoperatively in the two studied groups, but this decrease was more among intra venous oxytocin only group than intra venous oxytocin plus intra uterine misoprostol Hct value decreased significantly among both groups, manifested by the highly significant p value in comparison of pre and postoperative Hct in the two groups (*p≤0. 05*). There was more loss in postoperative Hct value of oxytocin group 30.14±3.7 than misoprostol plus oxytocin intrauterine group 31.38±2.8 (p≤0.05).

The present study shows that there was no statistically significant difference between the two studied groups regarding need for additional ecbolic. This with agreement with Vimala et al. (2006) In the misoprostol group 32% required extra ecbolics while in the oxytocin group 36% and p=0.673.

In a double-blind, non-inferiority, Multicenter study included 9348 women including Shatby Maternity Hospital concluded that intravenous oxytocin should be used when available, but 800 µg sublingual misoprostol could be an effective first-line treatment alternative when oxytocin is not available (11).

There was no statistically significant difference between the two studied groups regarding need for blood transfusion. that there was statistically significant difference (P ≤ 0.05). between the two studied groups regarding side effects of drugs with higher shivering among intra venous oxytocin plus intra uterine misoprostol than intra venous oxytocin only (47.9% versus 4.3%) while headache and vomiting were more common among intra venous oxytocin only than intra venous oxytocin plus intra uterine misoprostol (26.1% and 17.4% versus 13.1% and 8.6% respectively).

According to Hofmeyr the incidence of side effects with misoprostol was dose-dependent and that efforts should be undertaken to establish the smallest effective and safe dose of the drug (12). Shivering and pyrexia are common adverse effects of misoprostol use, occurring in 30% to 70% of cases (13,14).

In our study, shivering were the pronounced side effects associated with misoprostol plus oxytocin group when compared to oxytocin. The number of women who experienced shivering was higher in the misoprostol group (11 cases representing 47.9% of the misoprostol group vs. 4 cases only representing 17.4% of the oxytocin group), this difference is considered highly significant as the P value was ≤0.05.

In the present study there were no statistically significant differences between the two groups as regared intraoperative complications, and there was no any major

complication, such as need for blood transfusion, surgical intervention for PPH and maternal mortality, in either group.

Misoprostol has been used for more than a decade for prophylaxis and control of PPH. Many studies were done worlwide to compare between oxytocin and misoprostol as regards their role in prevention and management of postpartum hemorrhage and many studies were done to assess the effectiveness of the different routes of administration of misoprostol for prevention and control of PPH, but there is a lack of consensus about the optimum dose and the best route of administration.., The oral administration (Hamm et al., 2005) was assessed for the control of the third stage of labour in the distribution of caesarean products. Rectal misoprostol administration was explored in a report by (Conde. Agudel et al., 2013), which successfully treated 7 PPH patients with 800 µg of rectal misoprostol following caesarean delivery (16,17).

A study was done in this study, Intrauterine misoprostol efficacy was compared to placebo, and both groups got 10 IU oxytocin as an IV infusion. The current research had a larger number of patients in each group compared with this research (120 vs. 100). Like our report, it covered full-term low-risk PPH women who witnessed CS whether or not labour had begun and omitted high-risk PPH patients. Comparison was made between the two classes over the need for additional uterotonics, lack of haemoglobin and hematocrit levels, and the adverse effects. Results revealed that the use of intrauterine misoprostol reduced the need for additional uterotonics by 50%, reducing the depletion of haemoglobin and decreasing the amount of hematocrit by 39.6% and 40.6% respectively (15,18).

In a study conducted in China intrauterine administered misoprostol was found to be effective in reducing blood loss intra-operatively and after 2 hours of the cesarean section with no adverse reactions In this randomised trial 180 cases were randomly allocated to three classes of hospital-patients who underwent elective caesarean section and were at risk for postpartum haemorrhage, 800 microgm misoprostol intrauterine administration group, 20 IU IV group oxytocin infusion and 600 microgm group Misoprostol oral administration, with 60 cases in each category. Including our Blood Loss and Mediation Research medication side effects were observed during the operation and within the first 2 hours after operation. Comparison between groups based primarily on blood loss calculation, decrease in levels of haemoglobin / hematocrit 2 hours after surgery, need to add other uterotonics and drug adverse effects. Effects revealed that blood loss of the misoprostol group intraoperatively and 2 hours after surgery was slightly smaller than that of the oxytocin group (P= 0.01), and no adverse reactions were observed in two groups (19).

Misoprostol provides many benefits over oxytocin or ergometrine including that it has a long shelf life, is safe at room temperature, is light sensitive, needs no special storage or transport requirements, is orally active and can be given to patients with hypertension. These benefits of misoprostol make it an important replacement agent to be used in third stage laboratory management of atonic postpartum hemorrhage (20).

Conclusion

Combined with oxytocin injection intrauterine misoprostol during caesarean section may limit blood loss intraoperative, avoid postpartum haemorrhage and mitigate any additional uterotonic medication requirements. A minor side effect such as shivering that subsided spontaneously has been reported.

References

1. Gülmezoglu AM, Forna F, Villar J, Hofmeyr GJ. (2019): Prostaglandins for preventing postpartum haemorrhage. Cochrane Database Syst Rev; 3: CD000494.
2. Afolabi BB, Lesi FE, Merah NA. (2018): Regional versus general anaesthesia for caesarean section. Cochrane Database Syst Rev; 4: CD004350.
3. Lumbigaman P, villar J, Piaggio G, Gulmezoglu AM, Adetoro L, Carroli G. (2002): Side effects of oral misoprostol during the first 24 hours effect administration in the third stage of labor. BJOG;109: 1222-6.
4. Lurie S, Mamet Y. (2010): Cesarean sections in the days of the Mishna and Talmud. Isr J Obstet and Gynecol; 12:111-23.
5. World health organization (WHO) (2012): Recommendations for the prevention of postpartum hemorrhage. Geneva, Switzerland: WHO.
6. Khan R, El Refaey H, Sharma S, Sooranna D, Stafford H. (2014): Oral, rectal and vaginal pharmacokinetics of misoprostol. Obstet Gynecol; 103: 866–70.
7. El rafaey H, Rodeck C. (2012): Postpartum hemorrhage: definition, medical and surgical management a time for change. Br Med Bull; 67(1): 205–17.
8. Vimala N, Mittal S, Kumar S. Sublingual misoprostol versus oxytocin infusion to reduce blood loss at cesarean section. Int J Gynaecol Obstet 2006; 92(2):106-10.
9. Fiala C, Swahn M, stephansson O, Gemzell – Danielson K. (2009): The effect of non-steroidal anti-Inflammatory drugs on medical abortion with mifepristone and misoprostol at 13-22 weeks gestation. Hum Repord; 20: 3072–7.
10. Khawaja M, Jurdi R, Kabakian-Khasholian T. (2017): Rising trends in cesarean section rates in Egypt. Birth; 31(1):12-6.
11. Kreutner A, Del-Bene V, Delamar D, Bodden J, Loadholt C. (2009): Perioperative cephalosporin prophylaxis in cesarean section: effects on endometritis in the high-risk patient. Am J Obstet Gynecol; 134:925-35.
12. Hofmeyr GJ, Gülmezoglu AM, Novikova N, Linder V, Ferreira S, Piaggio G. (2009): Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose – related effect. Bull World Health Organ;87(9):666-77.

13. Afolabi BB, Lesi FE, Merah NA. (2011): Regional versus general anaesthesia for caesarean section. Cochrane Database Syst Rev; 4: CD004350
14. Luesley DM, Baker PN. (2004): Obstetrics and Gynecology, An evidence –Based Text for MRCOG. United States: CRC Press.
15. Royal College of Obstetricians and Gynecologist (RCOG). Caesarean section, NICE clinical guideline. London: RCOG; 2014.
16. Lopes T, Spirtos N, Naik R, Monaghan J. (2011): Bonney's gynaecological surgery. 11th ed. United States: Wiley-Blackwell.
17. Lucas DN, Yentis SM, Kinsella SM. (2009): Urgency of cesarean section: a new classification. J R Soc Med; 93: 346-50.
18. Walsh JA. (2008): Evolution and the Cesarean Section Rate. Am Biol Teach; 70(7): 401–40.
19. Winikoff B, Dabash R, Durocher J, Darwish E, Nguyen TN, León W, et al. Treatment of post-partum haemorrhage with sublingual misoprostol versus oxytocin in women not exposed to oxytocin during labour: a double-blind, randomised, non-inferiority trial. Lancet 2010; 375(9710):210-6.
20. Rajasekar D, Hall M. Urinary tract injuries during obstetric intervention. Br J Obstet Gynecol 2007; 104:731.