Research Article

Effectiveness of Oral Misoprostol to Prevent Postcesarean Section Urinary Retention

Efektivitas Misoprostol Per-oral terhadap Perubahan Residu Urin sebagai Pencegahan Retensio Urin Pascaseksio Sesarea

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Abstract

Objective: To determine the effect of misoprostol on the incidence of urinary retention in post-cesarean section patients by measuring maternal residual urine volume 6 hours after catheter removal.

Methods: This was a single-blind randomized controlled trial, at Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Palembang Hospital from October 2016 to February 2017. Samples were patients who underwent cesarean section, either elective or emergencies treated at Department of Obstetrics and Gynecology Hospital, Dr. Mohammad Hoesin Palembang. Subjects were allocated into two groups: treatment group (receiving misoprostol) and placebo group. Urinary retention is diagnosed if post-voiding residual urine volume after Foley catheter removal was >200 ml. Statistical analysis was performed using SPSS 17.0

Results: There were no differences in mean time between of urination between control group (placebo) and 600μg oral misoprostol group. The average of urine volume and residual urine volume between control group (placebo) and 600μg oral misoprostol group was significantly different. 600μg misoprostol orally can increase the amount of urine and reduce the volume of urinary residue after cesarean section.

Conclusion: 600μg oral misoprostol can increase urine volume and reduce volume of residual urine post-cesarean section.

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Keywords: cesarean section, misoprostol, urinary retention

Abstrak

***Tujuan**: Untuk mengetahui pengaruh misoprostol terhadap kejadian retensi urin pada pasien operasi seksio sesarea dengan mengukur volume residu urin maternal 6 jam setelah kateter dilepaskan.*

***Metode**: Penelitian uji klinik acak berpembanding (Randomized Controlled Trial) secara single blind (tersamar tunggal) ini dilakukan di Departemen Obstetri dan Ginekologi RSUP Dr. Mohammad Hoesin Palembang mulai bulan Oktober 2016 sampai dengan Februari 2017. Sampel penelitian adalah semua pasien seksio sesarea, baik elektif maupun emergensi yang dirawat di Departemen Obstetri dan Ginekologi RSUP Dr. Mohammad Hoesin Palembang. Subjek dialokasikan menjadi 2 kelompok yaitu kelompok penanganan yang menerima misoprostol dan kelompok plasebo. Retensio urin didiagnosis jika volume residu urin pascaberkemih setelah kateter Foley dilepaskan >200 ml. Analisis statistik dilakukan dengan menggunakan SPSS 17.0*

***Hasil**: Tidak terdapat perbedaan rerata waktu urinasi antara kelompok kontrol (plasebo) dengan misoprostol peroral 600μg.Terdapat perbedaan rerata jumlah urin, dan volume residu urin antara kelompok kontrol (plasebo) dengan misoprostol peroral 600μg. Misoprostol per oral 600μg dapat meningkatkan jumlah urin dan mengurangi volume residu urin pascapersalinan seksio sesarea.*

***Kesimpulan**: Misoprostol per oral 600μg dapat meningkatkan jumlah urin dan mengurangi volume residu urin pascapersalinan seksio sesarea*

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***Kata kunci**: misoprostol, retensio urin, seksio sesarea*

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INTRODUCTION

Postpartum urinary retention (PUR) is an obstetric case that is often encountered in clinical practice. The reported PUR prevalence varies from 1.7 to 17.9% focusing on PUR after vaginal delivery. Groutz et al. studied 125 women with postpartum voiding difficulties, as many as 38% of maternal women with the aid of vacuum instrumentation, 27% with spontaneous labour, and 15% with cesarean section.[1,2]

According to Weissman, factors including episiotomy, birth trauma, and severe perineal lacerations are not sufficient enough to induce PUR. On the contrary, there is some evidence to indicate the strong correlation between cesarean section and

PUR incidence. Kermans et al. stated the prevalence of post-cesarean section PUR is higher than vaginal delivery (2.1% vs 3.2%). Intraoperative bladder manipulation is thought to be the cause of weak detrusor muscle contractions. Patients terminated abdominally tend to be unable to empty the bladder due to inadequate contraction of detrusor muscles postoperative; patients are also reluctant to contract the abdominal wall to start urinary expenditure. Epidural anaesthesia may also decrease or exclude sensations of urgency from the need for urination during labour and the postpartum period.[3-7]

Inaccuracies or delays in diagnosis and management of PUR can cause excessive distension of the bladder, detrusor muscle damage, and increase risk of urinary tract infections, long-term voiding dysfunction and renal injury.[3]

Prostaglandin (PGS) is essential to improve detrusor muscle contraction. Misoprostol is an analogue of prostaglandin E1 (PGE1) synthetic. It has various advantages, including relatively affordable price, widely available, has long half-life, and stable at room temperature. Kelly et al. reported that within three months of therapy using oral PGS analogue 600 mg per day, 56% of patients reported improvement of interstitial cystitis symptoms, especially voiding disturbance due to pain and urine retention.[8-10]

Until today, effectiveness of misoprostol in preventing and overcoming urinary retention after cesarean section at Dr Mohammad Hoesin Palembang has not been studied. Therefore, this study aimed to determine the effect of misoprostol on the incidence of urinary retention in patients with cesarean section by measuring maternal residual urine volume 6 hours after catheter removal.

METHODS

This single-blind randomised controlled trial was conducted at the Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Palembang Hospital in October 2016 until February 2017.

Samples were all patients underwent elective and emergency cesarean sections, treated in Department of Obstetrics and Gynecology, Dr. Mohammad Hoesin Palembang Hospital. Inclusion criteria were patients undergoing cesarean sections at Dr. Mohammad Hoesin Palembang hospital by lower uterine segment incision, with regional anaesthesia, and those willing to participate in this research and signed informed consent. On the contrary, patients with urinary tract infections, having previous voiding problems prior to caesarean section, patients with severe preeclampsia, diabetes mellitus, renal dysfunction, and indications of cesarean section; those with prolonged labor, history of cesarean section, polyhydramnios, multiple pregnancies, and induction of labor with misoprostol were excluded from the study. Patient who has a habit or a history of smoking and alcohol consumption were also excluded from the study.

Patients were dropped out from the analysis if experiencing allergic or hypersensitivity during administration of misoprostol and suffered from urosepsis. Based on samples calculation, 15 samples were needed in each group. Sample was chosen by simple random sampling.

All post-cesarean patients who were treated at Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Palembang Hospital and met the inclusion criteria were asked to sign the informed consent, subjects then being matched based on age, parity, and gestational age. Simple random sampling was applicated to allocate subjects who received misoprostol and placebo. Sample did not know in which treatment group the belonged to.

Treatment group received 600 mcg misoprostol per day, administered orally after the patient completed a cesarean section. It was divided into three doses; 200 mcg orally after cesarean section, 200 mcg orally within 8 hours after the first dose, 200 mcg in 8 hours after administration of the second dose. Control group received a placebo in the form of three tablets of starch material. Placebo tablet was administered the same way as misoprostol. Foley catheter installed for 24 hours in post-cesarean section patients. After 24 hours post-surgery, catheter was removed, and patient was asked to urinate. Time interval between urination and time of catheter removal was then recorded. Patient was asked to collect urine in a bottles and researcher would measure the amount of urine volume in the bottle using a measuring cup. After the first voiding (after Foley catheter was removed), residual urine volume was measured by catheter. Catheterization was done using 16F Foley catheter as soon as voiding. Urine residues was collected in urine bag to measure urine volume. If the residual urine volume was >200 ml,

patient could be diagnosed with urinary retention after cesarean section. If the patient was not able to urinate spontaneously 6 hours after Foley catheter was removed, patient could be diagnosed with urinary retention after cesarean section. Patients underwent catheterisation and urine volume was measured.

Data was collected using forms previously provided, and then it was analysed using X^2 test for dichotomous variables and t tests for continuous variables. To determine the significance of differences between residual urine volume between misoprostol group and placebo group, data tes normality was performed with Shapiro Wilk test. If data were normally distributed, the unpaired t-test would be used. If data were not normally distributed, non-parametric Mann-Whitney test would be used. Differences were considered significant if $p < 0.05$. All data were analysed using SPSS version 18.

RESULTS

Population of this study were 30 pregnant women who underwent cesarean section and met inclusion and exclusion criteria. 15 women were located in the treatment group and 15 women as control in the placebo group. After follow-up, no research subject was dropped out or withdrawal from this study. Mean of urination time between control and treatment group was not significantly different (p = 0.589) (Table 1).

Table1. Comparison of Oral Misoprostol 600 μg and Placebo Group Based on Urination time

Variable	600 μg Oral Misoprostol	Placebo	p*
Time (Hour)	2.467 ± 0.972	2.667 ± 1.029	0.589*

**Independent T test, p = 0.05*

Mean urine volume between control group (placebo) and treatment group was significantly different (p = 0.029) (Table 2). Mean of urine volume was higher in treatment group.

Table 2. Comparison of 600 μg Oral Misoprostol and Placebo Group Based on Urine Volume

Variable	600 μg Oral Misoprostol	Placebo	p*
Urinary Volume (cc)	425.33 ± 71.20	320.00 ± 157.21	0.029*

**Independent T-test, p = 0.05*

Mean of residual urine volume between control group (placebo) and treatment group was significantly different (p = 0.001) (Table 3). Mean of residual urine volume was lower in treatment group.

Table 3. Comparison of 600 μg Oral Misoprostol and Placebo Group Based on Residual Urine Volume

Variable	600 μg Oral Misoprostol	Placebo	p*
Urinary Volume Residue (cc)	112.67 ± 28.59	147.33 ± 24.33	0.001*

**Independent T-test, p = 0.05*

DISCUSSION

Urinary retention after cesarean section is the inability to urinate 6 hours after Foley catheter removal or the volume of residual urine is > 200 ml. There are two parameters to diagnose urinary retention in this study including urination time, interpreting the time interval since Foley catheter removal until the patient can void spontaneously and residual volume, which is the amount of residual urine post spontaneous urination, as measured by catheterisation methods.

Before treatment, the characteristics of research subjects were statistically researched, the results of which, age (p = 0.407), body mass index (p = 0.489), and parity (p = 0.244) between the two groups did not differ significantly. It confirms that the differential effectiveness of 600μg oral misoprostol with placebo in preventing the occurrence of postpartum urinary retention is not influenced by demographic characteristics.

This study also showed there are no differences between the mean time urination between the control group (placebo) and misoprostol orally 600 μg (p = 0.589), in which both the misoprostol group and placebo, all pregnant women after cesarean section were able to urinate 6 hours after the catheter Foley released. The results of this study differs from the research conducted by Azami and Gatut in 2013 which showed differences between the mean time urination between the control group (placebo) with 600μg oral misoprostol (p = 0.010). PGS role in relaxation-contraction and sensitivity to stimuli urinary bladder has been widely studied, PGS released during or immediately after the occurrence of bladder distention, and PGS also regulates smooth muscle contraction and modulates neuronal transmission in urinary tract.[11,12]

Therefore, it can be concluded that misoprostol can increase sensitivity to stimuli urinary bladder, that is distended bladder with urine, and accelerates urination time in the study samples.

The was no difference of urination time in both study groups (misoprostol vs placebo), this might be caused by several factors, such as, the whole research samples were from pregnancies with no disorders that affect micturition (examples: UTI, cystitis, neurological disorders, prolonged labor, renal dysfunction, preeclampsia, smoking, alcohol, etc.) so that the samples were all under normal urination condition.

Intraoperative bladder manipulation occurred minimally. It was mentioned earlier that one of the exclusion criteria for the study was pregnancies with complication, so the cesarean section operation may take place smoothly without any difficulty that may involve manipulation of bladder.

Fluid intake in this study could not be controlled by the researcher. It is known that fluid intake pre-operative or post-operative determines urine production which then would affect the urination time. However, the calculation of urine time of all samples were after catheter removal, which means all samples at the beginning of the calculation of urination time had an empty bladder.

Both groups were installed foley catheters until 24 hours post-operative. A study conducted by T Mohammad Rizki in 2009 showed a significant association between the length of catheter insertion with urinary retention, where the faster the settled catheter was removed, the incidence of urinary retention was increased by $p = 0.038$ ($p < 0.05$).

A small amount of samples. A study with 30 samples, with each group of 15 samples, may be less representative of the population, so no time difference in urination was found. This is one of the weaknesses of the study, so it is expected that in the next study should involve a larger sample size.

Prevention of urinary retention in obstetric cases can be done in several ways, among others, by overcoming postpartum pain, by installing a Foley catheter for 24 hours or by administration of PGS. The release of PGS by the bladder can be stimulated by a variety of factors, including neuropeptides (substance P, neurokinin A), and inflammatory factor (bradykinin), which causes vesicular contractions and facilitates urinary reflex.[4]

In this study statistical analysis showed that there was a difference in the mean number of urine volume between the control group (placebo) with 600 μg oral misoprostol, in which the urine volume of group who received 600 μg peroral misoprostol was more than the group who received placebo. The results of this study were slightly different from the Azami and Gatut research in 2013 where the results showed no difference in the mean volume of urine between the control group (placebo) with 600 μg per oral misoprostol ($p = 0.051$). However, the same result was found the amount of urine volume in the misoprostol group was higher than those of the placebo group. This difference is probably due to the research of Azami and Gatut route of misoprostol was suppository. After oral administration, the half-life of misoprostol ranges from 20 to 40 minutes, then decreases rapidly within 120 minutes and remains low whereas at rectal administration is less than 20 minutes.[8,12]

Another possible cause is the uncontrollable fluid intake in this study as discussed earlier. After oral administration, misoprostol is faster and almost entirely absorbed by the gastrointestinal tract, plasma peak levels are achieved in 30 minutes, while the half-life ranges from 20-40 minutes, then decreases rapidly within 120 minutes and remains low. Misoprostol plays a role in opening Ca2 + ion channels so that extracellular Ca2 + ions can enter easily into intracellular and bind to calmodulin. This bond further activates the formation of MLC kinase which facilitates the formation of P-myosin. P-myosin will bind to actin causing contraction of detrusor muscle. Detrusor muscle contractions will trigger the function of the bladder to return to normal.[9]

In addition to urinary and urine volume time, another parameter for assessing postpartum urinary retention is the volume of urine residue > 200 ml. With statistical analysis, this study showed that there was a difference in mean residual urine volume between the control group (placebo) and 600 μg oral misoprostol, in which the volume of urine residues of the group receiving peripheral misoprostol was 600 μg less than those receiving placebo, but no residual volume was found > 200 ml in both misoprostol and placebo groups.

The results of this study were not much different from the research done by Azami and Gatut in 2013 where the results showed that there was a difference of average urine volume between the control group (placebo) and 600 μg ($p < 0.001$) oral misoprostol, whereas the volume of urine residues of the group receiving 600 μg oral misoprostol less than those receiving placebo and no residual volume > 200 ml was found in either the misoprostol or placebo group.[12]

So it can be concluded that in this study 600μg oral misoprostol can increase the amount of urine volume and reduce the volume of residual urine after cesarean section.

The majority side effect of misoprostol in this study (20% of 15 samples) was shivering. These findings are consistent with the study of Azami and Gatut (2003) who found 38% of shivering incidents. Other adverse effects were diarrhoea, Wagner (1985) has documented adverse drug events of oral route misoprostol in the gastrointestinal tract and suggested that rectal route delivery is safer to prevent the adverse effects of misoprostol in the gastrointestinal tract. Other possible causes of diarrhoea in this study include electrolyte imbalances, gastroenteritis-associated diseases that may be suffered by the patient and undetected during the study.

The results of the fisher exacts analysis found no significant association between the types of intervention and the incidence of drug side effects, suggesting that the adverse effects of drugs on the study could be "brutal" and not necessarily caused by misoprostol. The patient's subjectivity bias for shivering perception can disrupt the analysis of drug side effects, and this bias is difficult to control. A larger sample size is needed to determine if side effects do occur, and what are the side effects that may result from misoprostol administration.

Some disadvantages in this study besides the small number of samples is not to include patients with PUR (+). All samples did not experience PUR, and the effectiveness analysis of misoprostol was done on non PUR samples. Secondly, no misoprostol was administered in different doses, so this study could not determine the best dose of misoprostol for PUR handling, as well as the possible toxic effects based on misoprostol dosage. Further research is expected to include post-cesarean serum PUR population with larger sample quantities and provide varying doses of misoprostol intervention.

CONCLUSION

There is no difference in mean time of urination between the control group (placebo) with 600μg oral misoprostol. There is an average difference in the amount of urine volume, and the volume of residual urine between the control group (placebo) with 600μg oral misoprostol. 600μg oral misoprostol can increase the amount of urine and reduce the volume of urinary residue after cesarean section.

REFERENCES

1. Kekre AN, Vijayanand S, Dasgupta R, Kekre N. Postpartum urinary retention after vaginal delivery. Int J Gynecol Obstet. 2011; 112: 112-5.
2. Groutz A, Hadi E, Wolf Y, Maslovitz S, Gold R, Lessing JB, et al. Early postpartum voiding dysfunction: incidence and correlation with obstetric parameters. J Reprod Med. 2004; 49(12): 960-4.
3. Buckley BS, Lapitan MCM. Drugs for treatment of urinary retention after surgery in adults (Review). Cochrane Database Syst Rev. 2010(10): 1-27.
4. Kearney R, Cutner A. Postpartum voiding dysfunction. Obstet Gynecol. 2008; 10: 71-4.
5. Weissman A, Grisaru D, Shenhav, Peyser RM, Jaffa AJ. Postpartum surveillance of urinary retention by ultrasonography: the effect of epidural analgesia. Ultrasound Obstet Gynecol. 1995; 6: 130-4.
6. Kermans G, Wyndaele JJ, Thiery M, De Sy W. Puerperal urinary retention. Acta Urol Belgica. 1986; 54: 376-85.
7. Ulmstein U. Prostaglandins and the urinary tracts.Acta Obstet Gynecol Scand Suppl. 1983; 113: 55-8.
8. Tang OS, Gemzell-Danielsson K, Ho PC. Misoprostol: Pharmacokinetics profiles, effects on the uterus, and side-effects. Int J Gynecol Obstet. 2007; 99: s160-7.
9. Anderson K, Arner A. Urinary bladder contraction and relaxation: physiology and pathophysiology. Physiol Rev. 2004; 84: 935-86.
10. Kelly MRA, Johnston SR, Keane PF. Clinical response to an oral prostaglandin analogue in patients with interstitial cystitis. Eur Urol. 1998; 34: 53-6.
11. Ruan YC, Zhou W, Chan HC. Regulation of smooth muscle contraction by the epithelium: role of prostaglandins. Physiol. 2011; 26: 156-70.
12. Azami DA, Gatut H. Post Void Residual Reduction by Administering Misoprostol during Post Caesarean Section. Maj Obstet Ginekol, 2013; 21(3): 104-8.