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EFFICACY AND SAFETY OF POSTOPERATIVE INTRAVESICAL ADMINISTRATION OF TRANEXAMIC ACID AFTER TRANSURETHRAL RESECTION OF THE PROSTATE*

TRANSÜRETRAL PROSTAT REZEKSİYONU SONRASI POSTOPERATİF İNTRAVEZİKAL TRANEKSAMİK ASİT UYGULAMASININ ETKİNLİĞİ VE GÜVENLİĞİ

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ABSTRACT

Objective: To evaluate the safety and efficacy of postoperative intravesical administration of tranexamic acid after transurethral resection of the prostate.

Material and Method: The data of 112 patients who underwent surgery for lower urinary tract symptoms associated with benign prostatic obstruction (BPO) were retrospectively analysed. We formed two groups: Group 1 consisted of 57 patients who received tranexamic acid by irrigation fluid after the operation; group 2 consisted of 55 patients who did not receive tranexamic acid. Demographic data of patients and prostate characters, as well as operative and postoperative data were analysed. Postoperative bleeding in all patients was evaluated using the haemoglobin levels at the preoperative, and at 0- and 24-h postoperative were evaluated and noted.

Result: The mean ages of the patients were 66.9±7.2 (55-81) years in the intervention group, and those in the control group were 68.6±7.6 (55-80) years. There were no significant differences between the groups for demographic data, prostate volume and International Prostate Symptom Score (IPSS). The reduction in Hb at 24 hours postoperatively was greater in the control group compared to the tranexamic acid (TXA) group. Statistically significant differences were found between the two groups in terms of postoperative haemoglobin decrease, bladder irrigation time and total amount of irrigation fluid. There were no statistically significant differences between each group regarding the operation, weight of resected adenoma, hospitalization time and catheter removal time.

ÖZET

Amaç: Benign prostat hiperplazili hastalarda transüretral prostat rezeksiyonu sonrası postoperatif intravezikal traneksamik asit uygulamasının güvenlik ve etkinliğini değerlendirmek.

Gereç ve Yöntem: Benign prostat hiperplazisine bağlı alt üriner sistem semptomları nedeniyle ameliyat edilen 112 hastanın verileri geriye dönük olarak incelendi. İki grup oluşturuldu: Grup 1'de operasyon sonrası irrigasyon sıvısı ile traneksamik asit uygulanan 57 hasta, grup 2'de traneksamik asit uygulanmayan 55 hasta mevcuttu. Hastaların demografik verileri, prostat özellikleri, operatif ve postoperatif verileri analiz edildi. Tüm hastalarda ameliyat sonrası takiplerindeki kanama miktarları; preoperatif ve postoperatif 0. ve 24. saatlerde hemoglobin düzeyleri kullanılarak değerlendirildi ve not edildi.

Bulgular: Traneksamik asit grubundaki hastaların yaş ortalaması 66,9±7,2 (55-81) yıl, kontrol grubundakiler ise 68,6±7,6 (55-80) yıl idi. Demografik veriler, prostat hacmi ve Uluslararası prostat semptom skoru açısından gruplar arasında anlamlı fark yoktu. Postoperatif 24 saatte hemoglobindeki azalma, traneksamik asit grubuna kıyasla kontrol grubunda daha fazlaydı. Postoperatif hemoglobin düşüşü, mesane irrigasyon süresi ve toplam irrigasyon sıvısı miktarı açısından iki grup arasında istatistiksel olarak anlamlı fark bulundu. Ameliyat süresi, rezeke edilen adenomun ağırlığı, hastanede kalış süresi ve kateter çıkarma süresi açısından gruplar arasında istatistiksel olarak anlamlı fark yoktu.

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Conclusion: A postoperative follow-up process with less bleeding and complications is possible with tranexamic acid added to the intravesical irrigation fluid used after transurethral prostate resection (TURP) surgery.

Keywords: Tranexamic acid, transurethral resection of the prostate, irrigation fluid, postoperative bleeding

Sonuç: Transüretral prostat rezeksiyonu ameliyatı sonrası kullanılan intravezikal irrigasyon sıvısına eklenen traneksamik asit ile ameliyat sonrası daha az kanama ve komplikasyon ile takip süreci mümkündür.

Anahtar Kelimeler: Traneksamik asit, transuretral prostat rezeksiyonu, irrigasyon sıvısı, postoperatif kanama

INTRODUCTION

Lower urinary tract symptoms (LUTS) are a common complaint in aging men and occur most frequently associated with benign prostatic obstruction. Especially surgical treatment is performed in cases resistant to medical treatment (1, 2). Despite the recent development of alternative surgical techniques, transurethral prostate resection (TURP) is still accepted as the gold standard for the surgical treatment of benign prostatic obstruction (BPO). However, bleeding is a major perioperative complication, and transfusion rates after TURP have been shown to be around 0.4-7.1% in patients. The amount of bleeding varies depending on the patient's use of anticoagulant medication, comorbidity, size of the prostate, duration of the operation, and the amount of resected tissue (3, 4).

Many interventions have been recommended to reduce perioperative bleeding in prostate surgery such as intravenous oestrogen, erythropoietin, finasteride, intraprostatic vasopressin, controlled hypotension, and the use of antifibrinolytics (5).

Bleeding associated with urinary tract surgery is thought to be due to the fibrinolytic effect of high plasminogen concentration in the urine. Therefore, the use of tranexamic acid (TXA) has been investigated in previous studies to reduce intraoperative and postoperative bleeding in prostate surgeries. However, it has not been adequately accepted in urology practice (6, 7).

In this study, we aimed to investigate the effect of tranexamic acid, which was used in the irrigation fluid postoperatively, on reducing the amount of perioperative bleeding in bipolar TURP.

MATERIAL and METHODS

We included 112 patients operated on for BPO-related lower urinary tract symptoms and designed two groups with similar characteristics. The study was designed by scanning data of patients on whom bipolar TURP for benign prostatic obstruction was performed between February 2018 and July 2022 retrospectively. All operations were performed by two expert endourologists in a tertiary hospital. Group 1 consisted of 57 patients who had tranexamic acid in the irrigation fluid following the operation; group 2 consisted of 55 patients who did not have tranexamic acid in the irrigation fluid. Approved written informed consent describing the surgical procedure, benefits, and potential risks appropriately was read and completed by all study patients prior to surgery. Ethics committee approval was obtained from Istinye University Clinical Research Ethics Committee (Date: 07.12.2022, No: 3/2022.K-91). The study was conducted in accordance with the ethical standards set forth in the 1964 Declaration of Helsinki and its subsequent amendments. We performed a digital rectum examination, a routine blood examination and urine test, prostate-specific antigen (PSA) levels, a transrectal ultrasound scan, and International Prostate Symptom Score (IPSS). The haemoglobin levels of the patients at the preoperative, and at 0- and 24-h postoperatively were evaluated and noted. Inclusion criteria were as follows: age ≤ 81, Qmax≤10 mL/h, IPSS≥16, and prostate volume measured by transrectal US between 40-100 mL. The exclusion criteria were suspected/confirmed bladder or prostate cancer, neurogenic bladder, previous lower urinary tract surgery (urethral and/or prostate), serious comorbidities (unstable angina, symptomatic CHF, poorly controlled COPD, recent (less than six months ago) myocardial infarction or stroke), coagulopathy.

When the operation was over, a 22F 3-way urethral catheter was inserted and bladder irrigation was continued until the postoperative flush was cleared. While 5 ampoules of tranexamic acid (5 mL 250 mg/1 ampoule) were applied to the first postoperative irrigation fluid (0.9% Sodium Chloride Irrigation, 3000 mL), 3 ampoules of tranexamic acid were added to the postoperative maintenance irrigation fluids. In total, 17-29 ampoules of tranexamic acid were added in irrigation fluids in all patients of the intervention group.

Statistical analysis

Statistical analyses were performed with SPSS version 18.0 (SPSS, Inc., Chicago, IL, USA) and data were displayed as mean±standard deviation (SD) (range). The chi-square test, Manne-Whitney U test, and one-way analysis of variance (ANOVA) were used for statistical comparisons. A 5% level of significance was used for all statistical testing. A P-value<0.05 was considered significant.

RESULTS

Data from 57 (51%) patients treated with TXA and 55 (49%) control patients were analysed. The mean age of

the patients was 66.9±7.2 (55-81) years in the intervention group, and those in the control group was 68.6±7.6 (55-80) years. Body mass index (BMI) was calculated as 30.5±3.6 (21-36) in the intervention group and 28.8±4.1 (22-35) in the control group, respectively. While 46 (81%) patients had ASA I-II and 11 (19%) patients had ASA III-IV in the intervention group, 47 (85%) patients had ASA I-II and ASA III-IV was 8 (15%) patients in the control group. The prostate volumes of the patients were 69.6±10.9 (40-92) mL and 66±11.3 (48-91) mL, respectively. There were no statistical differences between each group in age, BMI, IPSS, prostate size and patients' comorbidity. Demographic data and preoperative results of patients are shown in Table 1. The reduction in Hb at 24 hours postoperatively was statistically significant in the control group compared to the TXA group ($p<0.001$). The mean duration of operation was 73.8±14.5 (40-110) minutes in the intervention group and 76.3±17.1 (48-125) in the control group. The weight of resected adenoma was 35.1±7.8 grams in group 1 and 34.7±6.4 grams in group 2. The mean hospitalization time of patients was 1.8±0.7 (1-3) days and 2±0.8 (1-5) days, respectively. Catheter removal times were 2.4±0.7 days and 2.8±1 days in group 1 and group 2, respectively. There were no statistical differences between each group regarding the duration of the operation, weight of resected adenoma, hospitalization time, and catheter removal time. Postoperative bladder irrigation time was 12.4±5.1 hours in the intervention group, while it was 15.5±7.3 hours in the control group. According to our analysis of patients' data, statistically significant differences were found between the two groups in postoperative bladder irrigation time and the total amount of irrigation fluid (Table 2). No patient had haematuria requiring blood transfusion in both groups.

DISCUSSION

The prostate tissue, which has a rich blood supply, contains large venous sinuses. During prostate resection, these venous sinuses are opened, fibrinolytic enzymes pass into the vascular system and fibrinolysis is activated. Bleeding becomes inevitable with fibrin degradation (7-9).

TXA is a synthetic derivative of lysine and is an antifibrinolytic. Its mechanism of action is to prevent the formation of plasmin by binding to plasminogen, to prevent the breakdown of fibrin polymers, and to stabilize blood clots, respectively. Thus, it reduces blood loss and the need for transfusion in surgeries. Thanks to this effect, TXA is used in acute trauma, cardiac surgery, orthopaedics and liver surgery operations (5, 7, 10). Although it was used in some previous studies in urological surgery, it did not gain much interest in the urology practice.

Despite the developing technology in TURP operations, blood loss continues to be a problem. Significant bleeding can increase surgical morbidity and mortality. TXA, which is used effectively in reducing blood loss in different surgical branches, has also been used in TURP operations recently, but its effectiveness has been a matter of debate (11, 12). In the studies, the route of administration of TXA was performed intravenously, as in other surgical specialties. However, in our study, TXA was added to irrigation fluids by the intravesical route, and its efficacy and safety were evaluated.

In the literature, there are studies that evaluated the decrease in haemoglobin after TURP surgery and found a significant difference in the TXA group (13), as well as studies stating that there was no difference (14). In the present study, we found that the urine colour was lighter, and the amount of bleeding decreased with TXA added to the irrigation fluid in the postoperative follow-ups. It showed that the decrease in Hb at the postoperative 24th hour was statistically less significant in the TXA group ($p<0.001$).

Some studies found a statistical decrease in the volume of irrigation fluid used intraoperatively with intravenous TXA administered perioperatively (12, 13). However, there have also been studies that applied TXA with the same method and did not detect any difference (15, 16). Unlike our study, TXA was applied only in the postoperative period and was added to the irrigation fluid. There was a statistical difference in the postoperative total amount of

Table 1: Preoperative demographic characteristics of the patients

	Tranexamic acid (n=57)	Control (n=55)	P value
Age (years)	66.9±7.2 (55-81)	68.6±7.6 (55-80)	0.67
Body mass index	30.5±3.6 (21-36)	28.8±4.1 (22-35)	0.29
ASA category I + II (n)	46	47	0.44
ASA category III + IV (n)	11	8	0.17
Preoperative haemoglobin (g/dl)	13.9±0.9	14.2±0.8	0,52
Prostate volume (ml)	69.6±10.9 (40-92)	66±11.3 (48-91)	0.15
IPSS	22.5±2.3	22.1±2.6	0.61

ASA: American Society of Anaesthesiologists, IPSS: International Prostate Symptom Score

Table 2: Comparison of postoperative parameters and complications

	Tranexamic acid (n=57)	Control (n=55)	P value
Haemoglobin (g/dl)			
preoperative	13.9±0.9	14.2±0.8	0.52
postoperative 0-h	12.1±1	12.5±1.3	0.21
postoperative 24-h	11.8±1.1	10.6±1.4	0.001
Duration of operation (min)	73.8±14.5 (40-110)	76.3±17.1 (48-125)	0.45
Postoperative bladder irrigation time (h)	12.4±5.1	15.5±7.3	0.001
Total amount of irrigation fluid (L)	18.44±2.16	24.08±3.5	0.001
Weight of resected adenoma (g)	35.1±7.8	34.7±6.4	0.62
Hospitalization time (day)	1.8±0.7 (1-3)	2±0.8 (1-5)	0.37
Catheter removal (day)	2.4±0.7 (2-5)	2.8±1 (1-6)	0.35

irrigation fluid and bladder irrigation time in the intervention group. We state that our study differs from the other studies in this aspect.

In addition, the effect of intravenous TXA, which is applied to provide better haemostasis and better imaging during surgery, was evaluated in some studies in the literature, and significantly shorter operative times were found in the intervention group (7, 11, 13). In our study, TXA was applied to the postoperative irrigation fluid and therefore its effect on the operation time could not be evaluated.

On the other hand, some studies have shown that TXA may be associated with postoperative neurological complications in a dose-dependent manner. While it has been reported that using TXA may increase the risk of epilepsy in children undergoing cardiac surgery (10), in another study it was shown that the use of TXA may cause complications such as convulsions of the central nervous system in a dose-dependent manner (17). There were no neurological complications in any of the patients after the operation in our study. We attribute this situation to the fact that the route of administration is not intravenous, but intravesical (into the bladder irrigation fluid) and its minimal passage into the vascular system. Another important complication of administering TXA to patients undergoing prostate surgery is the thromboembolic risk. It has been stated that this risk exists especially in patients with thrombophilia (18). Although studies in the literature have shown that TXA does not increase the risk of thromboembolic complications, its effect on this complication remains unclear (19). In our study, we conclude that the TXA application method is safe, considering that systemic transmission is minimal.

The main limitations of the study were the small sample size, and the inability to evaluate total and mean blood losses. Further studies are needed on the use of intravesical TXA after TURP operation.

CONCLUSION

The use of intravesical TXA offers a safe postoperative follow-up process with less bleeding and lower irrigation fluid volumes after TURP surgeries. In addition, we think that intravesical use of TXA is superior to intravenous use in terms of systemic complications. Further studies supporting the results of this study will be required.

Ethics Committee Approval: This study was approved by Istinye University Clinical Research Ethics Committee (Date: 07.12.2022, No: 3/2022.K-91)

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REFERENCES

1. Coskuner ER, Ozkan TA, Koprulu S, Dillioglugil O, Cevik I. The role of the bipolar plasmakinetic TURP over 100 g prostate in the elderly patients. Int Urol Nephrol 2014;46(11):2071-7. [CrossRef]
2. Mebust WK, Holtgrewe HL, Cockett AT, Peters PC. Transurethral prostatectomy immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3, 885 patients. J Urol 2002;167(1):999-1003. [CrossRef]
3. Sun F, Sun X, Shi Q, Zhai Y. Transurethral procedures in the treatment of benign prostatic hyperplasia: A systematic review and meta-analysis of effectiveness and complications. Medicine (Baltimore) 2018;97(51):e13360. [CrossRef]

4. Yang TY, Chen M, Lin WR, Li CY, Tsai WK, Chiu AW, et al. Preoperative treatment with 5α-reductase inhibitors and the risk of hemorrhagic events in patients undergoing transurethral resection of the prostate - A population-based cohort study. Clinics (Sao Paulo) 2018;73:e264. [CrossRef]
5. Mina SH, Garcia-Perdomo HA. Effectiveness of tranexamic acid for decreasing bleeding in prostate surgery: a systematic review and meta-analysis. Cent European J Urol 2018;71(1):72-7. [CrossRef]
6. Kumsar S, Dirim A, Toksöz S, Sağlam HS, Adsan O. Tranexamic acid decreases blood loss during transurethral resection of the prostate (TURP). Cent European J Urol 2011;64(3):156-8. [CrossRef]
7. Jendoubi A, Malouch A, Bouzouita A, Riahi Y, Necib H, Ghedira S, et al. Safety and efficacy of intravenous tranexamic acid in endoscopic transurethral resections in urology: Prospective randomized trial. Prog Urol 2017;27(16):1036-42. [CrossRef]
8. Nielsen JD, Gram J, Holm-Nielsen A, Fabrin K, Jespersen J. Post-operative blood loss after transurethral prostatectomy is dependent on in situ fibrinolysis. Br J Urol 1997;80(6):889-93. [CrossRef]
9. Karakose A, Aydogdu O, Atesci YZ. BiVap saline vaporization of the prostate in men with benign prostatic hyperplasia: our clinical experience. Urology 2014;83(3):570-5. [CrossRef]
10. Martin K, Breuer T, Gertler R, Hapfelmeier A, Schreiber C, Lange R, et al. Tranexamic acid versus ε-aminocaproic acid: Efficacy and safety in paediatric cardiac surgery. Eur J Cardiothorac Surg 2011;39(6):892-7. [CrossRef]
11. Karkhanei B, Musavi-Bahar SH, Bayat M, Kaseb K, Rezaee H, Moradi A, et al. Safety and efficacy of intraoperative administration of intravenous tranexamic acid in transurethral resection of prostate: a double-blind, randomised, placebo-controlled trial. J Clin Urol 2020;13(2):125-31. [CrossRef]
12. Vezhaventhan G, Soundarya G, Saravanan K, Govindarajan P. Is tranexamic acid effective in reducing TURP related blood loss? A prospective study. Int J Curr Res Life Sci 2018;7(6):2226-28.
13. Samir M, Saafan AM, Afifi RM, Tawfick A. Can high-dose tranexamic acid have a role during transurethral resection of the prostate in large prostates? A randomised controlled trial. Arab J Urol 2021;20(1):24-9. [CrossRef]
14. Longo MA, Cavalheiro BT, de Oliveira Filho GR. Systematic review and meta-analyses of tranexamic acid use for bleeding reduction in prostate surgery. J Clin Anesth 2018;48:32-8. [CrossRef]
15. Meng QQ, Pan N, Xiong JY, Liu N. Tranexamic acid is beneficial for reducing perioperative blood loss in transurethral resection of the prostate. Exp Ther Med 2019;17(1):943-7. [CrossRef]
16. Gupta A, Priyadarshi S, Vyas N, Sharma G. Efficacy of tranexamic acid in decreasing primary hemorrhage in transurethral resection of the prostate: A novel combination of intravenous and topical approach. Urol Ann 2021;13(3):238-42. [CrossRef]
17. Murkin JM, Falter F, Granton J, Young B, Burt C, Chu M. High-dose tranexamic acid is associated with nonischemic clinical seizures in cardiac surgical patients. Anesth Analg 2010;110(2):350-3. [CrossRef]
18. Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ, Fergusson DA, et al. Antifibrinolytic use for minimising perioperative allogeneic blood transfusion. Cochrane Database Syst Rev 2011;(1):CD001886. [CrossRef]
19. Sharma V, Katznelson R, Jerath A, Garrido-Olivares L, Carroll J, Rao V, et al. The association between tranexamic acid and convulsive seizures after cardiac surgery: a multivariate analysis in 11 529 patients. Anaesthesia 2014;69(2):124-30. [CrossRef]