Global Journal of Medicine
2024; 5(1):21-30.
ISSN Online: 2766-8878. ISSN Print: 2766-8886.
Website: http://naturescholars.com
Email: Glo_J_Med@126.com
Publisher: Scholars Publishing, LLC

Research Article

Tranexamic Acid for Reducing Bleeding in Transurethral Resection of The Prostate: A Meta-Analysis and Systematic Review

Xin-Zhi Zhou[1] and Zhi-Ping Yu[1*]

[1]Operating Room of Jingzhou Central Hospital, Jingzhou, 434000, Hubei, China.

***, Correspondence**
Zhi-Ping Yu, BSN, Operating Room of Jingzhou Central Hospital, Jingzhou, 434000, Hubei, China. Phone number：86+15377180870. Email: 517057424@qq.com.
Received: November 28, 2023; Accepted: March 1, 2024; Published online: June 8, 2024.
Cite this paper: Xin-Zhi Zhou and Zhi-Ping Yu. (2024) Tranexamic Acid for Reducing Bleeding in Transurethral Resection of The Prostate: A Meta-Analysis and Systematic Review. *Global Journal of Medicine,* 5(1):21-30. http://naturescholars.com/gjm.050103. https://doi.org/10.46633/gjm.050103.

Abstract

Objective: The efficacy of tranexamic acid (TXA) for reducing bleeding during transurethral resection of the prostate is still inconclusive. To understand its efficacy and safety in transurethral resection of the prostate literature results were meta-analyzed and systematically reviewed. **Methods:** We searched PubMed, Web of Science, The Cochrane Library, and Embase database, and finally retrieved 9 articles, and screened titles and abstracts according to our inclusion and exclusion criteria. Only randomized controlled trials (RCTs) were included in the analysis, and the trials should include at least 2 subgroups: the TXA group and the control group. **Results:** Nine RCTs were eligible for this meta-analysis and systematic review. The results of the meta-analysis showed that, compared with the control group, the TXA group had higher hemoglobin 24 hours after surgery [SMD=0.55, 95%CI (0.18, 0.92), P=0.003], and less intraoperative blood loss [SMD=- 2.20, 95%CI (-3.45, -0.96), P=0.0005]. Blood transfusion rate was lower [SMD=0.53, 95%CI (0.30, 0.96), P=0.04], while other aspects such as hemoglobin loss at 24h after operation [SMD=-0.08, 95%CI (-0.29, 0.13), P=0.46], operation time [SMD=-0.28, 95%CI (-0.83, 0.27), P=0.31], hospital stay [SMD=0.07, 95%CI (-0.11, 0.24), P=0.45] had no significant difference. **Conclusion:** Tranexamic acid can reduce blood loss and blood transfusion rate during transurethral resection of the prostate, and maintain a higher hemoglobin level 24 hours after surgery, without increasing the risk of thromboembolism and other complications. High clinical application value was obtained for clinical recommendation.

Keywords: Tranexamic Acid; Transurethral Resection; Prostate; Temoglobin; Bleeding.

Introduction

Benign prostatic hyperplasia (BPH) is one of the most common paralytic diseases that plague middle-aged and elderly men (1). Mild benign prostatic hyperplasia can still be controlled by drugs such as Q-receptor blockers and 5Q-reductase inhibitors. With the progress of the disease, the obstruction of the urinary tract becomes more and more serious, and the drug intervention is no longer effective, and it is necessary to surgically remove part of the hyperplastic prostate. Transurethral resection of the prostate (TURP) has high surgical safety and fast postoperative recovery. Advantages have been popularized worldwide and are recognized as the gold standard for the treatment of benign prostatic hyperplasia (2,3). However, due to the abundant blood supply in the prostate, especially the venous drainage (4), intraoperative bleeding is unavoidable, and the amount of bleeding directly affects the postoperative prognosis and recovery of patients. In severe cases, TUR syndrome and blood loss may even occur. Sexual shock (5), so how to better control intraoperative bleeding is also one of the important indicators to measure the success of the surgery.

At present, there are many methods for controlling intraoperative bleeding, such as improving the surgical method and using the laser to remove the prostate (6). In addition, the use of hemostatic drugs in the perioperative period is also a feasible intervention. Studies have shown that an important reason for bleeding after TURP is the increased activity of the fibrinolytic system. Surgery will stimulate a high concentration of plasminogen activators in the urinary tract, which in turn activates the fibrinolytic system. Fibrinolytic drugs can effectively reduce bleeding during TURP (7). TXA is a synthetic antifibrinolytic drug that binds to plasminogen about 10 times stronger than aminocaproic acid and can block the interaction of plasminogen and plasmin on the surface of fibrin, thereby preventing fibrinolysis. Protein proteolysis, thereby reducing intraoperative bleeding (8). Multiple studies have shown that TXA is an effective drug in reducing bleeding and blood transfusion in various surgical procedures, including cardiac surgery (9), orthopedic surgery (10), and oral surgery (11).

The efficacy of TXA in controlling bleeding and transfusion in TURP is still inconclusive. To understand its efficacy and safety in TURP, we performed a meta-analysis and systematic review of published randomized controlled trials (RCTs).

Method

1 Search strategy

Preferred reporting items based on systematic reviews and meta-analyses (12).We conducted a systematic review and meta-analysis.

We searched foreign language databases PubMed, the Cochrane Library, and Embase databases in July 2022 to screen for studies on the effects of TXA in TURP for bleeding control and transfusion. Search keywords are as follows: [(“tranexamic acid” or“AMCHA”or“trans-4-(Aminomethyl) cyclohexane carboxylic acid” or "t-AMCHA” or "t-AMCHA” or "AMCA" or "Davidoff" or "cyklokapron" or "ugurol" or “KABI 2161” or "spoof" or "transmit"）and(“transurethral resection of the prostate” or "prostate transurethral resection"or“transurethral prostate resection” or "transurethral prostatectomy" or "transurethral microwave thermotherapy" ” or “transurethral thermotherapy”or“TURP”)].

This meta-analysis was limited to published RCT studies, and there were no restrictions on language or publication year. In addition, we browsed other articles on related topics.

2 Inclusion and exclusion criteria

Inclusion criteria include (1) Eligible randomized controlled trials (RCTs), which should include at least 2 groups of tranexamic acid and placebo; (2) Outcome indicators include 24h postoperative hemoglobin loss and 24h

postoperative hemoglobin level, one or more of intraoperative blood loss, blood transfusion rate, operation time, and hospital stay. Exclusion criteria included: (1) articles were conference papers, reviews, letters, etc.; (2) studies did not contain the outcome indicators required for this analysis; (3) full-text literature was not presented.

3 Quality Assessment

We assessed the quality of the included RCTs using the Cochrane Risk of Bias Assessment Tool recommended in the Cochrane Handbook. The quality of each RCT was evaluated one by one in seven aspects: random sequence generation, allocation concealment, blinding of investigators and subjects, blinded evaluation of study outcomes, completeness of outcome data, selective reporting of study results, and other biases, and classify the assessment results into "low risk", "unclear" and "high risk".

4 Data extraction

Two investigators Xinzhi Zhou (ZXZ) and Zhiping Yu (YZP) independently performed data extraction, screened the titles and abstracts of relevant studies, excluded studies that did not meet the criteria, and further screened each article by browsing the full text. Differences between investigators on research evaluation issues were resolved through discussion, and if results were still in dispute, a third person should be involved in the deliberations. The extracted data included: the first author's name, publication time, number of experimental and control groups, age, prostate volume, 24h postoperative hemoglobin loss, 24h postoperative hemoglobin level, intraoperative blood loss, blood transfusion rate, operation time, and hospital stay, etc.

5 Statistical analysis

Statistical analysis was performed using RevMan 5.3 software (Cochrane Collaboration, Oxford, UK), and the results were considered significant if two-sided P<0.05. Heterogeneity between results from studies included in this meta-analysis was assessed using the χ test and the I^2 statistic, both of which were used to determine statistical significance. If the χ test shows P<0.1 or the I^2 statistic shows a ratio >50%, then there is significant heterogeneity and a random effects model will be used. If no significant heterogeneity was observed, a fixed-effects model was used.

2 Results

1 Study selection

After searching PubMed, Web of Science, The Cochrane Library, and Embase databases, we finally retrieved 9 articles and screened titles and abstracts according to inclusion and exclusion criteria, excluding a total of 8 articles（Figure1）. We then assessed the full-text content of the remaining literature and finally identified 9 articles for meta-analysis。（Table1 and 2）

2 Meta-analysis

2.1 postoperative hemoglobin loss(24h)

Four studies reported 24h postoperative hemoglobin loss. Heterogeneity analysis showed I^2=0%, P=0.40 (Figure 2), which showed no heterogeneity, so a fixed-effects model was used. Compared with the control group, the TXA group did not reduce the hemoglobin loss at 24 h after the operation [SMD=-0.08, 95%CI (-0.29, 0.13), P=0.46].

2..2 postoperative hemoglobin level(24h)

Six studies reported 24h postoperative hemoglobin levels. Heterogeneity analysis showed that I^2=74%, P=0.001 (Figure 3), with high heterogeneity, so a random effects model was used. Compared with the control group, patients in the TXA group had significantly higher hemoglobin levels at 24 h after surgery [SMD=0.55, 95%CI (0.18, 0.92), P=0.003].

2.3 Intraoperative blood loss

Five studies reported intraoperative blood loss. Heterogeneity analysis showed that I^2=96%, P<0.00001 (Figure 4), with high heterogeneity, so a random-effects model was used. Compared with the control group, the TXA group had significantly less intraoperative blood loss [SMD=-2.20, 95%CI (-3.45, -0.96), P=0.0005].

2.4 Blood transfusion rate

Five studies reported transfusion rates. Heterogeneity analysis showed that I^2=2%, P=0.4 (Figure 4), and the heterogeneity was low, so a fixed-effects model was used. Compared with the control group, the blood transfusion rate was significantly lower in the TXA group [SMD=0.53, 95%CI (0.30, 0.96), P=0.04].

2.5 Operation time

Eight studies reported operative time. Heterogeneity analysis showed that I^2=92%, P<0.00001 (Figure 4), with high heterogeneity, so a random-effects model was used. There was no difference in operative time in the TXA group compared with the control group [SMD=-0.28, 95%CI (-0.83, 0.27), P=0.31].

2.6 Length of hospital stay

Five studies reported the length of hospital stay. Heterogeneity analysis showed that I^2=36%, P=0.18 (Figure 4), and the heterogeneity was low, so a fixed-effects model was used. Compared with the control group, there was no difference in the length of hospital stay in the TXA group [SMD=0.07, 95%CI (-0.11, 0.24), P=0.45].

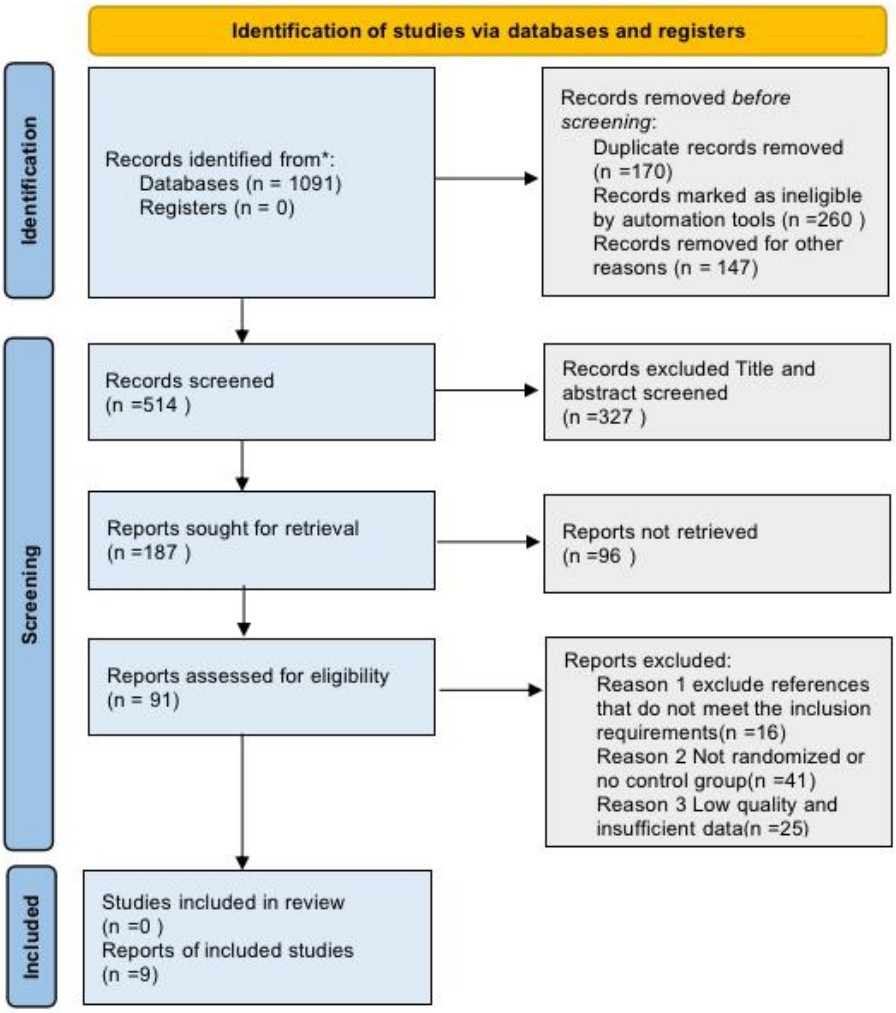

Figure 1. Literature screening flow chart.

Table 1 Basic characteristics of included studies

Study	Year	Research area	Age		People		Prostate volume	
			TXA	Control	TXA	Control	TXA	Control
Gupta (13)	2020	India	68.2±8.49	66.51±9.38	35	35	56.87±14.91	51.20±17.03
Tawfick (14)	2022	Egypt	69.36±7.88	68.88±7.82	25	25	70.28±9.17	68.88±9.27
Karkhanei (15)	2019	Iran	66.43±7.86	69.63±9.67	35	35	36.62±16.29	39.14±19.90
Jendoubi (16)	2017	Tunisie	67.31±7.72	71.13±9.06	30	30	47.76±16.41	59.07±30.62
Meng (17)	2019	China	71.4±5.4	70.7±8.5	30	30	73.3±8.3	66.6±3.9
Mirmansouri (18)	2016	Iran	72.72±9.79	69.52±10.28	40	40	56±14.8	50.87±20.7
Samir (19)	2022	Egypt	64.66±5.87	65.75±5.48	95	91	108.32±16.64	107.09±16.21
Pravin (20)	2016	India	56.86±6.09	57.23±5.40	40	40	38.07±3.83	38.27±3.91
Rannikko (21)	2004	Finland	71.33±6.81	68.67±9.09	70	66	48.67±19.68	52.33±19.70

Table 2 Intervention of included studies

Study	Intervention Program	
	TXA	Control
Gupta (13)	Intravenous TXA 500 mg after induction of anesthesia, followed by TXA 500 mg per 3 L of lavage fluid	NR
Tawfick (14)	During the operation, receive 0.1% TXA 1000mg (10mL) dissolved in 1L sterile flushing solution (glycine) flushing solution, postoperative local administration of TXA 500mg (5mL) dissolved in 100mL normal saline	During the operation, 10 mL of distilled water was dissolved in 1 L of sterile flushing solution (glycine), and 5 mL of distilled water was locally administered to dissolve in 100 mL of normal saline after surgery.
Karkhanei (15)	Intravenous infusion of TXA 15 mg/kg for 20 min after induction of anesthesia, followed by infusion of TXA at a rate of 1 mg/kg/h until 5 h after surgery	NR
Jendoubi (16)	TXA 10 mg/kg intravenously 30 min before surgery, then 1 mg/kg/h by continuous infusion until 24 h after surgery	receive isotonic saline at the same rate
Meng (17)	Administer 1 g TXA in 200 ml normal saline after	Receive 200 ml of saline at the same rate

	induction of anesthesia at a drip rate of 20-30 drops/min	
Mirmansouri (18)	Intravenous TXA 15mg/kg 20min before surgery, then TXA infusion at a rate of 1mg/kg/h until 5h after surgery	NR
Samir (19)	TXA was administered as an IV loading dose of 50 mg/kg within 20 min immediately before induction of anesthesia, followed by a maintenance dose of 5 mg/kg/h until completion of TURP	The same regimen received the same dose of saline
Pravin (20)	TXA 500mg was injected 30min before surgery and after surgery	NR
Rannikko (21)	Oral 2g TXA 3 times on the day of surgery and the first day after surgery	NR

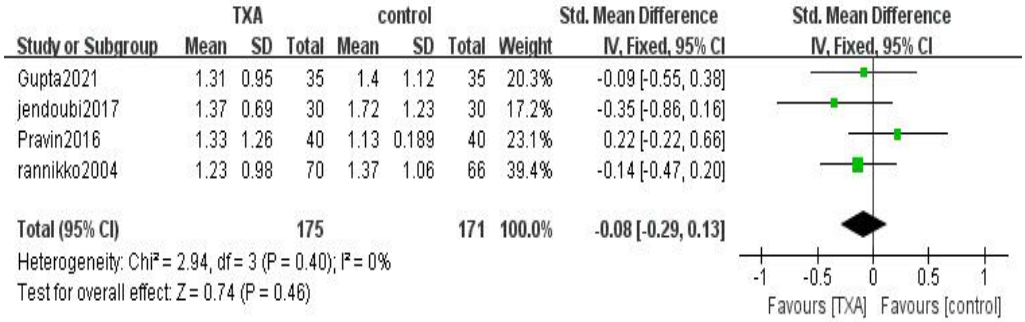

Figure 2. Postoperative hemoglobin loss (24h).

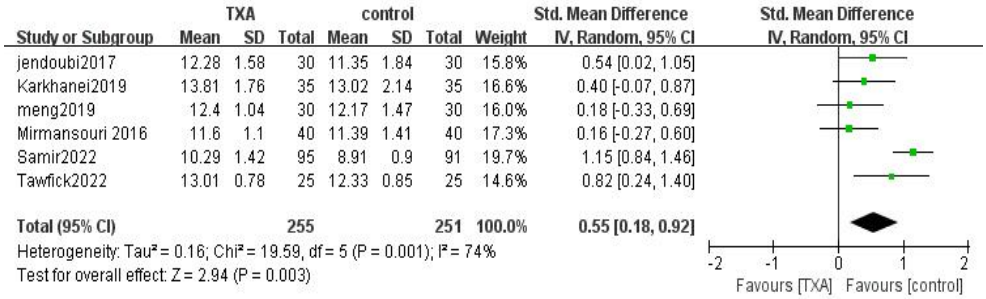

Figure 3. Postoperative hemoglobin level (24h).

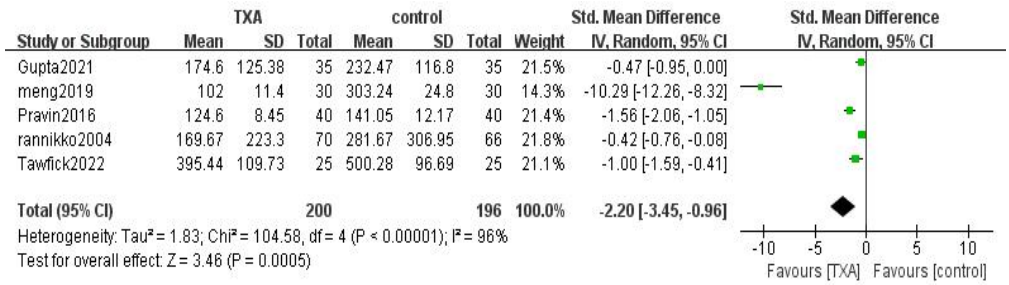

Figure 4. Intraoperative blood loss.

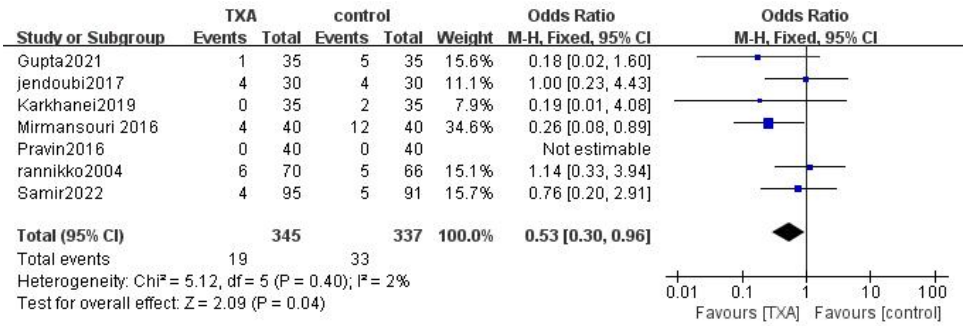

Figure 5. Blood transfusion rate.

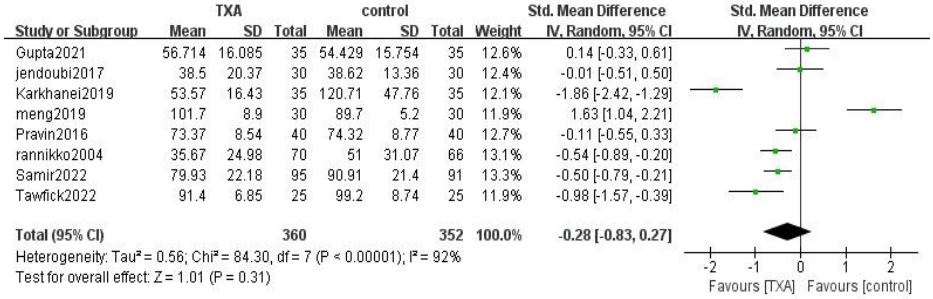

Figure 6. Operation time.

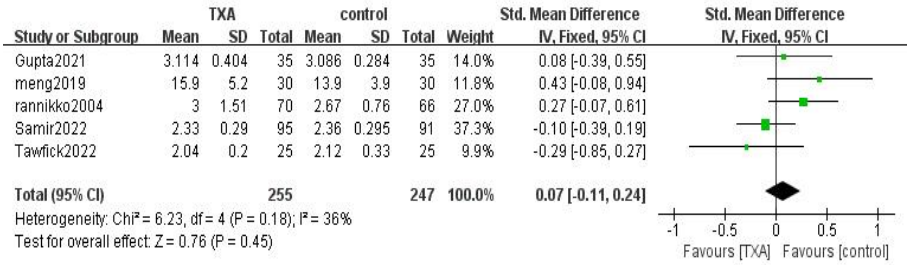

Figure 7. Hospital stay.

Discussion

We are a study to systematically evaluate the safety and efficacy of tranexamic acid in reducing bleeding during transurethral resection of the prostate. Through this meta-analysis, we found that intraoperative use of tranexamic acid not only reduces intraoperative blood loss in patients with transurethral prostatectomy but also has a large advantage in the need for perioperative blood transfusions, in addition to, Intraoperative use of tranexamic acid did not increase the risk of any postoperative thromboembolic events or other adverse effects. Therefore tranexamic acid is effective in preventing perioperative blood loss compared with antiretroviral drugs in surgically treated urethroprostatectomy patients.

Based on 9 studies with a total of 792 patients, there are 6 outcome indicators in this meta-analysis, including the patient's 24h postoperative hemoglobin, intraoperative blood loss, blood transfusion rate, hemoglobin loss, operation time, and hospital stay. There were three main outcome indicators, all of which had good heterogeneity and were statistically significant. However, we found that the remaining 3 outcome measures were not ideal, and the current analysis has limitations. It includes the analysis of 24h postoperative hemoglobin loss, the overall operation time, and the hospitalization time of patients. There is great

heterogeneity among the studies, and this problem cannot be resolved after subgroup analysis. Therefore, it is concluded that tranexamic acid Acids did not have a great advantage in reducing 24h hemoglobin loss in patients and in reducing operative time and hospital stay. We recommend high-quality clinical trials to support the intervention of tranexamic acid in patients undergoing urethroprostatectomy.

Current limitations of this study include: the number of available articles is too small, specific procedural analysis is not feasible due to the limited number of included studies, and larger, practical clinical trials are still needed to evaluate TXA in urethroprostatectomy patients effect in. Furthermore, in the quality assessment of the included studies, a high proportion of studies were found to be at unclear risk of bias. For example, the estimated 24h hemoglobin loss in this study showed a high degree of heterogeneity that we could not eliminate by sensitivity or subgroup analysis, so different measurement methods must be considered in this question, requiring higher quality and better reported clinical trials.

Conclusion

Tranexamic acid can reduce blood loss and blood transfusion rate in transurethral prostatectomy, and maintain a higher hemoglobin level 24 hours after surgery, without increasing the risk of thromboembolism and other complications in patients, with a high clinical application value.

Declarations

1. ***Consent to publication***
   We declare that all authors agreed to publish the manuscript in this journal based on the signed Copyright Transfer Agreement and followed publication ethics.
2. ***Ethical approval and consent from participants***
   Not applicable.
3. ***Disclosure of conflict of interests***
   We declare that no conflict of interest exists.
4. ***Funding***
   None
5. ***Availability of data and material***
   We declare that the data supporting the results reported in the article are available in the published article.
6. ***Authors' Contributions***
   Authors contributed to this paper with the design (XZZ), literature search (ZPY), drafting (XZZ), revision (ZPY), and editing (XZZ) and final approval (XZZ and ZPY).
7. ***Acknowledgement***
   None.
8. ***Authors' biography***
   None.

References

1. Devlin C M, Simms M S, Maitland N J. Benign prostatic hyperplasia - what do we know? [J]. BJU international, 2021, 127(4): 389-399.
2. Lerner L B, Mcvary K T, Barry M J, et al. Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA GUIDELINE PART II-Surgical Evaluation and Treatment [J]. The Journal of urology, 2021, 206(4): 818-826.
3. Lerner L B, Mcvary K T, Barry M J, et al. Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA GUIDELINE PART I-Initial Work-up and Medical Management [J]. The Journal of urology, 2021, 206(4): 806-817.
4. Aaron L, Franco O E, Hayward S W. Review of Prostate Anatomy and Embryology and the Etiology of Benign Prostatic Hyperplasia [J]. The Urologic clinics of North America, 2016, 43(3): 279-288.
5. Gratzke C, Bachmann A, Descazeaud A, et al. EAU Guidelines on the Assessment of Non-neurogenic Male Lower Urinary Tract

Symptoms including Benign Prostatic Obstruction [J]. European urology, 2015, 67(6): 1099-1109.
6. Yu J, Jeong B C, Jeon S S, et al. Comparison of Efficacy of Different Surgical Techniques for Benign Prostatic Obstruction [J]. International neurourology journal, 2021, 25(3): 252-262.
7. Nielsen J D, Gram J, Holm-Nielsen A, et al. Post-operative blood loss after transurethral prostatectomy is dependent on in situ fibrinolysis [J]. British journal of urology, 1997, 80(6): 889-893.
8. Ortmann E, Besser M W, Klein A A. Antifibrinolytic agents in current anaesthetic practice [J]. British journal of anaesthesia, 2013, 111(4): 549-563.
9. Habbab L M, Semelhago L, Lamy A. Topical Use of Tranexamic Acid in Cardiac Surgery: A Meta-Analysis [J]. The Thoracic and cardiovascular surgeon, 2020, 68(3): 212-218.
10. Reale D, Andriolo L, Gursoy S, et al. Complications of Tranexamic Acid in Orthopedic Lower Limb Surgery: A Meta-Analysis of Randomized Controlled Trials [J]. BioMed research international, 2021, 2021(6961540.
11. De Vasconcellos S J, De Santana Santos T, Reinheimer D M, et al. Topical application of tranexamic acid in anticoagulated patients undergoing minor oral surgery: A systematic review and meta-analysis of randomized clinical trials [J]. Journal of cranio-maxillo-facial surgery : official publication of the European Association for Cranio-Maxillo-Facial Surgery, 2017, 45(1): 20-26.
12. Liberati A, Altman D G, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration [J]. Annals of internal medicine, 2009, 151(4): W65-94.
13. Gupta A, Priyadarshi S, Vyas N, et al. Efficacy of tranexamic acid in decreasing primary hemorrhage in transurethral resection of the prostate: A novel combination of intravenous and topical approach [J]. Urology Annals, 2021, 13(3): 238-242.
14. Tawfick A, Mousa W, El-Zhary A F, et al. Can tranexamic acid in irrigation fluid reduce blood loss during monopolar transurethral resection of the prostate? A randomised controlled trial [J]. Arab Journal of Urology, 2022, 20(2): 94-99.
15. Karkhanei B, Musavi-Bahar S H, Bayat M, 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]. Journal of Clinical Urology, 2019, 13(2): 125-131.
16. Jendoubi A, Malouch A, Bouzouita A, et al. [Safety and efficacy of intravenous tranexamic acid in endoscopic transurethral resections in urology: Prospective randomized trial] [J]. Prog Urol, 2017, 27(16): 1036-1042.
17. Meng Q Q, Pan N, Xiong J Y, et al. Tranexamic acid is beneficial for reducing perioperative blood loss in transurethral resection of the prostate [J]. Exp Ther Med, 2019, 17(1): 943-947.
18. Mirmansouri A F F, Imantalab V, Et Al. A Survey on the Effects of Intravenous Tranexamic Acid on the Amount of Transfusion in Patients Undergoing T.U.R-P. [J]. Journal of Guilan University of Medical Sciences, 2016, 98(110-116.
19. Samir M, Saafan A M, Afifi R M, et al. Can high-dose tranexamic acid have a role during transurethral resection of the prostate in large prostates? A randomised controlled trial [J]. Arab Journal of Urology, 2022, 20(1): 24-29.
20. Pravin R P, S V Kansal, M Chaudhary,Et Al. Comparative study of role of pre-operative injection tranexamic acid in 80 cases of transurethral resection of prostate [J]. Int J Sci Study, 2016, 4(2): 167-170.

21. Rannikko A, Petas A, Taari K. Tranexamic acid in control of primary hemorrhage during transurethral prostatectomy [J]. Urology, 2004, 64(5): 955-958.