

PERIOPERATIVE HAEMORRHAGE IN TRANSURETHRAL RESECTION OF PROSTATE: IMPACT OF 5 ALPHA REDUCTASE INHIBITORS IN THE REDUCTION OF PERIOPERATIVE BLOOD LOSS

Mohamad Anish Ahamad,^{1*} Jonesh Tiwari,² Emran Ansari,³ Manisha Joshi⁴¹ Department of Urology, National Medical College and Teaching Hospital, Birgunj, Parsa, Nepal.² Seti Provincial Hospital, Dhangadhi, Kailali. Nepal.³ Birat Medical College, Biratnagar, Nepal.⁴ United Hospital, Kapilvastu, Nepal.**Date of Submission** : April 18, 2023**Date of Acceptance** : July 14, 2023**Date of Publication** : July 28, 2023***Correspondence to:**

Mohamad Anish Ahamad, Department of Urology, National Medical College and Teaching Hospital, Birgunj, Parsa, Nepal.

Phone: +977-9865067766

Email: anish7901@gmail.com

Citation:

Ahmad MA, Tiwari J, Ansari E, Joshi M. Perioperative Haemorrhage in Transurethral Resection of Prostate: Impact of 5 Alpha Reductase Inhibitors in the Reduction of Perioperative Blood Loss. Medphoenix. 2023;8(1):21-25

DOI: <https://doi.org/10.3126/medphoenix.v8i1.56873>**Conflict of interest:** None, **Funding:** None**Publisher:** National Medical College Pvt. Ltd. **MedPhoenix - Journal of National Medical College (JNMC); 2023,8(1), available at www.jnmc.com.np**

ISSN:2631-1992 (Online); ISSN:2392-425X (Print)



This work is licensed under a Creative Commons Attribution 4.0 International License.

**ABSTRACT****Introduction:** Benign prostatic hyperplasia (BPH) is an age dependent disorder characterized by hyperplastic changes in the tissue resulting in enlargement of the prostate that may lead to difficulty in micturition or impairment in the flow of urine from the bladder. Medical treatment is the primary option for the patient with mild to moderate voiding symptoms which consists of alpha blockers and 5-alpha reductase inhibitors either as mono-therapy or in combination therapy.**Materials and Methods:** A observational cross-sectional study was conducted in a teaching hospital. Total sixty-four patients were selected from hospital records. Group-A received Alpha blocker along with Dutasteride two weeks prior to transurethral resection of prostate for benign prostatic hyperplasia. Patients were followed up after 24 hours of surgery in which hematocrit levels were estimated. Blood loss was calculated by recording pre-operative and post-operative (after 24 hours) hematocrit level. Data were tabulated and analyzed by SPSS v25. Comparison of two groups' Group A Alpha-blocker with Dutasteride and Group B with Alpha-blocker only was done by applying independent sample t-test. A p-value ≤ 0.05 was taken as significant.**Results:** A total of 64 patients were enrolled for this study. Patients were divided into two groups i.e. Group-A (TURP with Alpha-blocker & Dutasteride) and Group-B (TURP with Alpha-blocker). Mean age of group-A patients was 66.4 ± 7.5 years and 66.5 ± 7.2 years in group-B. Mean blood loss of group-A patients was 158.3 ± 131.1 ml and 311.5 ± 150.7 ml in group-B with a p-value of 0.000054, which is statistically significant.**Conclusion:** Patients on Dutasteride have less perioperative bleeding during transurethral resection of prostate for benign prostatic hyperplasia.**Keywords:** Transurethral Resection of Prostate, Alpha-blocker, Dutasteride, Benign Prostatic Hyperplasia**INTRODUCTION**

Benign prostatic hyperplasia (BPH) sometimes also known as benign prostatic hypertrophy, is an age dependent disorder characterized by hyperplastic changes in the tissue resulting in enlargement of the prostate that may lead to difficulty in micturition or impairment in the flow of urine from the bladder.¹ Growth of prostate is dependent upon androgen hormone dihydrotestosterone which is active metabolite of testosterone that is formed by the action of two 5-alpha reducing isoenzyme, 5-alpha reductase type I and type II.² Traditional theory regarding benign prostatic hyperplasia suggests that as the prostate increases in size the capsule surrounding the gland prevents it from expanding radially and ultimately resulting in bladder outlet obstruction.²

Medical treatment is the primary option for the patient with mild to moderate voiding symptoms

which consists of alpha blockers and 5-alpha reductase inhibitors either as mono-therapy or in combination therapy.³ Phosphodiesterase type-5 inhibitor and anticholinergic agents as other alternatives. Type 1 and type 2 isoenzymes of 5 alpha-reductase are present throughout the body and Dutasteride, a dual 5 alpha-reductase inhibitor acts competitively and specifically on type 1 and type 2 isoenzymes to inhibit the conversion of testosterone to the more potent dihydrotestosterone.⁴

The American Urology Association recommends for surgical option if medical treatment fails or patient develops BPH related complications such as hematuria, urinary retention, recurrent urinary tract infection or bladder calculi.⁵ The different surgical approaches for the BPH comprises of open prostatectomy, transurethral resection of prostate (TURP), transurethral incision of

prostate (TUIP), holmium laser enucleation of prostate (HoLEP) and newer robotic techniques.⁶

BPH is characterized by increased proliferation of stromal and acinar cells around the urethra, prolonged by increased gland angiogenesis. The increased vascularity can result in massive bleeding during and after TURP. Finasteride α 5-ARI inhibits the conversion of testosterone to DHT and the resulting activation of androgen-controlled growth factor, which stimulates angiogenesis.⁷ Preoperative 5 alpha reductase inhibitor treatment has been reported to reduce this bleeding. It reduced the expression of VEGF and lowered the sub-urethral microvessel density of the prostate.⁸

MATERIALS AND METHODS

Observational cross-sectional study was conducted from 17th October 2022 to 16th April 2023. After approval of the research proposal, from ethical committee [Ref F-NMC/610/079-080], sixty-four patients fulfilling inclusion criteria were selected from outpatient, Urology unit, Department of Surgery, National Medical College and Teaching Hospital, Birgunj, Nepal. Patients were divided into two groups: thirty-two in each group, Group A comprising of patients who were receiving treatment alpha-blockers and dutasteride (0.5mg daily) for at least two weeks before surgery whereas Group B were receiving alpha-blocker only.

Patients were included, Age 55-80 years, unresponsive to medical therapy, enlarged prostate (40-70 grams) with absolute indication for surgery, PSA within normal limit and preoperative creatinine <1.5mg/dl and INR <1.5. Patients were excluded who had bleeding disorder, chronic liver disease and co-morbidities as hypertension and diabetes mellitus.

Informed consent about the study was taken from the patient. Demographic data/information was recorded from hospital record. Investigations included complete blood picture, urine complete examination and ultrasonography abdomen and pelvis. Pre-operative hematocrit of each study patient was recorded. surgery was performed by Uro-Surgeon under spinal anesthesia. As recommendation, cystoscopy was done first with proper lubrication, resection of prostate was done with monopolar resectoscope using glycine as irrigation fluid. After completion of resection of gland, proper hemostasis was done by coagulation electrode followed by three-way catheterization and irrigation with Normal saline was started. Patients were followed up after 24 hours of surgery in which hematocrit levels were estimated. Blood loss was calculated by recording pre-operative and post-operative (after 24 hours) hematocrit level.

Data were tabulated and analyzed by SPSS v25. The

quantitative data like age and duration of operation were presented in the form of mean. Qualitative variable like gender was presented as frequency and percentages. Comparison of two groups' Group A with Dutasteride and Group B without Dutasteride was done by applying independent sample t-test. A p-value ≤ 0.05 was taken as significant.

RESULTS

A total of 64 patients were enrolled for this study. Patients were divided into two groups i.e. Group-A (TURP with Dutasteride along with alpha-blocker) and Group-B (TURP with alpha-blocker only). Mean age of group-A patients was 66.4 \pm 7.5 years and 66.5 \pm 7.2 years in group-B.

Mean IPSS of group-A patients was 23.9 \pm 2.0 and 21.1 \pm 2.3 years in group-B with a p-value of 0.000006, which is statistically significant.

Mean blood hemoglobin of group-A patients was 12.9 \pm 1.7 g/dl and 12.9 \pm 2.1 g/dl in group-B with a p-value of 0.895, which is statistically insignificant.

Mean blood hematocrit at baseline of group-A patients was 38.5 \pm 4.3% and 38.9 \pm 5.6% in group-B with a p-value of 0.728, which is statistically insignificant.

Mean urine complete examination of group-A patients was 9.5 \pm 5.1 pus cells/HPF and 9.5 \pm 6.2 pus cells/HPF in group-B with a p-value of 0.965, which is statistically insignificant.

Mean ultrasound abdomen/pelvis of group-A patients was 56.1 \pm 11.1 gm prostate and 52.8 \pm 9.3 gm prostate in group-B with a p-value of 0.203, which is statistically insignificant.

Mean blood hematocrit after 24 hours of group-A patients was 35.4 \pm 4.0% and 32.9 \pm 6.8% in group-B with a p-value of 0.081, which is statistically insignificant.

Mean blood loss of group-A patients was 158.3 \pm 131.1 ml and 311.5 \pm 150.7 ml in group-B with a p-value of 0.000054, which is statistically significant.

In group-A, mean blood hematocrit at baseline was 38.5 \pm 4.3% and 35.4 \pm 4.0% after 24 hours with a p-value of 0.0000001, which is statistically significant.

In group-B, mean blood hematocrit at baseline was 38.9 \pm 5.6% and 32.9 \pm 6.8% after 24 hours with a p-value of 0.000067, which is statistically significant.

Table 1 : Comparing mean of parameters between two groups.

	Group A	Group B	P-Value
Mean age	66.4±7.5	66.5±7.2	0.948
IPSS	23.9±2.0	21.1±2.3	0.00006
Mean Blood hemoglobin	12.9±1.7 g/dl	12.9±2.9 g/dl	0.895
Mean Blood hematocrit baseline	38.5±4.3%	38.9±5.6%	0.728
Mean Prostate size	56.1±11.1gm	52.8±9.3gm	0.203
Mean Blood hematocrit after 24 hours	35.4±4.0%	32.9±6.8%	0.081
Mean Blood loss after 24 hours	158.3±131.1ml	311.5±150.7ml	0.00054

DISCUSSION

TURP still represents the gold standard in the surgical treatment of symptomatic BPH. One of the most important complications of TURP is intra- and perioperative bleeding, which sometimes leads to urine retention because of blood clots. BPH is characterized by increased proliferation of stromal and acinar cells around the urethra sustained by increased gland vascularity (neovascularity).

Some studies demonstrated the effect of finasteride in reducing BPH-related hematuria.^{9,10,11} Finasteride, which blocks the conversion of testosterone to dihydrotestosterone, decreases the activity of androgen-controlled growth factors responsible for angiogenesis.

This feature was used to prevent intra-operative bleeding in patients undergoing TURP. Some studies supported the pharmacological use of finasteride to reduce surgical blood loss.^{12,13} Dutasteride is an inhibitor of type 1 and 2 isoenzymes of 5-alpha reductase commonly used, as is finasteride, for treatment of symptomatic BPH.

Some studies attempted to resolve whether dutasteride could be used to reduce bleeding after TURP in the same way that finasteride is.^{13,14} Hahn et al used dutasteride for 2–4 weeks before TURP without significant reduction in blood loss compared to the placebo group.¹⁶

Various studies have been done but they show conflicting results. In one study use of 0.5 mg Dutasteride preoperatively resulted in significantly lower blood loss compared to control (p value <0.0491).¹⁷ While in another study they have found there was no difference in blood loss between treatment and control group (p value >0.98).¹⁸

Other authors have confirmed these results, concluding that a short-term treatment with dutasteride was not superior compared to the control group in decreasing TURP-related blood loss, and suggested that a longer

duration treatment will reduce intra-operative and postoperative bleeding.¹⁹

Martov found a significant reduction in blood loss in patients by using dutasteride for at least 1 month before TURP compared to the control group.²⁰ Kravchick demonstrated that 6 weeks of treatment with dutasteride reduced prostatic vascularity, especially in the peri-urethral area.²¹

In the study conducted by Kim lower mean blood loss was observed in the dutasteride group immediately after and 24 hours after surgery peri operative and post-operative bleeding were significantly reduced in the group taking dutasteride for 2 weeks before TURP.

There were no significant effects on prostate volume or resected prostate volume, statistically meaningful difference were not detected between the 2 groups in PT, aPTT, INR and BT and based on these results, dutasteride may only affect vascularity related bleeding during TURP.²²

Based on these evidences, we attempted to evaluate if pretreatment with dutasteride (0.5mg/day) for 2 weeks before TURP could reduce surgical bleeding.

The results of the present study showed that treatment with dutasteride for 2 weeks before TURP reduces surgical bleeding. No differences were found with regard to prostatic volume, prostate resected weight, and operation time between the groups A & B.

CONCLUSION

BPH is a common problem of the ageing males. Since from the start of the endoscopic resection of enlarged prostate i.e. TURP, the surgeons have been much concerned with the bleeding during and after the procedure. Many studies reported that preoperative Dutasteride has an impact on perioperative hemorrhage during TURP for benign prostatic hyperplasia but it is still controversial.

We conducted a study to observe if two weeks of pretreatment with Dutasteride significantly reduces perioperative bleeding during procedure. The results were compared with another group of patients undergoing TURP without having preoperative Dutasteride.

The result concludes that patients on Dutasteride has less perioperative bleeding during transurethral resection of prostate for benign prostatic hyperplasia.

REFERENCES

1. Dhingra N, Bhagwat D. Benign prostatic hyperplasia: An overview of existing treatment. Indian journal of pharmacology. 2011 Feb;43(1):6

2. Vignozzi L, Rastrelli G, Corona G, Gacci M, Forti G, Maggi M. Benign prostatic hyperplasia: a new metabolic disease?. *Journal of endocrinological investigation*. 2014 Apr;37:313-22.
3. Bishr M, Boehm K, Trudeau V, Tian Z, Dell'Oglio P, Schiffmann J, Jeldres C, Sun M, Shariat SF, Graefen M, Saad F. Medical management of benign prostatic hyperplasia: Results from a population-based study. *Canadian Urological Association Journal*. 2016 Jan;10(1-2):55.
4. Zaitu M, Tonooka A, Mikami K, Hattori M, Takeshima Y, Uekusa T, Takeuchi T. A dual 5 α -reductase inhibitor dutasteride caused reductions in vascular density and area in benign prostatic hyperplasia. *International Scholarly Research Notices*. 2013;2013..
5. Fonseca J, Martins da Silva C. The diagnosis and treatment of lower urinary tract symptoms due to benign prostatic hyperplasia by primary care family physicians in Portugal. *Clinical drug investigation*. 2015 Feb;35:19-27.
6. Michalak J, Tzou D, Funk J. HoLEP: the gold standard for the surgical management of BPH in the 21st century. *American journal of clinical and experimental urology*. 2015;3(1):26.
7. Gökçe Mİ, Kerimov S, Akıncı A, Hamidi N, Afandiyev F, Yaman Ö. Effect of dutasteride treatment on reducing blood loss and in perioperative period of open prostatectomy. *Turkish journal of urology*. 2015 Mar;41(1):24.
8. Kim KS, Jeong WS, Park SY, Kim YT, Moon HS. The effect of two weeks of treatment with dutasteride on bleeding after transurethral resection of the prostate. *The world journal of men's health*. 2015 Apr 1;33(1):14-9.
9. Ekman P. Finasteride in the treatment of benign prostatic hypertrophy: an update: New indications for Finasteride therapy. *Scandinavian Journal of Urology and Nephrology*. 1999 Jan 1;33(203):15-20.
10. Miller MI, Puchner PJ. Effects of finasteride on hematuria associated with benign prostatic hyperplasia: long-term follow-up. *Urology*. 1998 Feb 1;51(2):237-40.
11. Hagerty JA, Ginsberg PC, Harmon JD, Harkaway RC. Pretreatment with finasteride decreases perioperative bleeding associated with transurethral resection of the prostate. *Urology*. 2000;55(5):684-7.
12. Crea G, Sanfilippo G, Anastasi G, Magno C, Vizzini C, Inferrera A. Pre-surgical finasteride therapy in patients treated endoscopically for benign prostatic hyperplasia. *Urologia internationalis*. 2005;74(1):51-3.
13. Donohue JF, Sharma H, Abraham R, Natalwala S, Thomas DR, Foster MC. Transurethral prostate resection and bleeding: a randomized, placebo-controlled trial of role of finasteride for decreasing operative blood loss. *The Journal of urology*. 2002;168(5):2024-6.
14. Boccon-Gibod L, Valton M, Ibrahim H, Comenducci A. Effect of dutasteride on reduction of intraoperative bleeding related to transurethral resection of the prostate. *Progres en urologie: journal de l'Association francaise d'urologie et de la Societe francaise d'urologie*. 2005;15(6):1085-9.
15. Tuncel A, Ener K, Han O, Nalcacioglu V, Aydin O, Seckin S, et al. Effects of short-term dutasteride and Serenoa repens on perioperative bleeding and microvessel density in patients undergoing transurethral resection of the prostate. *Scandinavian journal of urology and nephrology*. 2009;43(5):377-82.
16. Hahn RG, Fagerström T, Tammela TL, Van Vierssen Trip O, Beisland HO, Duggan A, et al. Blood loss and postoperative complications associated with transurethral resection of the prostate after pretreatment with dutasteride. *BJU international*. 2007;99(3):587-94.
17. Pastore AL, Mariani S, Barrese F, Palleschi G, Valentini AM, Pacini L, et al. Transurethral resection of prostate and the role of pharmacological treatment with dutasteride in decreasing surgical blood loss. *Journal of endourology*. 2013;27(1):68-70.
18. Jamal A, Srinivasarao P, Dorairajan LN, Kumar S. Is transurethral resection of prostate made safer by preoperative dutasteride therapy? a randomized controlled trial. *International Journal of Contemporary Medical Research*.3:1254-7.
19. Shanmugasundaram R, Singh JC, Kekre NS. Does dutasteride reduce perioperative blood loss and postoperative complications after transurethral resection of the prostate?. *Indian Journal of Urology*. 2007 Jul 1;23(3):334-5.
20. Martov AG, Ergakov DV. The experience in dutasteride use before transurethral prostatic resection for large adenoma. *Urologiia (Moscow, Russia)*: 1999). 2008 Jul 1(4):46-8.
21. Kravchick S, Cytron S, Mamonov A, Peled R, Linov

L. Effect of short-term dutasteride therapy on prostate vascularity in patients with benign prostatic hyperplasia: a pilot study. *Urology*. 2009;73(6):1274-8.