Effect of Preoperative Finasteride on the Volume or Length Density of Prostate Vessels, Intraoperative and Postoperative Blood Loss during and after Monopolar Transurethral Resection of Prostate: A Dose Escalation Randomized Clinical Trial Using Stereological Methods

Alireza Aminsharifi,[1,2]* Alireza Salehi,[3] Ali Noorafshan,[4] Amirhossein Aminsharifi,[5] Khalil Alnajar[1]

Purpose: To evaluate the effects of two preoperative treatment courses with Finasteride on intraoperative and postoperative bleeding complications and prostate blood vessel characteristics in men who underwent transurethral resection of prostate (TURP) using monopolar energy.

Materials and Methods: Men scheduled for TURP were randomized into group 1 (control n = 25, no medication), group 2 and 3 (n = 20 in each, 5 mg Finasteride daily for 2 and 4 weeks before TURP; respectively). Hematocrit level in the irrigation fluid, weight of the resected prostate chips, decreases in blood hemoglobin (Hb) level 6 and 24 hours after the operation together with volume and length density of prostate vessels using stereological methods were compared.

Results: The three groups were matched regarding preoperative demographic data, resection time and weight of the resected tissue. Men who received preoperative Finasteride (groups 2 and 3) had significantly lower hematocrit levels in irrigation fluid than control group (control, 0.59 ± 0.85, group 2, 0.25 ± 0.4, group 3, 0.175 ± 0.16; *P* = .028; Power = .80). However, no statistically significant difference was found in hematocrit level in irrigation fluid between groups 2 and 3 (0.25 ± 0.4 vs. 0.175 ± 0.16, 95% confidence interval (CI) = -0.28-0.42; *P* = .68). These values were independent of the weight of the resected tissue and resection time. There were no significant differences between the three groups in the decrease in Hb 6 hours (*P* = .58) and 24 hours after TURP (*P* = .65). The stereological and histological characteristics of blood vessels in suburethral prostate tissue were similar in all three groups.

Conclusion: A 2-week preoperative course of daily Finasteride seems sufficient to significantly reduce intraoperative blood loss; this effect was independent of the weight of the resected tissue and resection time. Neither the 2-week nor the 4-week presurgical Finasteride regimen could significantly decrease postoperative blood loss, and neither regimen induced significant changes in characteristics of prostate tissue blood vessels.

Keywords: postoperative complications; prostatic hyperplasia; surgery; transurethral resection of prostate; methods; adverse effects; treatment outcome; hemorrhage.

INTRODUCTION

Transurethral resection of the prostate (TURP) is the gold standard procedure for the surgical management of symptomatic benign prostatic hyperplasia (BPH) intractable to medical therapy. Intraoperative and postoperative bleeding, one of the most common complications of TURP, may result in poor intraoperative visualization, hemodynamic instability, clot retention and the need for surgical reexploration.(1) During the previous 3 decades, several modalities such as instillation of coagulating or sclerosing agents (e.g. fibrin adhesives, premarin or phenol solution) as well as maneuvers such as catheter traction have been proposed to reduce the bleeding complications of TURP. These strategies, although they may be effective, can also be difficult to use or may have critical consequences such as scar formation in the prostatic fossa.(2) Thanks to the modulating effect of 5-alpha-reductase inhibitors on angiogenesis growth factors in the prostate, these agents have attracted attention for the treatment of BPH-associated gross hematuria. It has been shown that exposure of the prostate to Finasteride for as little as 2 weeks is associated with reduced expression of vascular endothelial growth factor (VEGF) (a potent angiogen-

Department of Urology,[1] Stem Cell and Transgenic Technology Research Center,[2] Department of Epidemiology,[3] and Histomorphometry and Stereology Research Center,4 Shiraz University of Medical Sciences, Shiraz, Iran.
[5] General Internal Medicine, Toronto General Hospital, Toronto, Canada.
*Correspondence: Shaheed Faghihi Hospital, Zand Street, Shiraz, Iran.
Tel: +98 917 7000656. Fax: +98 711 2331006. E-mail: aminsharifi_ar@yahoo.com.
Received June 2015 & Accepted November 2015

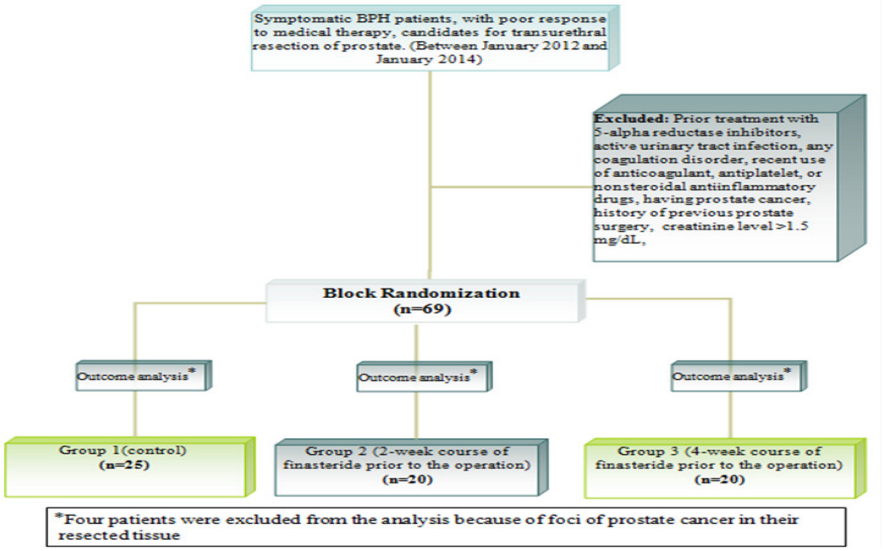

Figure 1. Patient allocation during study.

esis growth factor) and reduced microvascular density (MVD) in the prostate tissue.[3] A few recent studies have been designed to address the clinical effects of preoperative treatment with 5-alpha-reductase inhibitors on bleeding complications of TURP, with variable outcomes. An optimum preoperative treatment course has yet to be proposed.

In the present study we evaluated the potential effects of Finasteride on bleeding complications of TURP. We assessed two preoperative treatment courses to define an optimum dose, and analyzed intraoperative and postoperative variables to determine the amount of bleeding in both periods. At the same time, we used stereological and histological methods to evaluate the suburethral prostatic tissue with regard to blood vessel characteristics, and to gain insights into the physiopathological mechanisms of the effect of Finasteride.

MATERIALS AND METHODS

Ethics

Before the study we obtained approval from our institutional review board. All patients were informed about the purpose of the study and provided their informed consent.

Patients

Between January 2012 and January 2014, all men with an enlarged prostate who had moderate to severe lower urinary tract symptoms with a poor response to medical therapy with α1a-blockers were considered for inclusion. These patients referred to the university clinics of Shiraz University of Medical Sciences, Shiraz, Iran. The exclusion criteria were prior treatment with 5-alpha reductase inhibitors, active urinary tract infection, any coagulation disorder, and recent use of anticoagulant, antiplatelet, or nonsteroidal anti-inflammatory drugs. Men who were diagnosed as having prostate cancer or who had a history of previous prostate surgery, or with a creatinine level of > 1.5 mg/dL, were also excluded (**Figure 1**).

Study Design and Surgical Procedure

This clinical trial was designed in accordance with the CONSORT statement and guidelines. The patients were randomized by block randomization using sequentially numbered containers (block size = 3) to three groups. The random allocation sequence and participant enrollment and assignment to surgery were managed by different individuals (AS and MKA, respectively). Patients in group 1 (control) received no medication whereas those in group 2 and group 3 took 5 mg daily Finasteride (Soha pharmaceutical company, Karj, Iran), for 2 weeks and 4 weeks, respectively prior to TURP. The surgeon, histopathologist and laboratory technicians were blinded to the group assignment (**Figure 1**). Before the operation the patients' lower urinary tract symptoms were scored with the International Prostate Symptom Score (IPSS) Questionnaire. All patients underwent cystoscopic evaluation of the lower urinary tract, and prostate volume was recorded by transrectal ultrasonography just before TURP. The operation was done with the patient in the lithotomy position under general anesthesia in all cases. All surgeries were done by the same surgeon (AA) with a 24 French (F) resectoscope (Richard Wolf GmbH, Knittlingen, Germany) using monopolar energy.

Table 1. Characteristics of 65 men in a trial of finasteride to reduce intraoperative blood loss during transurethral resection of the prostate in Iran, January 2012 to January 2014.

Variables	Group 1 (Control)	Group 2 (Finasteride 2 Weeks)	Group 3 (Finasteride 4 Weeks)	*P* Value
Mean age ± SD, years	68.8 ± 11.3	66.1 ± 10.9	67.1 ± 6.0	.65
Mean PSA ± SD, ng/mL	2.95 ± 3.91	1.40 ± 1.29	3.80 ± 4.9	.13
Prostate volume, mL	43.8 ± 13.7	45.7 ± 16.04	49.2 ± 15.2	.49
Mean preoperative Hb, g/dL	13.8 ± 1.8	14.0 ± 1.75	14.6 ± 1.9	.31
Mean IPSS ± SD	22.6 ± 7.21	23.1 ± 7.22	21.6 ± 8.54	.35

Abbreviations: IPSS, International Prostate Symptom Score; PSA, prostate specific antigen; SD, standard deviation; Hb, hemoglobin.

Study Outcomes

Demographic data as well as prostate-specific antigen (PSA) level, IPSS score, prostate volume and operative time were recorded. To evaluate intraoperative bleeding (primary outcome), the returned irrigation fluid was collected from the initiation until the termination of prostate resection and hematocrit level was measured in a 10-mm sample. The weight of the resected prostate chips was also recorded. To estimate overall postoperative blood loss, the decrease in blood hemoglobin (Hb) level was calculated by comparing preoperative Hb with 6-hour and 24-hour postoperative Hb.

Stereological Study

The stereological methods were used to obtain length density and volume density of the vessels per mm3 of the prostate tissue. The method provides reliable, comparable quantitative data.[4,5] The estimation of microvessel volume density does not require isotropic uniform random (IUR) sections, but IUR sections are necessary to estimate length density of the vessels. These sections were obtained by the orientator method.[4,5] Briefly, to generate IUR sections, tissue samples of the prostate cylinder were located in the center of a circle with 10 equidistant divisions around the circumference. A random number between 0 and 10 was selected and the each piece of tissue was excised in the selected direction. The first cut edge of the tissue was placed parallel to the 0–0 direction of a second circle with 10 sine-weighted nonequidistant divisions around the circumference. A new random number between 0 and 10 was chosen and a specimen was cut in the new direction. This new cut surface was the isotropic face of the tissue. The tissue pieces were embedded in a paraffin block from the isotropic face, and sections (4 µm thick-

Table 2. Intraoperative, postoperative and stereohistomorphologic variables in 65 men in a trial of finasteride to reduce intraoperative blood loss during transurethral resection of the prostate in Iran, January 2012 to January 2014.

Variables	Group 1 (Control)	Group 2 (Finasteride 2 Weeks)	Group 3 (Finasteride 4 Weeks)	*P* Value
Resection time, min	43.4 ± 20.7	39.3 ± 10.9	42.3 ± 15.4	.69
Mean irrigating fluid hematocrit, %	0.59 ± 0.85	0.25 ± 0.4	0.175 ± 0.16	.028 (Power = 0.80)
Mean resection weight, g	14.4 ± 3.9	14.9 ± 4.7	15.7 ± 6.1	.65
Mean irrigating fluid hematocrit/g resection weight	0.044 ± 0.068	0.018 ± 0.017	0.012 ± 0.012	.04 (Power = 0.89)
Mean irrigating fluid hematocrit/min resection time	0.016 ± 0.022	0.007 ± 0.006	0.004 ± 0.004	.02 (Power = 0.93)
Mean postoperative hemoglobin decrease, g/dL				
Preoperative-6 hour postoperative	0.88 ± 0.65	0.73 ± 0.74	0.98 ± 0.93	.58
Preoperative-24 hour postoperative	1.38 ± 0.79	1.13 ± 0.96	1.24 ± 0.98	.65
Stereological and histological vascular findings in the suburethral prostate tissue				
Mean volume density of the vessels, mm^3/mm^3	0.04 ± 0.02	0.06 ± 0.02	0.03 ± 0.01	.41
Mean length density, mm/mm^3				
Vessels smaller than 10 µm in diameter	46.8 ± 26.6	51.0 ± 26.5	62.5 ± 29.8	.63
Vessels larger than 10 µm in diameter	13.7 ± 7.6	11.1 ± 3.4	12.5 ± 7.3	.35

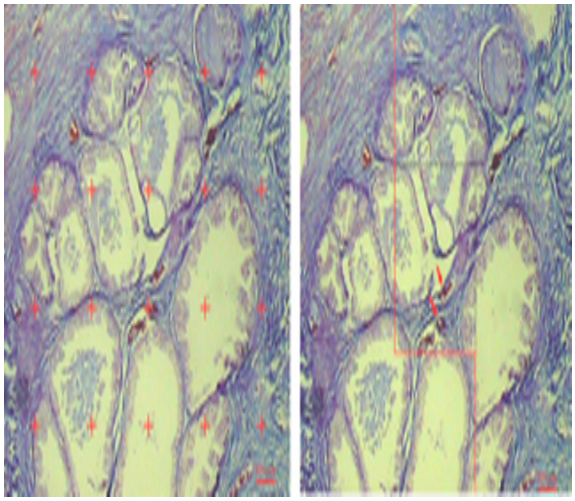

Figure 2. Stereological estimates of prostatic tissue stained with Heidenhain's AZAN trichrome stain. Left) Point-counting method; Right) Length density estimate of vessels using the counting frame. The arrows indicate accepted vessel profiles.

ness) were cut and stained with Heidenhain's AZAN trichrome. Volume density of the microvessels was estimated with the stereological software. The stereological probes consisted of points that were superimposed on the images of the tissue sections, and were viewed on a monitor at a final magnification of 1800 × (**Figure 2**). Volume density (Vv) was obtained with the following formula:[4,5]

Vv (vessels) = P(vessels) / P(reference)

where P(vessels) indicates the number of points hitting the vessels and P(reference) is the number of points hitting the prostatic tissue.

To estimate the length density of the vessels. (Lv (vessels)), an unbiased counting frame was superimposed on the images of the tissue sections viewed on a monitor and the following formula was used (**Figure 1**): Lv (vessels) = 2ΣQ/ΣA

where ΣQ is the total number of vessel profiles counted that fell within the counting frame and did not touch the left and lower borders, and ΣA is the area of all counting frames. Vessel diameters were measured on the vessels sampled in the unbiased counting frame used to estimate length. The diameter was measured perpendicular to the long axis of vessels where the vessel was widest. Length density was categorized as less than or more than 10 µm to distinguish between capillaries and larger vessels.

Statistical Analysis

Parametrical tests were used as long as their assumptions were verified. Selected endpoints were compared among the three treatment groups with one-way ANOVA. To search for possible differences in different variables within groups, one-way ANOVA and paired t-tests were used. The stereological data were analyzed with the Mann-Whitney *U* test. All data analyses were done with Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 16.0 software and study power was calculated with SAS® v. 9.1 software.

RESULTS

During the study period, 69 patients were randomized to one of the three groups. Four patients were excluded from the trial because of foci of prostate cancer in their resected tissue, and data for the remaining 65 patients (group 1 n = 25, groups 2 and 3, n = 20 each) were analyzed (**Figure 1**). All three groups were similar with regard to preoperative demographic data including age, IPSS, PSA, prostate volume, and preoperative serum Hb level (**Table 1**). There were no differences between groups in resection time, weight of the resected tissue or hospital stay, and no patient required intraoperative or postoperative blood transfusion (**Table 2**).

In patients who received preoperative Finasteride (groups 2 and 3), hematocrit in irrigation fluid was significantly lower than in control group (*P* = .028; Power = 0.80). However, no statistically significant differences were found in hematocrit level in the irrigation fluid between groups 2 and 3 (0.25 ± 0.4 vs. 0.175 ± 0.16, 95% confidence interval [CI] = -028-0.42; *P* = 0.68) (**Table 2**). The amount of intraoperative bleeding per gram of resected prostate (irrigation fluid hematocrit/weight of the resected prostate) was significantly greater in the control group (*P* = .04; Power = 0.89), and was similar in groups 2 and 3 (0.018 ± 0.017 vs. 0.012 ± 0.012, 95% CI = -0.02-0.033; *P* = .69) (**Table 2**). To adjust for the effect of resection time on intraoperative bleeding, we divided the irrigation fluid hematocrit by resection time. Again, intraopertive blood loss per minute of resection time was significantly higher in the control group (*P* = .02; Power = 0.93) and was similar in men who receive Finasteride for 2 weeks and 4 weeks (0.007 ± 0.006 versus 0.004 ± 0.004, 95% CI = -0.0066-0.011; *P* = .59) (**Table 2**). The change in serum Hb level was determined by comparing postoperative and preoperative values. Serum Hb decreased significantly 6 and 24 hours after TURP in all three groups (*P* < .001); however, there were no significant differences between the three groups in the decrease in Hb 6 hours (*P* = .58) and 24 hours after the operation (*P* = .65) (**Table 2, Figure 3**). There was no relationship between the postoperative decrease in Hb and resection time or

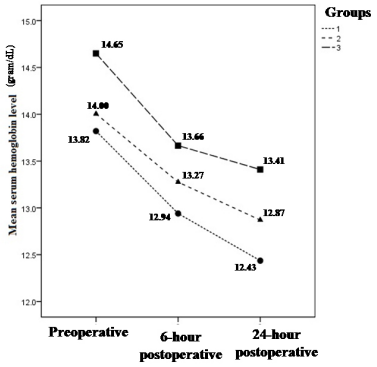

Figure 3. Preoperative, 6-hour and 24-hour postoperative hemoglobin values in three groups. Serum hemoglobin decreased significantly 6 and 24 hours after transurethral resection of prostate in all three groups; however, there were no significant differences between the three groups in the decrease in hemoglobin 6 hours and 24 hours after the operation.

weight of the resected tissue. No major complications were observed in any of the patients during their hospital course. The stereological and histological characteristics of blood vessels in the suburethral prostate tissue were similar in all three groups (**Table 2, Figure 2**).

DISCUSSION

Human fetal and animal studies have established that vascularity in the prostate is influenced by dihydrotestosterone (DHT), which induces the expression of vasoactive mediators such as VEGF by prostatic epithelial and stromal cells.[3,6,7] Increased VEGF expression and MVD in the suburethral prostatic tissue have been proposed as the main mechanisms of BPH-related intractable hematuria, i.e. the primary indication for TURP in 12% of patients.[7,8] This mechanism also explains why in these patients, hematuria recurs frequently (more than 60% in 1 year) if left untreated.[8] As a 5-alpha reductase inhibitor, Finasteride reduces the level of intraprostatic DHT. Lekas and colleagues have shown that after 10 weeks of treatment with Finasteride for prostate hyperplasia, MVD in the suburethral region as well as the level of VEGF are significantly reduced.[6] This angiostatic effect was also observed by Donohue and colleagues. after a 2-week treatment course before TURP.[3] Interestingly, Häggström and colleagues also noted a reduction in VEGF expression; however, consistent with Sandfeldt and colleagues they found no change in MVD after 3 months of treatment with Finasteride before TURP.[9,10] Using contrast-enhanced magnetic resonance imaging in an animal model, Jia and colleagues noninvasively evaluated prostatic suburethral microcirculation. In their dynamic imaging method, they found reduced blood perfusion after a 3-month course of Finasteride.[11]

Interest in presurgical medical interventions with 5-alpha-reductase inhibitors to reduce bleeding during or after TURP has paralleled our increased understanding of prostatic microcirculation. Perhaps Hagerty and colleagues were the first who, as early as 2000, subjectively described the potential benefits of preoperative treatment with Finasteride for 2 to 4 months for significant postoperative bleeding events, namely the need for blood transfusion, clot retention and persistent gross hematuria requiring treatment.[2] Özdal and colleagues in a comprehensive randomized clinical trial, documented the promising effects of 4-week presurgical treatment with Finasteride on both intraoperative and early postoperative bleeding in patients who underwent TURP. By measuring Hb concentration in the irrigation fluid and the postoperative decrease in Hb as surrogate markers of intraoperative and postoperative bleeding, respectively, they found that this benefit was independent of the resected prostate volume.[12]

Using similar surrogate markers, Donohue and colleagues demonstrated that a 2-week course of preoperative Finasteride significantly reduced intraoperative blood loss. However, they discerned no significant difference in the early postoperative decrease in Hb.[13] In contrast, Sandfeldt and colleagues after a 3-month presurgical course of Finasteride, found neither a decrease in average intraoperative blood loss nor any difference in MVD in the resected prostate tissue.[10]

Meanwhile, Lund and colleagues reported no benefit with a 3-month presurgical course of Finasteride in terms of a postoperative decrease in Hb.[14] Crea and colleagues reported a smaller postoperative decrease in Hb after a preoperative course of 8-10 weeks.[15] On the other hand, Pastore and colleagues found that a 6-week course of dutasteride prior to TURP was beneficial with regards to postoperative decrease in Hb.[16] Recently, the effectiveness of an 8 week course of dutastride before bipolar TUPR for reduction of preoperative blood loss was shown only in patients with large prostate (> 50 mL).[17]

There is no consensus regarding the optimum duration of preoperative treatment. Different trials have used courses ranging in duration between 2 weeks and 4 months. The discrepancies among studies were addressed in a recent Cochrane systematic review by Aboumarzouk and colleagues.[18] They found only 4 valid randomized clinical trials[3,10,12,13,18] and noted that the effect of Finasteride in different studies varied with regard to intraoperative and postoperative bleeding, and also with regard to histopathologic features of the pros-

tate tissue. To address the potential effect of Finasteride on bleeding complications of TURP and to determine whether this effect is dose dependent, we designed a 3-arm randomized trial to compare a 2-week versus a 4-week treatment course with a control group. We also recorded intraoperative and postoperative variables and used stereological and histological methods to compare blood vessel characteristics. We found that both 2-week and 4-week courses of Finasteride were able to significantly reduce intraoperative blood loss, and that the effect was independent of the weight of the resected tissue and resection time. However, the two regimens did not differ significantly in terms of reducing intraoperative blood loss. This finding is consistent with that of Donohue and colleagues,[13] and suggests that a course longer than 2 weeks may add no additional benefits in terms of reducing intraoperative blood loss. In our trial, there were no statistically significant differences between the three groups in the decrease in Hb after the operation. In other words, the potential positive effect of Finasteride was evident only during the operation. This finding parallels the results of some of previous studies.[13,14]

In contrast to Donohue and colleagues who observed significantly reduced MVD in prostate specimens treated with Finasteride for a period as short as of 2 weeks,[3] our findings with a computerized stereological and histological technique showed that both 2-week and 4-week courses of Finasteride were too short to affect the characteristics of the suburethral blood vessels. Previously, Sandfeldt and colleagues and Häggström and colleagues separately found no changes in MVD after treatment with Finasteride for 3 months.[9,10] Because a 2-4 week period is considered too brief to produce any significant involution of the prostatic tissue, we postulate that the Finasteride-induced reduction in intraoperative blood loss may originate mainly from a decrease in blood flow perfusion in the suburethral microcirculation. Further dynamic imaging studies with contrast-enhanced magnetic resonance imaging[11] will be necessary to elucidate the mechanism that underlies the angiostatic effect of short-course Finasteride treatment. Moreover, the impact of these preoperative protocols on the overall treatment costs seems worthy to be addressed.

CONCLUSIONS

In the present 3-arm randomized clinical trial, a 2-week preoperative course of daily Finasteride seemed sufficient to significantly reduce intraoperative blood loss; this effect was independent of the weight of resected tissue and resection time. Neither the 2-week nor the 4-week presurgical Finasteride regimen could significantly decrease postoperative blood loss, and neither regimen induced significant changes in the characteristics of prostate tissue blood vessels in stereological and histological studies.

Key Messages

1. A 2-week preoperative course of daily Finasteride seemed sufficient to significantly reduce intraoperative blood loss during transurethral resection of prostate.
2. This effect was independent of the weight of resected tissue and resection time.
3. Neither the 2-week nor the 4-week presurgical Finasteride regimen could significantly decrease postoperative blood loss, and neither regimen induced significant changes in the characteristics of prostate tissue blood vessels in stereological and histological studies.

ACKNOWLEDGMENTS

This study was supported by Shiraz University of Medical Sciences. The protocol has been registered in www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT01627522). This report is based on research done in partial fulfillment of the requirements for the specialty degree in urology (Dissertation no. 89-01-01-2395) awarded to Dr. Alnajar. We thank K. Shashok (Author AID in the Eastern Mediterranean) for improving the use of English in the manuscript.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. 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;167:999-1003.
2. Hagerty JA, Ginsberg PC, Harmon JD, Harkaway RC. Pretreatment with Finasteride decreases perioperative bleeding associated with transurethral resection of the prostate. Urology. 2000;55:684-9.
3. Donohue JF, Hayne D, Karnik U, Thomas DR, Foster MC. Randomized, placebo-controlled trial showing that Finasteride reduces prostatic vascularity rapidly within 2 weeks. BJU Int. 2005;96:1319-22.
4. Tschanz S, Schneider JP, Knudsen L. Design-based stereology: Planning, volumetry and sampling are crucial steps for a successful study. Ann Anat. 2014;196:3-11.
5. Karbalay-Doust S1, Noorafshan A. Stereological study of the effects of nandrolone decanoate on the rat prostate.

Micron. 2006;37:617-23.

6. Lekas AG, Lazaris AC, Chrisofos M, et al. Finasteride effects on hypoxia and angiogenetic markers in benign prostatic hyperplasia. Urology. 2006 ;68:436-41.
7. Pareek G, Shevchuk M, Armenakas NA, et al. The effect of Finasteride on the expression of vascular endothelial growth factor and microvessel density: a possible mechanism for decreased prostatic bleeding in treated patients. J Urol. 2000;169:20-3.
8. Foley SJ, Soloman LZ, Wedderburn AW, et al. A prospective study of the natural history of hematuria associated with benign prostatic hyperplasia and the effect of Finasteride. J Urol. 2000;163:496-8.
9. Häggström S, Tørring N, Møller K, et al. Effects of Finasteride on vascular endothelial growth factor. Scand J Urol Nephrol. 2002;36:182-7.
10. Sandfeldt L, Bailey DM, Hahn RG. Blood loss during transurethral resection of the prostate after 3 months of treatment with Finasteride. Urology. 2001;58:972-6.
11. Jia G, Heverhagen JT, Polzer H, et al. Dynamic contrast enhanced magnetic resonance imaging as a biological marker to noninvasively assess the effect of Finasteride on prostatic suburethral microcirculation. J Urol. 2006;176:2299-304.
12. Ozdal OL, Ozden C, Benli K, Gökkaya S, Bulut S, Memiş A. Effect of short-term Finasteride therapy on peroperative bleeding in patients who were candidates for transurethral resection of the prostate (TUR-P): a randomized controlled study. Prostate Cancer Prostatic Dis. 2005;8:215-8.
13. Donohue JF, Sharma H, Abraham R, Natalwala S, Thomas DR and Foster MC. Transurethral prostate resection and bleeding: A randomized, placebo controlled trial of the role of Finasteride for decreasing operative blood loss. J Urol. 2002;168:2024-6.
14. Lund L, Møller Ernst-Jensen K, Tørring N, Erik Nielsen J. Impact of Finasteride treatment on perioperative bleeding before transurethral resection of the prostate: a prospective randomized study. Scand J Urol Nephrol. 2005;39:160-2.
15. Crea G, Sanfilippo G, Anastasi G, Magno C, Vizzini C, Inferrera A. Pre-surgical Finasteride therapy in patients treated endoscopically for benign prostatic hyperplasia. Urol Int. 2005;74:51-3.
16. Pastore AL, Mariani S, Barrese F, et al. Transurethral resection of prostate and the role of pharmacological treatment with dutasteride in decreasing surgical blood loss. J Endourol. 2013;27:68-70.
17. Busetto GM, Giovannone R, Antonini G, et al. Short-term pretreatment with a dual 5α-reductase inhibitor before bipolar transurethral resection of the prostate (B-TURP): evaluation of prostate vascularity and decreased surgical blood loss in large prostates. BJU Int. 2015;116:117-23.
18. Aboumarzouk OM, Aslam MZ, Wedderburn A, Turner K, Hughes O, Kynaston HG. Should Finasteride Be Routinely Given Preoperatively for TURP? ISRN Urol. 2013;2013:458353.