

Original Research Article

Role of dutasteride (5-alpha-reductase inhibitor) in patients undergoing transurethral resection of prostate

Shafeen Majid Koul*, Imtiaz Shah, Omer Khurshid, Shehwar Majid Koul, Momin Shah

Department of Surgery, Acharya Shri Chander College of Medical Sciences Sidhra, Jammu and Kashmir, India

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*Correspondence:

Dr. Shafeen Majid Koul,

E-mail: drshafeenkoul@gmail.com

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ABSTRACT

Background: Bladder outflow obstruction due to benign prostate hyperplasia is the commonest urological condition affecting men over 50 years of age. Medical therapy is usually the first line management of BPH. The most frequent complication is encountered is perioperative bleeding and postoperative bleeding. Preoperative use of 5-alpha-reductase inhibitors like dutasteride to reduce surgical bleeding is still a topic of debate. The aim of this study was to evaluate whether pretreatment with dutasteride for 4 weeks prior to surgery can reduce surgical blood loss as well as post op blood loss and complications.

Methods: A total of 60 patients with BHP who were to undergo TURP were enrolled and randomized into 2 groups. The dutasteride group consisted of 30 patients who were treated with dutasteride (0.5mg) for 4 weeks before surgery and the control group consisted of 30 patients.

Results: The preoperative hemoglobin levels of cases and controls was done followed by postoperative hemoglobin. The average fall in hemoglobin was 0.9mg/dl in cases and 2.1mg/dl in controls. Concluding that group of patients taking dutasteride (cases) peri and post-operative surgical bleeding was significantly reduced on pretreatment of dutasteride for 4 weeks before TURP.

Conclusions: Many other surgical treatments are being developed for BHP, but TURP is the gold standard treatment. However, morbidity and blood loss are major potential complications and taking dutasteride 4 weeks prior to transurethral resection of prostate can be effective in reducing its complications.

Keywords: Benign prostatic hyperplasia, Bleeding, Dutasteride, TURP

INTRODUCTION

Symptomatic BPH is initially treated with pharmacotherapy with alpha adrenergic blockers, 5 alpha reductase inhibitors, or a combination of both. 5 alpha reductase has 2 isoenzymes type 1 and type 2 present throughout the body and dutasteride, a dual 5 alpha reductase inhibitor acts competitively and specifically on type 1 and type 2 iso enzymes to inhibit the conversion of testosterone to the more potent dihydrotestosterone.¹⁻³ In comparison with finasteride, a 5 alpha reductase inhibitor

selectively acting on type 2 isoenzyme, dutasteride is a 45 fold greater inhibitor of type 1 5 alpha reductase and a 2.5 fold greater inhibitor of type 2 5 alpha reductase.⁴⁻⁶

Benign prostatic hyperplasia (BHP) is a histological diagnosis that refers to the proliferation of smooth muscles and epithelial cells within the prostatic cell transition zone, with testosterone and DHT as primary androgen responsible in elderly men. Patients with BHP who do not respond to pharmacotherapy undergo TURP, the gold standard for surgical management of BHP, in

order to improve the symptoms of BOO. It has been seen that dutasteride reduced the prostatic tissue growth and suppresses the androgen controlled vascular endothelial growth factor (VEGF) leading to decreased angiogenesis and less prostatic bleeding.⁴⁻⁶

METHODS

Patients who underwent TURP for symptomatic BPH between January 2017 to July 2017 were enrolled in the study. All patients whose voiding symptoms did not improve after 3 months of treatment with alpha blockers underwent TURP. Subjects were excluded if they had renal failure, a history of using finasteride or dutasteride, previous invasive procedures of the prostate and patients on aspirin or antiplatelet drugs.

None of the patients in cases as well as the control had abnormal prostate specific antigen i.e. (≤ 4). Ultrasonography of abdomen and pelvis was performed to evaluate the prostate volume before undergoing TURP along with post voidal residual urine and bladder capacity. A routine hematological profile was done including hemoglobin before TURP and hemoglobin after TURP, PSA, prothrombin time (PT), activated partial thromboplastin time (Aptt), bleeding time (BT), international normalized ratio (INR), renal function tests (RFT), fasting blood sugar, electrolytes were also performed along with total leucocyte count (TLC) and differential leucocyte count (DLC).

Sixty patients were scheduled to undergo TURP were enrolled and divided into two groups. 30 patients (group 1) received dutasteride for 4 weeks before surgery and 30 patients (group 2) served as controls. Transurethral resection of prostate was performed under spinal anesthesia with a 26F Karl Storz double channel resectoscope. The prostate was resected from 11 o'clock position to 6 o'clock position both sides, median lobe was resected first using 1.5% glycine as irrigating fluid, with the depth of resection extending as far as the prostatic capsule. Hemoglobin (Hb) was checked one day before surgery and one day after surgery. Postoperative care was carried out using a 22 Fr 3 way indwelling foley's catheter which was inflated with approximately 20 to 25ml normal saline and a continuous 0.9% normal saline/1.5% glycine was used for bladder irrigation until the urine was clear for 12 to 48 hours in the postoperative period. The catheter was removed on third postoperative day and patients were discharged after voiding clear urine on removal of the catheter and thereafter.

The length of hospitalization, number of days of continuous bladder irrigation with normal saline, indwelling foley's catheter, international prostate specific score, quality of life, and caliber of urinary stream was assessed. The independent student's t-test and paired t-test was used to compare the categorical variables and a p-value of less than 0.05 was considered statistically significant.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were summarized as Mean \pm SD and categorical variables were expressed as frequencies and percentages. Graphically the data was presented by bar diagrams. Student's independent t-test and Paired t-test was employed to analyze the statistical differences in parametric data. A P-value of less than 0.05 was considered statistically significant.

RESULTS

None of the patients taking dutasteride suffered from side effects, there were no significant differences between the two groups i.e. (group 1) dutasteride administered group and (group 2) control group with respect to prostate volume, resected prostate volume, PSA, The length of hospitalization, number of days of continuous bladder irrigation, indwelling foley's catheter, international prostate specific score, quality of life, and peak flow rate. There were no postoperative side effects such as TURP- syndrome, acute urinary retention due to blood clots, blood transfusion was not required per operatively as well as post operatively in both the groups. The two groups had similar PT, Aptt, BT, and INR when checked the day before surgery. The mean operation time was almost 45 minutes and all the patients had continuous bladder irrigation immediately after TURP.

Table 1: Comparison based on preoperative Hb (g/dl) in cases and controls.

Hb (g/dL)	Mean	SD	Min	Max	P-value ^{\$}
Cases	12.6	1.85	8.0	15.7	0.475
Controls	12.9	1.63	9.2	15.5	

\$: P-value by Student's Independent t-test

Table 2: Intra-group comparison based on drop in Hb (g/dL) in cases and controls.

Group	Preop Hb		Post Hb		P-value
	Mean	SD	Mean	SD	
Cases	12.6	1.85	11.7	1.79	0.082
Controls	12.9	1.63	10.8	1.27	<0.001*

*Statistically Significant Difference (P-value<0.05); \$: P-value by Paired t-test

Comparison of preoperative hemoglobin Hb (gm/dl) was done in cases and controls, P value was calculated by independent student t-test (Table 1).

An intra group comparison based on drop in hemoglobin i.e. preoperative hemoglobin and postoperative hemoglobin in cases and controls was done with paired t-test, where p value was statistically significant in controls i.e. less than 0.001 (Table 2).

Average drop in hemoglobin Hb (g/dl) among two groups were calculated using students independent t-test where P value was found to statistically significant i.e. 0.001 (Table 3).

Table 3: Average drop in Hb (g/dL) postoperatively among two groups.

Drop in Hb (g/dL)	Mean	SD	Min	Max	P-value
Cases	0.9	0.342	0.4	2.2	0.001*
Controls	2.1	0.816	0.5	3.8	

*Statistically Significant Difference (P-value<0.05); \$: P-value by Student's Independent t-test

Concluding that group of patients taking dutasteride (cases) peri and post-operative surgical bleeding was significantly reduced on pretreatment of dutasteride for 4 weeks before TURP. The mean hospital stay, duration of indwelling urethral catheter and continuous bladder irrigation was the same in both the groups.

Both the groups had improved maximum urinary flow rate, volume of residual urine, international prostatic symptom score and quality of life.

DISCUSSION

TURP has long been the gold standard for surgical treatment of symptomatic BPH. Bleeding is the most common complication during TURP and in the post-operative period. Sometimes uncontrolled bleeding makes voiding difficult due to acute urinary retention of urine by the blood clots.

In BPH there is increased proliferation of stromal and acinar cells around the urethra, prolonged by increased gland androgen. The increased vascularity can result in massive bleeding during and after TURP. Dutasteride, a BPH medication is a 5 alpha reductase inhibitor. It inhibits the conversion of testosterone to DHT and the resulting activation of androgen controlled growth factors which stimulate angiogenesis. A significant reduction in blood loss when dutasteride was taken for over a month before surgery.⁷ In other studies it was observed that dutasteride treatment for 2 weeks before TURP reduced micro vessel density in the sub urethral region.⁸ Kravchick found that the vascularity of the prostate, especially in the periurethral area, was reduced after taking dutasteride for 6 weeks.⁹

Hahn showed that the perioperative administration of dutasteride had no effects on micro vessel density in prostate tissue of BPH patients given preoperative dutasteride for 2-4 weeks compared with placebo controls in a prospective randomized and multicenter study, where MVD was counted by the number of micro vessels.¹⁰

Zaitzu did a retrospective study to investigate effects of dutasteride administration before transurethral resection

of prostate in Japanese BPH patients. Serum PSA levels were less than 4.0ng/ml. the study did not detect differences in glandular density and the proportion of intraglandular area regardless of dutasteride administration. Such in the dutasteride treatment group, the period of dutasteride administration was 16.3+/-8.1 weeks and reduction on prostate volume was 28.2 %/-30.2%. No significant difference in operation time, amount of intravenous crystalloid infusion during TURP.¹¹

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.¹²

According to pastore patients with BPH who were to undergo TURP were enrolled and randomized into 2 groups. The dutasteride group comprising of 71 patients was treated with dutasteride 0.5mg/dl for 6 weeks before surgery and control group comprising of other 71 patients did not receive dutasteride.

The results showed that pretreatment with dutasteride for 6 weeks before TURP reduces the surgical bleeding considerably, as increased vascularity can result in massive bleeding during TURP. Pastore excluded the duration of continuous bladder irrigation and indwelling foley's catheter use and concluded that taking dutasteride before surgery is sufficient to reduce prostate tissue vascularity and treatment schedule can be used routinely to decrease TURP surgical bleeding.¹³

Our study corresponds to the study done by Pastore et al, concluding that dutasteride taken 4 weeks before TURP caused reduction in bleeding perioperatively as well as postoperatively, which reduces postoperative complications and may also reduce the post-operative hospital stay thus reducing the morbidity and mortality and allows better patient management with the benefits of minimally access surgery.

CONCLUSION

Many other surgical treatments are being developed for BHP, but TURP is the gold standard treatment. However, morbidity and blood loss are major potential complications and taking dutasteride before TURP can be effective in reducing its complications.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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