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The role of dutasteride in reducing complications of transurethral resection of prostate

Shyamal Shah* **and P. Periasamy**

Department of Urology, Chettinad Super Speciality Hospital, Rajiv Gandhi Salai OMR, Kelambakkam, Chennai-603103, Tamil Nadu, India

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Abstract: *Purpose:* To evaluate the superiority of dutasteride over a placebo in patients having their prostate removed during transurethral resection for benign prostate hyperplasia. *Material and Methods:* The study included a total of 30 patients, with 15 patients allocated to each group (group placebo and group B-Dutasteride). Group A received a placebo for two weeks before surgery and two weeks after surgery and group B received dutasteride respective time slots. *Result:* TURP tissue weight among the placebo and Dutasteride groups, the mean resected tissue weights were 25.86 and 29.6 grams, respectively. The study also examined micro vessel density (MVD) in the suburethral portion of prostatic tissue, which was found to be highest in the placebo group (22.05) compared to the Dutasteride (16.2) group. In the hyperplastic portion of prostatic tissue, MVD was slightly higher in the placebo group (16.04) than in the Dutasteride (14.86) group. *Conclusions:* Preoperative treatment with dutasteride for two weeks before TURP reduces surgical bleeding and length of hospitalization after TURP. This pre-treatment can be used to decrease surgical bleeding associated with the TURP.

Keywords: Dutasteride, Preoperative dose, Microvascular density, TURP.

Introduction

The prostate is an important male reproductive system accessory gland with a pyramidal fibromuscular and glandular structure. It extends from the base of bladder to the urethral sphincter externally, surrounding the prostatic urethra. During foetal development, before 20 weeks of gestation, the prostate is originally categorised into 5 morphological lobes: anterior, posterior, two laterals, and a central one. However, in adult males, only three lobes remain: two lateral lobes, which are accessible via rectal examination, and a median lobe that extends into the urethra, forming the crista urethralis [1].

The prostate is largely an exocrine gland with an unknown endocrine role. It produces around 0.5 ml of the entire 3 ml of seminal fluid. Key secretory proteins produced by the prostate include prostate-specific antigen (PSA) and acid phosphatase, both of which are instrumental in diagnosing and evaluating prostate carcinoma [2]. The exact prevalence and incidence of benign prostatic hyperplasia (BPH) are difficult to quantify due to its progressive nature. As we age, the prostate continues to expand under the influence of dihydrotestosterone and testosterone, which can obstruct bladder outlet and cause infections in the lower urinary tract [3]. The treatment of BPH depends on symptom severity and associated complications. Absolute indications for intervention include recurrent urinary infections, Repeated haematuria, azotemia, and acute urine retention [4].

Since dihydrotestosterone plays a crucial role in prostate enlargement, androgen suppression therapy is an effective treatment strategy. Medications such as 5-alpha reductase inhibitors (e.g., finasteride and dutasteride) inhibit the conversion of testosterone to dihydrotestosterone, thereby decreasing prostate growth. Haematuria in BPH is associated with the density of microvessels in the prostatic cell membrane. According to studies, Dutasteride may lessen recurrent gross haematuria in BPH by inhibiting

androgen-controlled vascular endothelial growth factor (VEGF), which lowers angiogenesis. Both Type 1 and type 2 isoenzymes are inhibited by dutasteride. Research indicates that Dutasteride, similar to Finasteride, may also reduce bleeding complications associated with TURP [5].

Material and Methods

Study Location: Department of Urology, Chettinad Hospital and Research Institute, Chengalpattu District.

Study Population: Patients who were admitted with enlargement of Benign prostate and volume of more than 30 cc.

Study Design: This is a prospective, single-centre, randomized, double-blinded, placebo-controlled interventional study.

Study Duration: The study duration is two years from March 2023 to March 2025. Participants were randomized into two groups using a computer-generated random number table:

- *Group A:* Received a placebo for two weeks before surgery and two weeks after surgery.
- *Group B:* Received Dutasteride0.5 mg twice daily for two weeks before transurethral resection of the prostate (TURP) and two weeks postoperatively.

All patients provided written informed consent. A comprehensive history was recorded, including LUTS symptoms, hematuria, past medical and surgical history, medication use, and family history.

Inclusion Criteria: Patients were eligible for the study if they met the following criteria:

- Males diagnosed with benign prostatic hyperplasia (BPH) and associated lower urinary tract symptoms (LUTS).
- Age above 40 years.
- Prostate weight >30 grams on ultrasonography (USG).

Exclusion Criteria: Patients were excluded if they met any of the following conditions:

- History of prior prostate surgery.
- Suspected prostate cancer or any prostate disease other than BPH.
- Previous treatment with 5-alpha reductase inhibitors.
- Use of antiplatelet or anticoagulant medications.
- Presence of bleeding disorders or liver disease.

Preoperative Investigations: Routine preoperative investigation done.

Intraoperative Parameters:

- *Operation time:* Measured from the start to the completion of prostate resection.
- *Resected prostate weight:* Weighed post-resection.
- *Histopathological Examination* was done by using resected prostate tissue which was preserved in 10% formalin, stained with hematoxylin and eosin (H&E), and examined for malignancy. Microvascular density (MVD) was assessed by counting stained blood vessels in 10 high-power fields (×400).
- Hemoglobin (Hb) and packed cell volume (PCV) were measured on first postoperative day.

Other complications such as clot retention, need of transfusion, failure to void and Urinary Tract Infections (UTI) were assessed post operatively

Statistical Analysis:

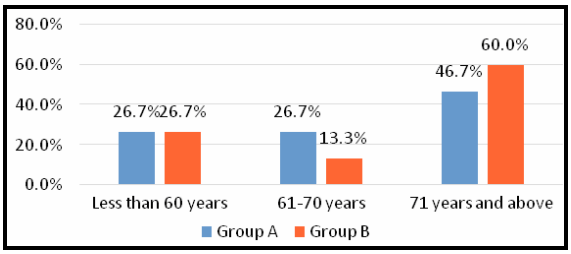
- Data were entered into an Excel (MS Office 2007) spreadsheet and was analysed using SPSS version 25.0
- The Chi-square test or Fisher's exact test was applied for categorical variables based on sample size.
- A p-value <0.05 was considered statistically significant.

Results

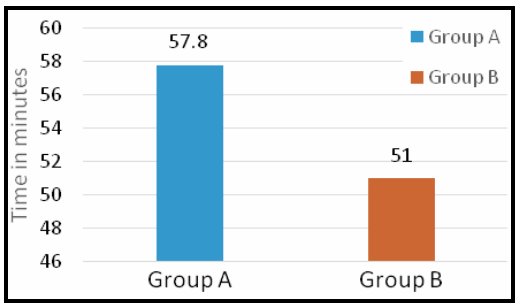
The study was carried out on 30 patients who underwent transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH) in the Department of Urology at Chettinad Hospital and Research Institute, over2 years (March 2023 to March 2025). The participants were randomly assigned to two groups: Group A received a Placebo drug (2 weeks before TURP and 2

weeks postoperatively) and Group B was given a Dutasteride tablet 0.5 mg at corresponding time intervals.

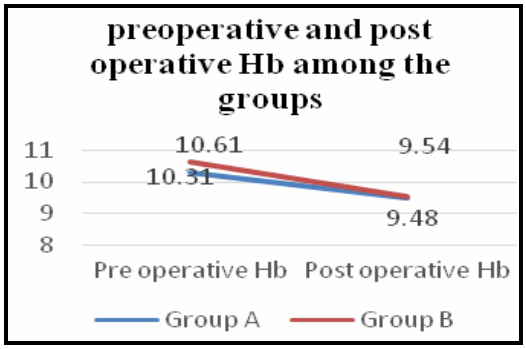
Graph-1: Age Group-wise distribution of the study subjects



Graph-2: Tissue Resection time among the study groups



Graph-3: Difference between the pre and postoperative Haemoglobin and PCV among the groups



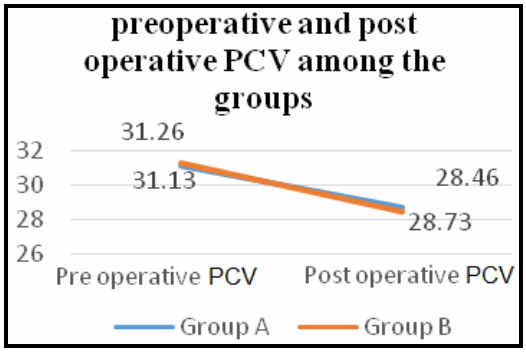


Table-1: Micro Vascular Density at Sub urethral portion among the study groups					
Micro Vascular Density	**Minimum (ml)**	**Maximum (ml)**	**Mean (ml)**	**Std. Deviation**	**p-value**
Group A (N=15)	17.18	28.17	22.05	2.89	0.001*
Group B (N=15)	13.68	23.34	16.2	2.84	

Table-2: Micro Vascular Density at Hyperplastic portion among the study groups					
Micro Vascular Density	**Minimum (ml)**	**Maximum (ml)**	**Mean (ml)**	**Std. Deviation**	**p-value**
Group A (N=15)	14.86	17.56	16.04	0.70	0.001*
Group B (N=15)	13.46	15.62	14.86	0.60	

Discussion

The primary aim of this randomized controlled trial was to determine whether preoperative administration of Dutasteride could reduce bleeding complications during transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH). Numerous studies have already established the role of Dutasteride in minimizing TURP-related bleeding. When analysing the results across the two study groups, demographic characteristics were comparable. Nearly 46% of participants were in the age group above 71 years and above, averaging 65.55 years (graph 1). A similar study conducted by Robert G. Hahn [6] reported a mean age of 67 years. Digital rectal examinations indicated that 61% of patients had Grade 2 benign prostate enlargement, with no significant differences among the groups.

The mean prostate volume recorded in this study group was 42.26 ml. A related study by J. A. Arratia-Maqueo [7] observed a mean prostate volume of 66.8 cm^3 in the Dutasteride group and 57 cm^3 the mean packed cell volume was 31.27%. There were no significant differences in prostate volume, preoperative haemoglobin, or packed cell volume among the groups (graph 3).

In terms of surgical parameters, Robert G. Hahn [8] reported an average TURP duration of 45 minutes and a mean resected prostate tissue weight of 25 grams. This study found comparable results, with a mean TURP duration in study group of 51 seconds and in placebo group of 57.8 seconds and a mean resected prostate weight in study group of 27.8 grams (graph 2). When analyzing TURP tissue weight among the placebo and Dutasteride groups, the mean resected tissue weights were 25.86 and 29.6 grams respectively. A statistically significant difference was observed between the placebo and the treatment groups, suggesting that preoperative administration of 5-alpha reductase inhibitors increases the amount of resected prostatic tissue during TURP.

The study also examined microvessel density (MVD) in the suburethral portion of prostatic tissue, which was found to be highest in the placebo group (22.05) compared to the Dutasteride (16.2) group (table 1). Research by A Bansal et al [9] similarly found MVD values of 20.2 ± 5.3 in the Dutasteride group and 14.0 ± 2.8 in the placebo group.

Additionally, a study by Je Hyeong Woo et al [10] in Korea reported an MVD of 22.19 in the placebo group versus 14.47 in the Dutasteride group, with a p-value of 0.026. In the hyperplastic portion of prostatic tissue, MVD was slightly higher in the placebo group (16.04) than in the Dutasteride (14.86) group (table 2). Je Hyeong Woo et al. [11] found similar results, reporting MVD values of 14.72 in the Dutasteride group and 15.24 in the placebo group ($p = 0.801$).

S. Sugie et al [12] observed MVD values of 17.5 ± 2.8 in the Dutasteride group patients and 16.7± 4.6 in the placebo group. Research suggests that 5-alpha reductase inhibitors suppress androgen-regulated vascular endothelial growth factor (VEGF), leading to reduced angiogenesis and lower micro vessel density. Despite significant blood loss in all two groups during TURP, no statistically significant differences were found when comparing preoperative and postoperative hemoglobin and packed cell volume (PCV) levels between the groups. The most accurate method to quantify blood loss during TURP is by measuring hemoglobin in the irrigation fluid, as hemoglobin concentrations in the fluid are typically 5–10% of whole blood levels. This study assessed blood loss by comparing preoperative and postoperative hemoglobin and PCV levels.

Postoperative clot retention was observed in 20%, 13.3% patients in groups 1, and 2 respectively. The requirement for postoperative blood transfusion was 16% and 10 % across the same groups. Research by R. Shanmugasundaram et al [13] found clot retention rates of 6–11% and a blood transfusion requirement of 1–3%, which were lower than those observed in this study.

Failure to void occurred in 6.7% patients in both the groups. Postoperative urinary tract infections (UTIs) were reported in 13.3% of placebo patients, 6.7% of Dutasteride patients. While these complications were more frequent in the placebo group, there were no statistically significant differences between groups. R. Shanmugasundaram et al [14] also reported acute urinary retention (AUR) rates of 11–17% and UTI rates of 20–30%, with no significant statistical differences. Dutasteride, a commonly used 5-alpha reductase inhibitor, is frequently administered preoperatively to reduce TURP-related bleeding. It reduces prostate size by inhibiting VEGF and decreasing microvessel density. However, Sandfeldt et al. [15] found no significant difference in blood loss during TURP following Dutasteride treatment.

Similar to this study, research by S Sugie et al [16] confirmed that Dutasteride reduces suburethral prostatic microvessel density in BPH patients. In recent study done by UK Dutt et al [17] MVD was lower in Dutasteride group than in placebo group. While some studies, including one by R. Shanmugasundaram et al [14], reported that Dutasteride did not significantly reduce bleeding complications in TURP despite

lower in gintraprostatic dihydrotestosterone (DHT) levels, other research has shown positive effects. Pastore AL and Mariani et al. [18] found that a six-week preoperative regimen of Dutasteride reduced surgical bleeding during TURP. However, J. A. Arratia-Maqueo et al. [19] reported no statistically significant differences in bleeding complications with Dutasteride use. A study by Je Hyeong Woo et al. [20] demonstrated that a short-term, two-week preoperative Dutasteride regimen significantly decreased suburethral prostatic microvessel density and reduced TURP-related bleeding.

This randomized study found that a two-week preoperative and two-week postoperative regimen of Dutasteride (0.5 mg twice daily) significantly decreased microvessel density in the suburethral portion of prostatic tissue in BPH patients. It also reduced TURP-associated bleeding complications, such as clot retention and blood transfusion requirements.

Conclusion

This study aimed to evaluate the effectiveness of preoperative Dutasteride in reducing intraoperative blood loss in patients undergoing TURP for benign prostatic hyperplasia with a prostate volume greater than 30cc. The results suggest that Dutasteride contributes to a significant reduction in surgical bleeding, potentially decreasing the need for blood transfusions and improving overall perioperative outcomes. Additionally, the analysis of postoperative complications, such as clot retention, urinary tract infections, urinary retention after catheter removal, and the requirement for blood transfusions, provides valuable insights into the broader implications of Dutasteride use in this surgical setting

Limitations: This study has some limitations that may affect the interpretation of the results. The sample size may be relatively small, limiting the generalizability of the findings to a broader population. Additionally, as a single-centre study, the results may not be widely applicable to different patient groups and healthcare settings. Variability in surgical expertise and patient-specific factors, such as comorbidities, could also influence intraoperative blood loss and postoperative outcomes. Furthermore, adherence to preoperative Dutasteride treatment may vary, potentially affecting the consistency of results.

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Conflicts of interest: There are no conflicts of interest.

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*All correspondences to: Dr. Shyamal Shah, Resident, Department of Urology, Chettinad Super Speciality Hospital, Rajiv Gandhi Salai OMR, Kelambakkam, Chennai-603103, Tamil Nadu, India. Email: shyamal.3637@gmail.com