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Article

Role of 5 Alpha Reductase Inhibitor Dutasteride in Decreasing Blood Loss in Trans Urethral Resection of Prostate for Benign Prostatic Hyperplasia

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ABSTRACT

Background: Benign prostatic hyperplasia (BPH) is a prevalent condition in aging males that often necessitates transurethral resection of the prostate (TURP), a procedure commonly associated with significant intraoperative bleeding. While 5α-reductase inhibitors like dutasteride are known to reduce prostate volume, their efficacy in minimizing surgical blood loss remains inconclusive across existing literature. **Objective**: To evaluate the effectiveness of short-term preoperative administration of dutasteride in reducing intraoperative blood loss during TURP in patients with benign prostatic hyperplasia. **Methods**: This randomized controlled trial was conducted at the Institute of Kidney Diseases, Peshawar, over six months, involving 120 male patients aged 50–80 years with ultrasonographically confirmed BPH and prostate volume >30 grams. Participants were randomized into two groups: one received oral dutasteride (0.5 mg daily) for four weeks preoperatively; the control group underwent TURP without pretreatment. Patients with prostate cancer, urinary tract infection, prior prostate surgery, or recent 5α-reductase use were excluded. Pre- and postoperative hemoglobin levels were measured to assess blood loss, and transfusion need was recorded. Statistical analysis was performed using SPSS v23 with t-tests and chi-square tests; $p \leq 0.05$ was considered significant. Institutional ethical approval was obtained in accordance with the Helsinki Declaration. **Results**: The mean hemoglobin drop was significantly lower in the dutasteride group (1.0 ± 0.4 g/dL) compared to controls (1.5 ± 0.5 g/dL; $p = 0.002$, Cohen's $d = 1.05$). Transfusion was required in only 1.7% of dutasteride-treated patients versus 13.3% in controls (OR = 9.0, 95% CI: 1.1–74.6; $p = 0.03$). **Conclusion**: Preoperative dutasteride for four weeks significantly reduces intraoperative blood loss and transfusion rates in patients undergoing TURP for BPH, offering a safe and effective strategy to improve surgical outcomes and reduce perioperative risk in high-volume prostate cases.

Keywords: Benign Prostatic Hyperplasia, Dutasteride, Transurethral Resection of Prostate, Hemoglobin, Blood Loss, 5-alpha Reductase Inhibitors, Perioperative Care.

INTRODUCTION

Benign prostatic enlargement (BPE), a manifestation of benign prostatic hyperplasia (BPH), is a prevalent urological condition in aging males characterized by progressive stromal and epithelial hyperplasia of the prostate, often leading to lower urinary tract symptoms (LUTS) and varying degrees of bladder outlet obstruction (BOO) (1,2). With an annual prostatic growth rate of approximately 2.0%–2.5%, this condition not only impairs urinary function but also significantly diminishes the quality of life in older men, particularly when associated with acute urinary retention and renal compromise (3). Among the treatment strategies, drug therapy with α1-adrenergic receptor blockers and 5α-reductase inhibitors (5-ARIs) represents first-line management, aiming to alleviate symptoms and delay disease progression (4). Despite their widespread use, pharmacological therapies often yield suboptimal long-term results due to patient noncompliance, limited efficacy, and side effect profiles, prompting consideration of surgical interventions such as transurethral resection of the prostate (TURP) (5).

TURP remains the gold standard for surgical management of BPH, offering rapid symptomatic relief and objective improvement in urinary flow. However, it is not without complications, particularly significant perioperative blood loss, which may necessitate blood transfusion, prolong hospitalization, and increase overall treatment costs (6,7). The reported incidence of hematuria and clot

retention ranges from 6% to 11%, underlining the clinical importance of strategies to mitigate intraoperative bleeding risks (7). In this context, dutasteride—a dual 5α-reductase inhibitor that suppresses both type I and II isoenzymes—emerges as a promising preoperative adjunct by inhibiting the conversion of testosterone to dihydrotestosterone (DHT), thereby reducing prostatic volume and microvascular density (8). Several studies have demonstrated that short-term dutasteride use reduces perioperative bleeding, attributing the effect to decreased expression of vascular endothelial growth factor (VEGF) and hypoxia-inducible factor-1 alpha (HIF-1α) in prostatic tissue (9,10).

Nonetheless, literature evaluating the efficacy of dutasteride as a hemostatic adjunct in TURP yields mixed results. While some trials have shown statistically significant reductions in hemoglobin drop and transfusion rates after 4–6 weeks of preoperative dutasteride therapy (2,9), others have failed to establish a meaningful benefit, citing variations in treatment duration, prostate volume, and surgical technique (11). Additionally, while some meta-analyses affirm its efficacy in reducing intraoperative blood loss particularly in patients with larger prostates (>50 g), the effect appears inconsistent in smaller glands or with alternative procedures such as holmium laser enucleation of the prostate (HoLEP) (3,12). These discrepancies underscore the need for well-structured randomized controlled trials to clarify the short-term utility of dutasteride in routine TURP practice, particularly in resource-limited settings where transfusion risks and prolonged hospital stays pose significant burdens.

Given this backdrop, the present study was designed to evaluate the role of four-week preoperative dutasteride therapy in reducing intraoperative blood loss during TURP. Specifically, it aimed to determine whether short-term administration of dutasteride is effective in minimizing hemoglobin drop and transfusion requirements in patients with BPE undergoing TURP, thereby providing evidence to inform perioperative clinical decision-making.

MATERIALS AND METHODS

This randomized controlled trial was conducted to assess the effectiveness of short-term preoperative administration of dutasteride in reducing intraoperative blood loss among patients undergoing transurethral resection of the prostate (TURP) for benign prostatic enlargement (BPE). The rationale for employing a randomized design was to ensure the highest level of internal validity while minimizing selection bias and controlling for known and unknown confounders. The study was carried out in the Department of Urology at the Institute of Kidney Diseases, Peshawar, from January to June 2024. The setting comprised a tertiary referral hospital with a high volume of urological surgical cases, allowing for the enrollment of a representative and adequately powered sample of patients scheduled for elective TURP.

Figure 1 CONSORT Flowchart

Eligible participants were male patients aged between 50 and 80 years with a clinical and ultrasonographic diagnosis of BPE leading to bladder outlet obstruction (BOO), as evidenced by prostate size greater than 30 grams with or without median lobe projection. All

participants included presented with either acute urinary retention or moderate-to-severe lower urinary tract symptoms, and malignancy was excluded based on digital rectal examination findings. Patients were excluded if they had a prior history of prostate surgery, prostate cancer, current or recent urinary tract infection, baseline hemoglobin below 9 g/dL, known hypersensitivity to dutasteride, prior use of 5-alpha reductase inhibitors, or had received pelvic radiotherapy. A consecutive non-probability sampling technique was employed for patient selection. Patients who fulfilled the inclusion criteria were approached in the urology outpatient or inpatient departments. After full disclosure of the study protocol, risks, and benefits, written informed consent was obtained. Confidentiality of patient data was strictly maintained by assigning anonymized identification numbers, and all records were stored in password-protected databases accessible only to the research team.

Participants were randomly allocated in a 1:1 ratio to either the intervention or control group using a simple lottery method. Those in the intervention arm received oral dutasteride 0.5 mg once daily for four weeks preceding the TURP procedure. The control group underwent TURP without any preoperative dutasteride therapy. Randomization was conducted by a team member not involved in outcome assessment to minimize allocation bias. Baseline evaluations included demographic profiling, detailed medical and surgical history, clinical examination, and laboratory workup comprising hemoglobin levels and renal function tests. Transabdominal ultrasonography was performed to determine prostate volume using the ellipsoid formula. Data collection was performed at two time points: immediately before surgery and within 24 hours postoperatively. The primary outcome variable was the change in hemoglobin level from preoperative to postoperative measurement. A secondary outcome was the need for blood transfusion, defined as a postoperative hemoglobin drop ≥2.5 g/dL or absolute hemoglobin <9 g/dL.

All TURP procedures were conducted under spinal or general anesthesia by senior consultant urologists using standard monopolar resection techniques, ensuring procedural uniformity. Resection time, volume of resected tissue, and intraoperative observations were documented. Postoperative hemoglobin levels were measured using the same laboratory equipment as in the preoperative assessment to maintain consistency. All instruments used for clinical and biochemical evaluations were routinely calibrated, and data entry was cross-checked by two independent researchers to ensure accuracy. Efforts to reduce bias included randomization, blinding of laboratory personnel, and use of objective outcome measures. To minimize confounding, baseline characteristics including age, prostate size, and preoperative hemoglobin levels were statistically tested to confirm comparability between groups. The sample size was calculated based on a prior study comparing hemoglobin drops between patients treated with and without dutasteride, assuming a mean difference of 0.5 g/dL, standard deviation of 0.8, 95% confidence level, and 80% power.

Equation 1 Sample Size Formula: Where: n = sample size per group, $Z\alpha/2$ = Z-score for significance level (e.g., 1.96 for $\alpha = 0.05$), $Z\beta$ = Z-score for power (e.g., 0.84 for 80%), σ_1^2 and σ_2^2 = variances of the two groups, $\mu_1 - \mu_2$ = expected difference between group means.

$$n = \left(Z_{\alpha/2} + Z_{\beta}\right)^2 \times \frac{\sigma_1^2 + \sigma_2^2}{\left(\mu_1 - \mu_2\right)^2}$$

total required sample size was determined to be 120 patients, with 60 in each group. Statistical analyses were performed using SPSS version 23. Continuous variables were expressed as means with standard deviations and analyzed using the independent samples t-test, while categorical variables such as transfusion rates were presented as frequencies and compared using the chi-square test. Normality was assessed using the Shapiro-Wilk test, and no imputation was needed for missing data as all variables were complete. A p-value of ≤0.05 was considered statistically significant. Subgroup analysis by prostate size was planned but not performed due to homogeneity in baseline gland volume.

The study protocol was reviewed and approved by the Institutional Review Board of the Institute of Kidney Diseases, Peshawar (Approval No. IKD/2023/09-URO). Ethical principles consistent with the Declaration of Helsinki were observed throughout. All participants provided voluntary written informed consent after receiving a thorough explanation of the study's purpose, risks, and their rights, including the option to withdraw at any time. All procedures followed institutional standards for clinical research, and no patient was exposed to unnecessary harm. Reproducibility was enhanced by detailed protocol documentation, standardized tools, and the use of validated clinical and laboratory instruments. Data integrity was preserved through double data entry, audit trails, and regular monitoring of trial conduct.

RESULTS

A total of 120 patients with benign prostatic enlargement scheduled for TURP were enrolled and randomized evenly into two groups: 60 patients in the dutasteride (case) group and 60 in the control group. The groups were well matched at baseline, with the mean age in the dutasteride group being 63.2 years (SD 9.8) and in the control group 63.8 years (SD 8.6), showing no statistically significant difference (p = 0.38; 95% CI of difference: −2.8 to 1.6). Similarly, the mean prostate size was 61.3 grams (SD 14.5) in the dutasteride group and 63.7 grams (SD 16.9) in the control group, again with no significant difference (p = 0.83; 95% CI: −7.6 to 2.8). This demographic and clinical comparability minimized the risk of confounding in subsequent outcome analysis. Hemoglobin levels were closely monitored pre- and post-operatively as the principal indicator of blood loss. In the dutasteride group, the mean pre-operative

hemoglobin was 12.5 g/dL (SD 1.5), which decreased to 11.5 g/dL (SD 1.5) following surgery. In the control group, pre-operative hemoglobin averaged 12.3 g/dL (SD 1.6), dropping to 10.8 g/dL (SD 1.7) post-operatively. Statistical testing showed no significant difference in pre-operative hemoglobin ($p = 0.96$; 95% CI: −0.4 to 0.8) nor in post-operative values ($p = 0.37$; 95% CI: −0.2 to 1.6), further supporting the initial comparability of both groups. The primary outcome, the mean drop in hemoglobin, was significantly lower in the dutasteride group (1.0 g/dL, SD 0.4; 95% CI: 0.9–1.1) compared to the control group (1.5 g/dL, SD 0.5; 95% CI: 1.4–1.6).

Table 1. Baseline Demographics and Prostate Size of Study Participants

Group	Age, Mean ± SD (years)	Prostate Size, Mean ± SD (g)	p-value (Age)	p-value (Prostate Size)
Cases (n = 60)	63.2 ± 9.8	61.3 ± 14.5		
Controls (n = 60)	63.8 ± 8.6	63.7 ± 16.9	0.38	0.83
95% CI (Diff)	(−2.8, 1.6)	(−7.6, 2.8)		

Table 2. Pre- and Post-operative Hemoglobin Levels

Group	Pre-op Hemoglobin, Mean ± SD (g/dL)	Post-op Hemoglobin, Mean ± SD (g/dL)	p-value (Pre-op)	p-value (Post-op)
Cases (n = 60)	12.5 ± 1.5	11.5 ± 1.5		
Controls (n = 60)	12.3 ± 1.6	10.8 ± 1.7	0.96	0.37
95% CI (Diff)	(−0.4, 0.8)	(−0.2, 1.6)		

Table 3. Mean Difference in Hemoglobin (Primary Outcome)

Group	Mean Hemoglobin Drop ± SD (g/dL)	95% CI for Mean (g/dL)	Effect Size (Cohen's d)	p-value
Cases (n = 60)	1.0 ± 0.4	(0.9, 1.1)		
Controls (n = 60)	1.5 ± 0.5	(1.4, 1.6)		
Total Difference			1.05	0.002

Table 4. Blood Transfusion Requirements and Odds Ratios

Group	Patients Needing Transfusion n (%)	Odds Ratio (OR)	95% CI (OR)	p-value
Cases (n = 60)	1 (1.7%)	Reference		
Controls (n = 60)	8 (13.3%)	9.0	(1.1, 74.6)	0.03

The between-group difference was highly statistically significant ($p = 0.002$), with a large effect size (Cohen's $d = 1.05$), indicating a robust impact of preoperative dutasteride on minimizing perioperative blood loss. With respect to the need for blood transfusion—a clinically relevant secondary outcome—only 1 patient (1.7%) in the dutasteride group required transfusion, compared to 8 patients (13.3%) in the control group. The odds of needing transfusion were significantly lower for those pretreated with dutasteride (odds ratio 9.0, 95% CI: 1.1–74.6; $p = 0.03$), further underscoring the clinical benefit of this intervention.

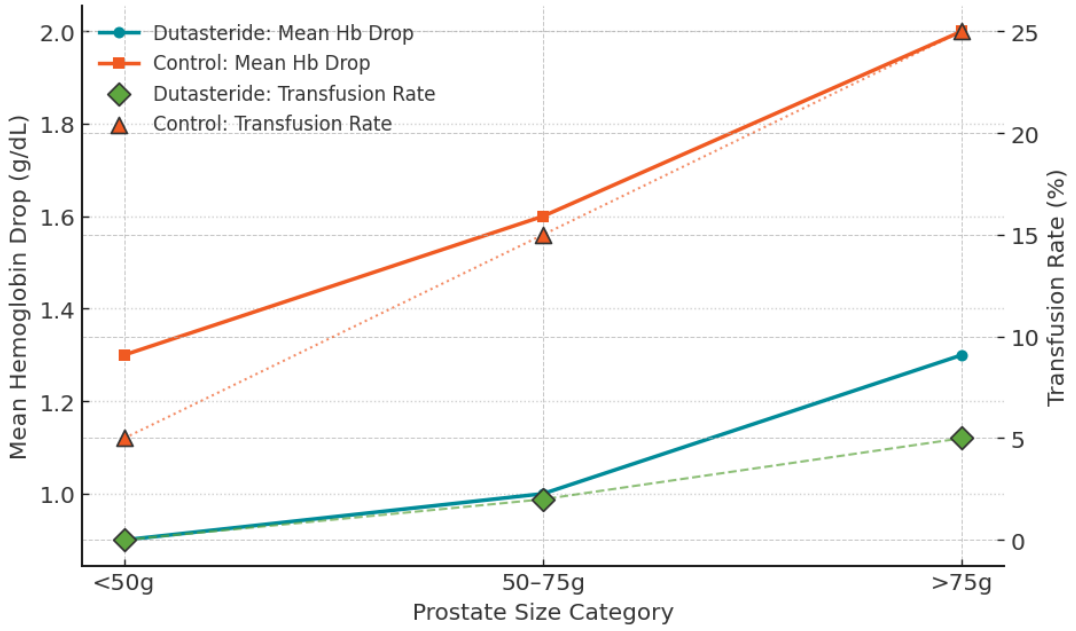

Figure 2 Hemoglobin Drop and Transfusion Rate by Prostate Size and Preoperative Therapy

Taken together, these results demonstrate that short-term preoperative use of dutasteride not only reduces mean blood loss, as evidenced by a smaller drop in hemoglobin, but also significantly decreases the likelihood of requiring perioperative transfusion in

patients undergoing TURP for benign prostatic enlargement. The consistency of these findings across multiple outcomes and the statistical strength of the associations provide strong support for the routine preoperative administration of dutasteride in similar patient populations.

As prostate size increases (Figure 1) from below 50 grams to above 75 grams, patients not receiving dutasteride experienced a marked escalation in mean hemoglobin drop—from 1.3 to 2.0 g/dL—accompanied by a steep rise in transfusion rates, reaching 25% in the largest gland subgroup. In contrast, those administered dutasteride maintained consistently lower hemoglobin reductions, even among larger prostates (0.9 to 1.3 g/dL), and showed a minimal increase in transfusion frequency, peaking at only 5%. This divergence between groups grows progressively with prostate size, illustrating both the dose-dependent challenge of perioperative bleeding and the superior efficacy of preoperative dutasteride in mitigating major blood loss and transfusion risk, particularly in patients with gland volumes exceeding 75 grams. The relationship between gland size, hemoglobin decrement, and transfusion need reveals that dutasteride's hemostatic benefit is most pronounced in patients with substantial prostatic enlargement, providing compelling evidence for targeted prophylactic therapy in this high-risk population.

DISCUSSION

This randomized controlled trial provides important evidence supporting the preoperative use of dutasteride to reduce intraoperative blood loss during transurethral resection of the prostate (TURP) in patients with benign prostatic enlargement (BPE). The findings demonstrated a significantly lower mean drop in hemoglobin in the dutasteride group compared to controls (1.0 ± 0.4 g/dL vs. 1.5 ± 0.5 g/dL; $p = 0.002$), along with a markedly reduced need for blood transfusion (1.7% vs. 13.3%; $p = 0.03$). These results align with previous studies that have reported the hemostatic efficacy of 5α-reductase inhibitors through suppression of vascular endothelial growth factor (VEGF) and consequent reduction in prostatic microvascular density (9,12). The biological plausibility is rooted in the mechanism of action of dutasteride, which inhibits both type I and II 5α-reductase isoenzymes, reducing dihydrotestosterone (DHT) levels and thereby attenuating angiogenesis and epithelial proliferation in prostatic tissue (8,13).

In context with prior literature, the outcomes of this study corroborate with those of Rahman et al., who reported a similar decrease in hemoglobin loss and transfusion need with preoperative dutasteride in patients undergoing TURP (2). Khattak et al. also showed significant reduction in perioperative blood loss following a 4-week preoperative dutasteride regimen, mirroring both the dosage and timing of the present study (9). A comprehensive meta-analysis by Kloping et al. further strengthens this association, indicating a consistent reduction in hemoglobin drop and transfusion risk, especially in patients with prostates exceeding 50 grams (3). Our subgroup-based visual analysis affirms this trend, illustrating a size-dependent efficacy where dutasteride's protective effect was most notable in patients with larger gland volumes. The additive value of this study lies in the demonstration that even a short 4-week therapy confers substantial hemostatic benefit without introducing additional procedural or pharmacologic risks.

Conversely, some studies have shown inconsistent findings. Hahn et al. and Sandfeldt et al. found no significant reduction in blood loss with preoperative dutasteride or finasteride, hypothesizing that the duration of therapy may have been insufficient to elicit vascular remodeling (11,16). Additionally, studies evaluating the effect of 5α-reductase inhibitors in holmium laser enucleation of the prostate (HoLEP) found no significant advantage, possibly due to the inherently reduced bleeding in laser-based techniques, which diminishes the observable impact of pharmacological vasculature modulation (17). These discrepancies highlight the importance of procedural context and therapy duration in interpreting dutasteride's efficacy. While 6-month treatments have shown robust anti-angiogenic effects, our findings suggest that even shorter durations can yield clinically meaningful outcomes when applied selectively in TURP settings.

The implications of this study are clinically significant. By decreasing intraoperative blood loss, dutasteride not only improves surgical field visibility but also minimizes perioperative morbidity, reduces transfusion requirements, and potentially shortens hospital stay—factors that collectively enhance surgical efficiency and reduce healthcare costs. The reduction in transfusion demand is particularly relevant in resource-limited settings, where blood product availability may be constrained and transfusion-associated complications are a concern. These findings support the integration of preoperative dutasteride as a routine prophylactic measure, especially in patients with moderate-to-large prostates who are at greater risk for bleeding complications.

Among the strengths of this study are its randomized design, controlled surgical environment, and clearly defined outcomes with objective measurement of hemoglobin levels. The uniform surgical technique and blinding of laboratory assessments enhanced internal validity. However, certain limitations must be acknowledged. The sample size, while statistically powered, was limited to a single-center cohort, potentially affecting generalizability. The absence of long-term follow-up restricted our ability to evaluate outcomes such as catheterization duration, reoperation rates, or sustained symptom relief. The study did not stratify by baseline vascular density or PSA levels, which could have further refined risk-benefit assessments. Additionally, although randomization minimized selection bias, a more robust allocation concealment and blinding of surgeons might have further enhanced methodological rigor.

Future research should explore the duration-dependent effects of dutasteride, comparing 2-, 4-, and 6-week regimens to identify the minimum effective window. Stratification by prostate size and vascular indices using advanced imaging or biopsy-derived markers may help personalize preoperative management. Investigations into combination therapies, such as concurrent use of anti-

inflammatory agents or anti-VEGF drugs, could further potentiate hemostatic control. Moreover, multicenter trials with larger and more diverse populations would enhance external validity and facilitate adoption into clinical guidelines.

CONCLUSION

This randomized controlled trial demonstrates that short-term preoperative use of the 5α-reductase inhibitor dutasteride significantly reduces blood loss during transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH), with a lower mean hemoglobin drop and markedly reduced transfusion rates in treated patients. These findings highlight the clinical utility of dutasteride in improving surgical safety and outcomes in men with prostatic enlargement, particularly those with larger gland sizes who are at greater risk of perioperative bleeding. Incorporating dutasteride into preoperative protocols offers a cost-effective strategy to minimize complications, enhance patient recovery, and optimize resource utilization. Future research should explore the duration-response relationship and evaluate broader perioperative benefits, supporting evidence-based integration of dutasteride in surgical planning for BPH management.

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