

Original Article

## Transurethral Resection of Prostate and Blood loss: Efficacy of Dutasteride in reducing perioperative blood loss.

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Doi: 10.29052/IJEHSR.v9.i2.2021.156-160

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**Received** 02/09/2020

**Accepted** 25/03/2021

**First Published** 14/04/2021



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### Abstract

**Background:** Benign Prostatic Hyperplasia (BPH) is the most common urological cause of urinary obstruction, affecting men above 50 years of age. Medical therapy used for managing BPH includes various medical regimes, including 5-alpha reductase inhibitors (5ARI), namely Dutasteride and more. This study aimed to evaluate the efficacy of four weeks' prior treatment with dutasteride on per-operative blood loss in patients of BPH undergoing transurethral resection of the prostate (TURP).

**Methodology:** A prospective observational study was conducted from January to December 2019 at the Kidney Centre, Karachi, Pakistan. A total of 64 patients were included and divided into two groups. Group A patients were those who had been taking dutasteride (0.5 mg/day) for four weeks or more before surgery, and group B patients were not taking dutasteride drug before surgery. All patients underwent standard TURP, and the intra-operative blood loss was calculated. The collected data was analyzed using SPSS version 22.0.

**Results:** In our study, there was a significantly less hemoglobin drop (1.2 gm vs. 2.2 gm) during prostate surgery in patients using dutasteride than those who were not using dutasteride.

**Conclusion:** This study has revealed that the use of dutasteride four weeks before surgery significantly reduces intra-operative bleeding.

### Keywords

Transurethral Resection, Dutasteride, Benign Prostatic Hyperplasia.



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## Introduction

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Dihydrotestosterone (DHT) has an obligatory role in the differentiation of the prostate during gestation and development of benign prostatic hyperplasia (BPH) in later years<sup>1</sup>. Clinical BPH is explained as hyperplasia of the prostate gland that leads to symptomatic or asymptomatic bladder outlet obstruction irrespective of the size of the prostate gland<sup>2</sup>. It is one of the commonest causes of lower urinary tract symptoms (LUTS) in men affecting the quality of life as a progressive disease of ageing due to the prostate gland's noncancerous proliferation and imbalance between the stroma and epithelium<sup>3</sup>. Alpha-blockers and the 5-alpha reductase enzyme inhibitors are used to treat LUTS with acceptable adverse effect profile in long-term use<sup>4</sup>. After failed medical treatment, surgical intervention is required as a mainstay of the treatment of BPH<sup>5</sup>. Although various endoscopic prostatic surgical techniques are being used, Transurethral Resection of Prostate (TURP) is considered a standard surgical modality for the treatment of BPH<sup>6</sup>. It is noted that patients after TURP are at increased risk for perioperative complications like infections, retrograde ejaculation, TUR syndrome, urethral stricture, hemorrhage, and clot retention<sup>7</sup>.

Hemorrhage (0.4% to 7%) is one of the most serious complications requiring blood transfusion, and sometimes auxiliary procedures are required for controlling bleeding (post-operative hemorrhage) and clot retention<sup>8</sup>. To minimize these complications, various methods have been postulated. Among various methods, the use of dutasteride is still unproven. Gökçe et al. reported markedly less bleeding in the dutasteride group of patients than other groups. They suggested that prior treatment with dutasteride for six weeks before surgery could decrease the blood loss after surgery<sup>9</sup>. Similar results have been reported with significantly lesser postoperative blood loss in patients taking dutasteride as compared to patients not taking dutasteride by Kim et al<sup>10</sup>. On the contrary, Yi-Ping et al. reported inconclusive results for its use and hence there is a need for

further studies to strengthen these recommendations<sup>11</sup>.

We planned to conduct a study to evaluate the efficacy of four weeks' prior treatment with dutasteride on per-operative blood loss in patients of BPH undergoing TURP versus without dutasteride pretreatment.

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## Methodology

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This prospective observational study was conducted from January to December 2019 at the Kidney Centre, Karachi, Pakistan, including 64 patients who underwent TURP. Patients between 50-80 years, with prostate size more than 50 gm, or those undergoing transurethral resection of the prostate, or those who were willing to enroll in the study were included. While patients with PSA  $\geq$  4.0, preoperative creatinine  $\geq$  1.5 mg/dl, INR  $\geq$  1.5, or patients with bleed disorders or active UTI and those undergoing simultaneous procedures along transurethral resection of the prostate were excluded from the study. Patients' data were collected prospectively from hospital records manually. Native ethical review board approval was taken before the study.

Written informed consent was obtained from every patient. All patients were on treatment with alpha-blockers before TURP. The size of the prostate gland was recorded via ultrasound within 10 days before surgery and surgery was performed by consultant urologists. Patients were divided into two groups: including Group A comprising of patients who were taking dutasteride (0.5 mg/day) for at least four weeks before surgery, along with alpha-blocker, and the other group B includes those patients who were taking alpha-blockers only. Pre-operative hemoglobin levels were recorded. The Operative procedure was done under standard anesthesia care. Initially, standard urethro-cystoscopy was done. After cystoscopy, serial Ureteral dilatation with adequate lubrication was done with metallic urethral dilators. Resection of the prostate was done with monopolar resectoscope using glycine as irrigation fluid. After resection of the prostate, adequate hemostasis was achieved by coagulation of prostatic bed, the

stream of urine was checked, and three-way hematuria catheter was introduced. Bladder irrigation was started with normal saline, and observation was done for the colour of effluent. Operative time was noted. After 24 hours, hemoglobin levels were checked. Laboratory values of hemoglobin after transurethral resection of the prostate were compared with preoperative hemoglobin levels as the main outcome variable to identify loss of blood during the procedure (peri-operative blood loss).

SPSS version 21.0 was used to analyze the data. Mean, and standard deviation was calculated for all continuous parameters like age, size of the prostate, duration of surgery, pre-operative and post-operative hemoglobin. Frequency and percentage were calculated for all categorical data like gender. Unpaired student t-test was applied to compare the mean difference of hemoglobin and

between two groups at pre-operative and postoperative value. A p-value  $\leq$  of 0.05 was considered statistically significant.

## Results

We included 64 patients in our study in which half of the patients were taking dutasteride along with alpha-blocker. The mean age was  $67.17 \pm 8.9$  years with a minimum of 42 years and a maximum value of 88 years. The Mean drop in hemoglobin in all patients undergoing TURP was  $1.7 \pm 0.8$  gm/dl. We found that both groups had a significant difference in the size of the prostate. It is also found a significant difference in hemoglobin after surgery and a difference in hemoglobin ( $p < 0.05$ ). In our study, there was significantly less hemoglobin drop following prostate surgery in patients using dutasteride as compared to those who were not (1.2 gm vs. 2.2 gm, respectively).

**Table 1: Differences of Mean of parameters between two groups of patients.**

Variables	No Dutasteride Use	Dutasteride Use	p-value
	Mean $\pm$ SD		
Age (Years)	66.2 $\pm$ 8.8	68.1 $\pm$ 9.1	0.399
Size of the prostate (gm)	73.5 $\pm$ 24.2	86.3 $\pm$ 19	0.021*
Operative time (min)	42.2 $\pm$ 16.8	44.8 $\pm$ 18.2	0.546
Hemoglobin before surgery (gm/dl)	12.8 $\pm$ 1.8	12.7 $\pm$ 1.4	0.803
Hemoglobin after surgery (gm/dl)	10.7 $\pm$ 1.8	11.6 $\pm$ 1.2	0.018*
Difference of Hemoglobin (gm/dl)	2.2 $\pm$ 0.6	1.2 $\pm$ 0.6	<0.001*

\*p-value < 0.05 is considered statistically significant.

## Discussion

Urinary obstruction due to BPH is one of the common urological symptoms affecting men over 50 years of age. Medical treatment used for managing BPH includes 5-alpha reductase inhibitor (5ARI), which works at the level of conversion of testosterone into its more potent form, dihydrotestosterone (DHT). These 5-alpha reductase inhibitors have been shown to decrease serum levels of DHT by 80–85% in 10–14 days<sup>14</sup>. The features of BPH include excessive production of stromal and acinar cells surrounding the urethra, sustained by increased formation of new vessels within the gland. Dutasteride, a non-selective 5-alpha reductase inhibitor (acts on type 1 and 2

isoenzymes), decreases the prostate gland's vascularity after six weeks of therapy<sup>12</sup>.

With the suppression of DHT, 5-alpha reductase inhibitors reduce the prostatic gland's size by decreasing glandular stroma and the fibromuscular component of hyperplastic tissue. This strategy is very effective as it reduces more than 30% of the overall size of the prostate in 6–12 months duration<sup>13</sup>. It has been observed that 5ARI reduces the androgen-dependent vascular endothelial growth factor (VEGF), which in turn leads to reduced growth of new vessels within the prostate gland and decreased vascular supply, which results in less prostatic bleeding<sup>14</sup>.

Like finasteride, dutasteride is also used for the treatment of LUTS, secondary to symptomatic BPH. Many studies have been conducted to compare the efficacy of dutasteride in decreasing blood loss during TURP in a similar way as finasteride. Hahn et al. stated that the use of dutasteride for one month prior to TURP was significantly helpful in reducing blood loss, similar to the placebo group. He reported that dutasteride is helpful in reducing serum levels of dihydrotestosterone (DHT) by nearly 90% in a one-month duration. He also reported more than 10 times lower levels of intra-prostatic DHT as compared to the placebo group, but he did not find any significant difference in blood loss, between the groups, either during or after TURP, which is in contrast to our study, as it showed beneficial less drop of hemoglobin in dutasteride using group. However, we did not measure the testosterone levels of the patients in our study<sup>15</sup>.

Boccon et al. reported similar facts and found no difference in a drop of hemoglobin between groups pretreated with dutasteride and the control group undergoing TURP<sup>16</sup>. Yi-ping et al. concluded the need for further data and studies to strengthen pre-treatment recommendation with dutasteride<sup>11</sup>. Furthermore, Gökçe et al. reported significantly lesser perioperative blood loss in patients undergoing TURP, pre-treated with dutasteride for six weeks, compared to the other group ( $1.93 \pm 1.34$  vs.  $2.72 \pm 1.43$ ,  $p=0.01$ ) as similar as results of our study<sup>9</sup>.

Moreover, in favour of dutasteride, Kravchick et al. also postulated about pretreatment of six weeks with dutasteride helped reduce blood loss during TURP by decreasing operative time and improving operative performance reduced prostatic vascularity, mainly in the periurethral area. But in contrast, our study did not report significant differences in operative time between the two groups<sup>17</sup>.

Martov and Ergakov also found highly favourable results and found the shorter operative duration (62 mins vs. 79 mins), removed tissue in larger volume (92 g vs. 85 g), lesser use of irrigation fluid

(16.7L vs. 19.3L), lesser duration of urethral catheterization (10.4 hours vs. 19.3 hours), low volume intraoperative blood loss (93.6 ml vs. 138.6 ml,  $p < 0.05$ ) in patients pretreated with dutasteride for one month as compared to control group<sup>18</sup>.

Future studies with larger sample size and randomized control design can give better insight and true representation of data.

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## Conclusion

This study demonstrates that the use of four weeks of dutasteride pre-treatment is effective in reducing perioperative blood loss in patients undergoing transurethral resection of the prostate.

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## Conflicts of Interest

The authors have declared that no competing interests exist.

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## Acknowledgement

The author(s) wish to acknowledge Dr. Bina Salman, Research Specialist, The Kidney Centre, Post Graduate Training Institute, Karachi-Pakistan.

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## Funding

The author(s) received no specific funding for this work.

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