



## Comparison of the Outcome of Transurethral Resection of Prostate with and Without Preoperative Finasteride

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### Abstract

**Background:** Transurethral Resection of Prostate (TURP) remains gold standard treatment option for BEP. But this procedure has got some expected complications, among them intra-operative and postoperative hematuria has a higher prevalence rate of 3.5-15.7%. So effective strategies and measures should be adopted to ensure better postoperative outcome in TURP patients in terms of reducing peroperative bleeding and its related catastrophes. Short term pre-treatment with finasteride can be an option suited best for TURP in reducing per-operative blood loss & for better postoperative outcome.

**Methods:** This was a hospital based quasi-experimental study conducted in the Department of Urology, Dhaka Medical College hospital, Dhaka in between January, 2021 to December, 2021 with 100 patients having enlarged prostate with moderate to severe LUTS aged within 50-80 years & with pre-operative prostate volume between 40-80 grams. The total sample size was divided in two groups. Whereby group A (n=50) had received 2 weeks of finasteride 5 mg once daily tablet and group B (n=50) was treated with vitamin-D3 2000 IU daily dose as a placebo prior to TURP. All of them underwent Trans-urethral Resection of Prostate. Post-operative follow up was designed as early post-operative follow up and follow up after 28 days of TURP.

**Results:** The baseline variables were comparable among the groups. Statistically significant differences were seen in the time duration of resection which was respectively  $43.97 \pm 8.79$  min and  $66.32 \pm 18.64$  min ( $p$  value  $< 0.0001$ ), in group A & B, also a significant difference was found in irrigation fluid during resection ( $10.50 \pm 2.40$  in group A versus  $19.20 \pm 0.54$  in group B,  $p$  value  $< 0.0001$ ). There was slightly greater postoperative hemoglobin drop in non finasteride group,  $10.85 \pm 0.5$  versus  $10.6 \pm 0.5$  gm/dl ( $p$  value of  $< 0.0001$ ). Three patient (6%) from group A and 12 (24%) patients from group B had encountered postoperative hematuria (with a  $p$  value of  $< 0.001$ ), 2 patient (4%) and 10 patients (20%) required blood transfusion from group A and B ( $p$  value 0.001), 2 patient (4%) and 6 patients (12%) encountered clot retention from group A and B. In the post-operative follow up after 4 weeks, QOL in IPSS were improved in 43 (90%) patient out of 50 in finasteride group, while 34 patient (70%) out of 50 in group B ( $p$  value  $< 0.001$ ). In same follow up, the mean  $\pm$  SD PVR in group A was  $15 \pm 4.6$  ml versus  $22 \pm 8.3$  ml in group B ( $p$  value  $< 0.001$ ). Q max on uroflowmetry done on 28th day after TURP, the Mean  $\pm$  SD  $18.2 \pm 1.4$  ml/sec in group A versus  $16.5 \pm 4.2$  ml/sec in group B ( $p$  value 0.0078).

**Conclusion:** Short term pre-treatment with finasteride was found effective to ensure better outcome in TURP by reducing intra-operative & post-operative blood loss along with better maximum flow rate & lesser amount of post voidal residue.

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## Introduction

Benign Enlargement of Prostate (BEP) is the most common disorder in men beyond fifth decade. Most men who reach their average expectancy will experience this condition in their lifetime<sup>1</sup>. It is also one of the most common cause of lower urinary tract symptoms in elderly men. It is well established that incidence of BEP related complications increases with age & number of aging populations is rising worldwide. No men under the age of 30 years had evidence of BEP & the prevalence of BEP is 88% in 80 years and reaching nearly 100% in 90 years of age<sup>2</sup>. BEP is characterized by the proliferation of prostatic epithelial and stromal cells within the transition zone of the prostate, which results in enlargement of the prostate gland which in turn leads to the compression of prostatic urethra and restriction of the urinary flow<sup>3</sup>.

The options for treatment of BEP are watchful waiting, medical therapy, minimally invasive therapy such as Transurethral Vaporization of Prostate (TUVP), Transurethral Microwave Therapy (TUMT), Transurethral Needle Ablation of Prostate (TUNA), Transurethral Incision of Prostate (TUIP), Laser Enucleation of Prostate (HoLEP), prostate stents, prostate urethral lift, convective radiofrequency water vapor thermal therapy, aqua-ablation, Transurethral Resection of Prostate (TURP) and open prostatectomy<sup>2</sup>. Among the options Transurethral Resection of the prostate is the gold standard of surgical management of BEP<sup>4</sup>. TURP remained as the most common surgical option for BEP worldwide<sup>5</sup>.

Monopolar TURP is the first leading technique for resection adopted worldwide, but it has got some disadvantages such as - TUR syndrome, bleeding which required blood transfusion, failure to complete the procedure, prolonged operation time, post-operative clot retention, return to operation room if severe clot retention, prolongs hospital stay and increases morbidity of the patient<sup>6</sup>. The amount of intra-operative and post-operative bleeding depends on the gland size, surgeon's expertise and duration of surgery. Intra-operative bleeding is usually controlled with electro-coagulation, but excessive intra and post-operative blood loss can cause hemodynamic instability that may increase morbidity and mortality associated with the procedure<sup>7</sup>.

Among 5 $\alpha$ -reductase inhibitors finasteride inhibits only 5 $\alpha$ -reductase type 2, the main enzyme for development of BEP and dutasteride inhibits both type

1 and 2<sup>8</sup>. Finasteride is a selective type-2 5 $\alpha$ -reductase inhibitor which prevents angiogenesis thus reduces prostate vascularity by interacting with the vascular endothelial growth factor (VEGF) and also reduces prostate volume. Finasteride significantly reduces suburothelial micro-vessel density and prostate vascularity with only 2-weeks therapy<sup>9</sup>.

Finasteride is an effective drug that may be considered for TURP patients with prostatic volume more than 30 cc and the duration of treatment ranges from 1-6 weeks depending on the prostatic volume<sup>10</sup>. Preoperative short course finasteride therapy reduces post-operative bleeding complications like postoperative blood loss, persistent hematuria, need for blood transfusion, clot retention and associated complications<sup>11</sup>.

Hagerty et al. (2000) were the first to report a reduction in blood loss during TURP in patients who were taking finasteride (5-ARI) pre-operatively<sup>12</sup>. Previous meta-analyses have demonstrated that preoperative finasteride administration could decrease hemoglobin reduction and hematocrit levels<sup>13</sup>. A United Kingdom-based survey, had revealed that 98% of the urologist uses finasteride to reduce hematuria of prostate origin and 4% of surgeon uses finasteride before TURP to achieve better hemostasis<sup>14</sup>. So this prospective study was designed to find out the efficacy of finasteride as preoperative short term therapy in reducing pre-operative and postoperative bleeding.

## Material and method

This was a hospital based quasi-experimental study conducted in the Department of Urology, Dhaka Medical College hospital, Dhaka in between January, 2021 to December, 2021 with 100 patients having enlarged prostate with moderate to severe LUTS aged within 50-80 years & with pre-operative prostate volume between 40-80 grams. There were two group of study subjects consisting of 50 subjects selected by purposive sampling in each group, one of the group was group A while another one was group B. Lottery was conducted for first two patient and were divided in two groups whereby the group A (n=50) was assigned for patients receiving 5 mg finasteride tablet as a once daily dose for two weeks before TURP and the group B (n=50) was assigned for patients receiving a placebo drug vit-D3 as 2,000IU dose once daily dose prior to TURP. It was found in several randomized studies that vitamin D-3 6000 IU taken orally daily for six months can reduce prostate volume<sup>15,16,17</sup>. In this

study only 2000 IU Vit-D3 administered orally for 2 weeks possibly having no effect on prostate volume. Rest of the patients were distributed in an alternative sequence of odd and even number to the groups. Patients who underwent prior prostate surgery or had a diagnosis of prostate cancer, chronic renal failure, patients who received finasteride, aspirin, coumadin or similar anticoagulants were excluded from the study.

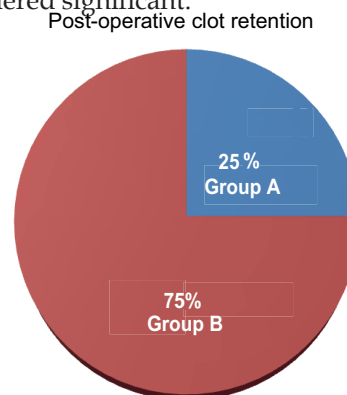
Per operative antibiotic was administered by operation theatre nurses as antibiotic prophylaxis as per pre-operative urine culture and sensitivity report. After proper painting and draping urethroscopy was performed by using 19-Fr cystoscope sheath (Karl Storz ,27026 DAK, Germany) & 30°(degree) Hopkins rod lens (The HOPKINS® telescope from KARL STORZ, Germany) to see any pathology in urethra & urinary bladder along with identification of anatomical landmark and morphology of adenoma. Urethral calibration was done as needed by Otis urethrotome (upto 28 Fr). Introduction of resectoscope was done either by blind approach or under vision. Assembled working element (with telescope, loop electrode, light cable, high frequency diathermy cord & camera) was introduced & after identification of the anatomical landmark the resection was started. Methodical resection was done by following the standard protocol to avoid excessive bleeding or any inadvertent events or injury. All the TURP in both experimental group and control group was done by monopolar mode of resection. Adequate care was taken during resection of apical tissue to avoid sub-trigonal injury. Along the procedure and after completion haemostasis was achieved by proper technique approached with a monopolar diathermy.

After completion of TURP, a 20/22 Fr tri-channel foley catheter was introduced following adequate lubrication, on table traction was given for 5-10 minutes. Catheter was fixed on the anterior compartment of the thigh. After completion of the procedure total amount of irrigation fluid used was measured in liter by counting the amount of irrigation solution bag required during TURP. The duration for resection was also recorded. Post-operative care & follow up was given to lessen or monitor any sorts of complications. Post-operative hemoglobin and hematocrit level was monitored by performing a complete blood count on the next morning following surgery (first post-operative day).

All of the 100 patients were followed up as per schedule(immediate, early post-operative & one month after) for search of any complication related to the intervention & for post TURP outcome in urology department, DMCH. All the collected data was

recorded in the predesigned data collection sheet and subjected to statistical analysis.

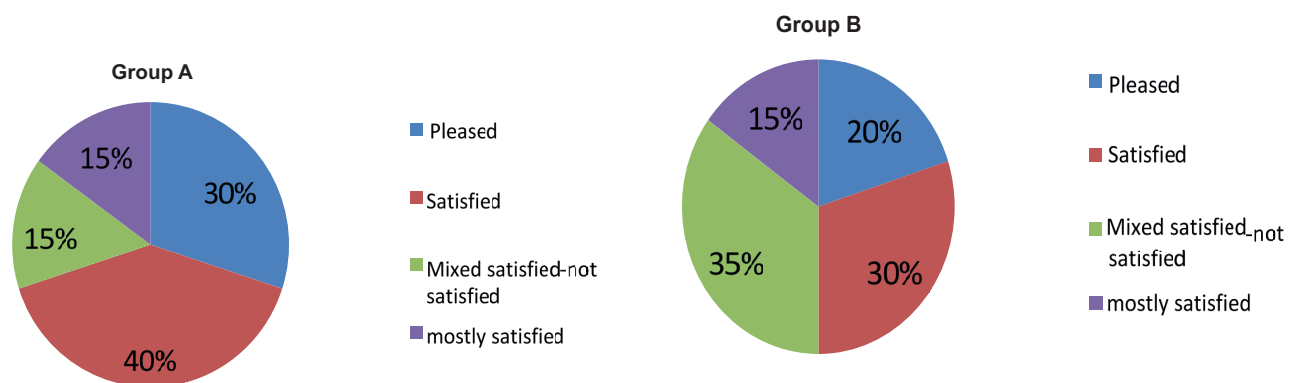
A predefined data sheet was designed to estimate & compare duration of resection, irrigation fluid used, post-operative haemoglobin & hematocrit level, clot retention, need for blood transfusion & post-operative post voidal residue (PVR), maximum urinary flow rate (Q max), Quality of Life (QOL). Data were processed and analyzed on SPSS (Statistical package for social science, Version-25.0). Tests of significance was done by independent sample t-test for quantitative outcome data and Chi-square test for categorical outcome data. Confidence interval was 95%. P-value of less than 0.05 was considered significant.



**Fig-1:** Postoperative clot retention between groups (n=100).

## Results

There was no significant difference regarding age and preoperative prostate volume among the groups. Statistically significant differences were seen in the time duration of resection which was respectively  $43.97 \pm 8.79$  min and  $66.32 \pm 18.64$  min (p value  $< 0.0001$ ), in group A & B, also a significant difference was found in irrigation fluid during resection ( $10.50 \pm 2.40$  in group A versus  $19.20 \pm 0.54$  in group B, p value  $< 0.0001$ ). There was slightly greater postoperative hemoglobin drop in non-finasteride group,  $10.85 \pm 0.5$  versus  $10.6 \pm 0.5$  gm/dl (p value of  $< 0.0001$ ). Three patient (6%) from group A and 12 (24%) patients from group B had encountered postoperative hematuria (with a p value of  $< 0.001$ ), 2 patient (4%) and 10 patients (20%) required blood transfusion from group A and B (p value 0.001), 2 patient (4%) and 6 patients (12%) encountered clot retention from group A and B. In the post-operative follow up after 4 weeks, QOL in IPSS were improved in 43 (90%) patient out of 50 in finasteride group, while 34 patient(70%) out of 50 in group B (p value  $< 0.001$ ). In same follow up, the mean  $\pm$  SD PVR in group A was  $15 \pm 4.6$  ml versus  $22 \pm 8.3$  ml in group B (p value  $< 0.001$ ). Q max on uroflowmetry done on 28 th day after TURP, the Mean  $\pm$  SD  $18.2 \pm 1.4$  ml/sec in group A versus  $16.5 \pm 4.2$  ml/sec in group B (p value 0.0078).



**Figure-2:** Comparison of post-operative Quality Of Life (QOL) score between two groups

**Table I:** Comparison of duration of resection, Irrigation fluid required during resection, Postoperative haemoglobin & hematocrit level between groups (n=100)

Parameter	Group A (n=50) Mean ± SD	Group B (n=50) Mean ± SD	p-value
Resection duration (min)	43.9 ± 8.7	66.3 ± 18.6	< 0.0001
Fluid use (liter)	10.5 ± 2.4	19.2 ± 5.2	< 0.0001
Post-operative haemoglobin level (g/ dl)	11.2 ± 0.5	10.6 ± 0.5	< 0.001
Post-operative hematocrit level	38.2±1.7	38.9±1.1	0.016

**Table II:** Comparison of Postoperative haematuria between groups (n=100)

Parameter	Group A (n=50)	Group B (n=50)	p-value
Postoperative haematuria (up to 3 <sup>rd</sup> post-operative day)	3(6%)	12 (24%)	
Postoperative blood transfusion	2 (4%)	10 (20%)	0.0007 0.001

**Table-3:** Comparison of pre-operative & post-operative Mean QOL in individual group (n=100)

Group	Pre-operative QOL Mean ± SD	Post-operative QOL Mean ± SD	P value
A	4.26 ± 1.03	1.48 ± 0.94	< 0.0001
B	4.96 ± 1.05	1.2 ± 1.05	< 0.0001

**Table-4:** Comparison of post-operative Q max and PVR between groups (n=100)

Criteria	Group A (n=50) Mean ± SD	Group B (n=50) Mean ± SD	p value
PVR(ml) Q max (ml/sec)	15±4.6 18.2±1.4	22±8.3 16.5±4.2	< 0.001 0.0078

## Discussion

It is evident that the data derived from statistical analysis in this study in general comparable with the other reported international studies on the outcome of TURP with and without pre-operative finasteride therapy for two weeks. Recent studies by other researchers have shown that short term pre-operative treatment with finasteride have a beneficial role to ensure better post TURP outcome. The bias in this kind of study is as the outcome of TURP not only depends on the pre-operative use of finasteride but also there are some other factors such as size of the prostate gland, time length of resection and experience of operating surgeon. In order to minimize this chances of bias, patients with comparable age and prostate volume were included in both groups. In most of the operation, Foley catheter was used as of 22 Fr and of same quality, as well as most of the surgery was performed by senior surgeons with nearly equal expertise.

Human studies with finasteride have shown a reduction in blood flow and vascular density<sup>18</sup>. Bleeding is expected during TURP, and it has been reported that approximately 4% of untreated patients may require blood transfusion after the procedure<sup>19</sup>. However, this may be decreased to a value close to 0% if patients have previously received finasteride. For patients treated by TURP, it was established that blood loss was markedly decreased in patient treated with finasteride compared with the non-treated patients, regardless the prostate volume<sup>11</sup>.

Finasteride reduces bleeding from prostatic origin, it was used before TURP to improve vision during the procedure, allow resection of more prostatic tissue, reduces intraoperative bleeding and post-operative hematuria which in turn improves post-operative urinary flow and patient satisfaction after surgery<sup>14</sup>.

In current study, the demographic and baseline characteristics were almost identical in both group. Age distribution was almost similar in both groups in this study. There was no significant difference in age between two group ( $p = 0.954$ ). Similar age in both groups was also found in a similar study<sup>20</sup>.

Pre-operative prostate volume of finasteride group was  $55.2 \pm 13.01$  gram and without finasteride group was  $51.9 \pm 8.7$  gram and that is statistically insignificant ( $p=0.139$ ). Aminsharifi et al. (2016) showed that Preoperative prostate size of control group was  $43.8 \pm 13.7$  gm. and experimental group was  $45.7 \pm 16.04$

gm. and that was statistically insignificant<sup>20</sup>. Comparing to previous study, this study sample values of prostatic volume was a bit higher, may be due to lack of awareness about disease process and its progression in the patients.

There was statistically significant difference in pre-operative haemoglobin level between two groups. Preoperative haemoglobin level of finasteride group is  $12.7 \pm 0.10$  gm/dl and without finasteride group is  $11.5 \pm 0.10$  gm/dl ( $p < 0.001$ ). This result is consistent with the study done by Aminsharifi et al. (2016) where they showed preoperative hemoglobin levels in control group and experimental group were  $13.8 \pm 1.8$  and  $14.00 \pm 1.75$  gm/dl, respectively which was statistically insignificant<sup>20</sup>. Penumatcha et al. (2020) showed that preoperative hemoglobin levels in control group and experimental group were  $12 \pm 0.55$  and  $12 \pm 0.35$  gm/dl, respectively which was statistically insignificant<sup>21</sup>. Haemoglobin value in current study population is less than normal as because of poor nutritional status along with delay in taking proper treatment in proper time.

The duration (Mean  $\pm$ SD) of resection in two groups were respectively  $43.97 \pm 8.79$  min &  $66.32 \pm 18.74$ . The statistical difference was significant with a p value of  $< 0.0001$ . Beside this, the irrigation fluid used in between two groups (The mean irrigation fluid used during operation in group A & B were respectively  $10.5 \pm 2.4$  liter &  $19.2 \pm 5.2$  liter) during resection was also found statistically significant ( $p$  value  $< 0.001$ ). The results of this study showed that the finasteride group patients had less bleeding during TURP, than the control group. This finding is in agreement with observation of similar studies<sup>11,12</sup>. As bleeding was reduced, visibility was improved during resection, the speed of resection was accelerated as well as less irrigation solution was consumed.

There was statistically significant difference of postoperative haemoglobin level between two groups that is  $11.2 \pm 0.5$  gm/dl in finasteride group and was  $10.6 \pm 0.5$  gm/dl in without finasteride group ( $p < 0.001$ ), Mean post-operative hematocrit was  $38.2 \pm 1.7$  in group A &  $38.9 \pm 1.1$  in group B, this p-value (0.016) was also significant statistically in this study. This result is consistent with the study done by Penumatcha et al. (2020) where they showed postoperative hemoglobin level of control group  $9 \pm 0.51$  gm/dl and experimental group  $10 \pm 0.50$  gm/dl. The difference was statistically significant ( $p=0.001$ )<sup>21</sup>.

Three (6%) patients encountered postoperative haematuria following TURP among the finasteride group and 12 (24%) in placebo group in this study which is statistically significant ( $p < 0.001$ ). Malik et al. (2010) showed that in 23(23%) patients gross haematuria was noted; in which 5 (5%) patients were from group A (Finasteride group) and 18 (18%) patients were from group B (non- Finasteride group) that is statistically significant<sup>22</sup>. The percentage of post-operative hematuria was higher in both the groups than the previous studies may be due to multifactorial causes. Patient may be involved in the process of not taking the drug regularly along with the skills of different surgeon's may vary in outcome. So, frequency and percentage were both in the higher ranges in this study population.

In this study there is statistically significant difference in required postoperative blood transfusion between two groups ( $p = 0.001$ ). Two (4%) and 10 (20%) patients required blood transfusion in group A and group B respectively. The result is similar with the study done by Malik et al. (2010) where they showed 16 (16%) out of 100 patients required blood transfusion; in which 4 (4%) patients were from group A (Finasteride group) and 12 (12%) patients were from group B (non-Finasteride group)<sup>22</sup>.

One (3.33%) patients encountered retention of urine in finasteride group and 8 (26.67%) patients without finasteride group due to clot after TURP in this study which is also significant statistically ( $p = 0.02$ ). Malik et al. (2010) showed that 25 (25%) patients out of 100, had postoperative clot retention and need for the Foley's Catheter wash was noted; in which 6 (6%) patients were from group A (Finasteride group) and 19 (19%) patients were from group B (non-Finasteride group) which was statistically significant<sup>22</sup>.

In this study, no patients required return visit to operation theater in finasteride group while 1 (2.5%) patients without finasteride group required clot evacuation after TURP. Malik et al. (2010) showed that 2 (2%) patients in non-finasteride group out of 100 cases suffered from severe postoperative hemorrhage & it was not controlled by conservative management<sup>22</sup>.

In this study, statistically significant difference ( $p$  value 0.017) in pre-operative IPSS (Quality of Life) score was observed between the group given finasteride therapy and the group not given finasteride therapy. The finasteride group showed greater improvement in QoL

than the control group with a statistically significant  $p$  value ( $p < 0.001$ ).

After TURP all 100 patients were followed up on 28 th day for post voidal residue (PVR) on ultrasonography and also the maximum urinary flow (Q max) on uroflowmetry. The mean  $\pm$  SD PVR in group A was  $15 \pm 4.6$  ml (Range 10-20 ml), which was  $22 \pm 8.3$  ml (Range 15-30 ml) in group B ( $p < 0.001$ ). On the uroflowmetry done on 28 th day after TURP, the Mean  $\pm$  SD Q max was  $18.2 \pm 1.4$  ml/sec (Range 16-20ml/sec) in group A and  $16.5 \pm 4.2$  ml/sec (Range 11-20ml/sec) in group B. ( $p = 0.0078$ ).

A significant difference was found between administration of finasteride versus placebo in post TURP outcome. There was less drop of postoperative hemoglobin with less blood loss in favor of finasteride group. Also the post-operative outcome was better in Finasteride group in terms of improvement in QoL, postoperative lesser PVR and higher Q max. The reason that finasteride could decrease intraoperative blood loss along with better outcome due to reduction of prostatic blood flow by down regulation of VEGF factor and reducing the sub-urethral prostatic Microvascular density. Some proportion of patient in finasteride group has suffered haematuria and clot retention, missing of dose of finasteride may be reason behind this event. The expertise of individual surgeon may also had a part in this phenomena.

### Conclusion

This study has showed that short course of Finasteride has ensured better post TURP outcome. There was significantly reduced amount of intra-operative blood loss & very minimum post-operative complications like ongoing hematuria, requirement for blood transfusion, clot retention and postoperative voiding failure in Finasteride group. The time duration for resection and the amount of irrigation fluid required for resection in TURP were also lesser in amount in the finasteride group. The short term therapy with finasteride is well tolerated by patients and has no major side effects.

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