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## The effect of preoperative finasteride therapy on perioperative blood loss in transurethral resection of Prostate for patients with benign prostatic hyperplasia

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### Abstract

**Background:** Benign prostatic hyperplasia (BPH) is an abnormal stromal and glandular proliferation of the prostate gland and is a common benign tumor found in men above 50 years of age. Most men who reach their average expectancy will experience this condition in their life time. The amount of intra-operative and postoperative bleeding depends on the gland size, surgeon's expertise and duration of surgery. Intraoperative bleeding is usually controlled with electro-coagulation, but excessive intra and perioperative blood loss can cause hemodynamic instability, that may increase morbidity and mortality associated with the procedure. Proliferation of the prostatic glandular tissue depends on the androgen dihydro-testosterone, hence inhibition of 5 $\alpha$ -reductase cause's reduction of gland volume that will indirectly reduce the duration of surgery and decrease the blood loss.

**Methods:** The study was conducted in the Department of Urology, Katuri Medical College, Guntur, Andhra Pradesh. One hundred patients who underwent TURP for symptomatic BPH from September 2015 to December 2019 fulfilling the inclusion and exclusion criteria were included in the study.

**Results:** They were randomized in to group A (received 2 weeks of preoperative tab. Finasteride 5 mg OD) and group B (placebo group), with a total of fifty patients in each group. In 70% of the patients in this study group, the prostatic weight was between 40 to 60 grams. 10 out of 50 patients in group A and 9 out of 50 patients in group B had prostatic weight of more than 60 grams. There is significant haemoglobin drop difference between the groups.  $p=0.001$ .it's statistically significant. Postoperative mean haemoglobin in group A & B were 10 grams and 9.4 grams/dl respectively. Postoperative mean PCV in both group A& B were 30 and 28%.

**Conclusions:** Pre-operative short course of finasteride therapy (Tab. finasteride 5 mg OD) definitely reduces the perioperative complications like intra and postoperative blood loss, persistent hematuria, need for blood transfusions, clot retention and postoperative voiding failure. It also decreases operative time, tissue microvessel density and post-operative UTI.

**Keywords:** Finasteride, TURP, haemoglobin

### Introduction

Benign prostatic hyperplasia (BPH) is an abnormal stromal and glandular proliferation of the prostate gland and is a common benign tumor found in men above 50 years of age. Most men who reach their average expectancy will experience this condition in their life time<sup>1</sup>. Like prostate cancer, BPH also very often occurs in the West compared to Eastern nations, such as Japan, China, and Asian countries like India. They are more common in blacks<sup>1</sup>. BPH is characterised by the proliferation of the prostatic epithelial and stromal cells within the prostatic transition zone, which results in enlargement of the prostate gland which in turn leads to compression of the prostatic urethra, and restriction of urinary flow<sup>2</sup>.

The amount of intra-operative and postoperative bleeding depends on the gland size, surgeon's expertise and duration of surgery. Intraoperative bleeding is usually controlled with electro-coagulation, but excessive intra and perioperative blood loss can cause hemodynamic instability, that may increase morbidity and mortality associated with the procedure<sup>9</sup>. Proliferation of the prostatic glandular tissue depends on the androgen dihydrotestosterone, hence inhibition of 5 $\alpha$ -reductase causes reduction of gland volume, that will indirectly reduce the duration of surgery and decrease the blood loss<sup>10</sup>. There have been few studies that have suggested the 5 $\alpha$ -reductase inhibitors finasteride and dutasteride to have anti-angiogenic properties and cause reduction of

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Intraprostatic and suburethral microvessel density<sup>11</sup>. Among 5 $\alpha$ -reductase inhibitors finasteride inhibits only 5 $\alpha$ - reductase type 2, the main enzyme for development of BPH. Dutasteride inhibits both 5 $\alpha$ -reductase type1 and 2. Studies have reported that patients<sup>5</sup> treated with finasteride prior to surgery have lesser bleeding following TURP than those who had been on dutasteride<sup>12</sup>.

Even though several studies have shown that preoperative short course of finasteride for BPH reduces perioperative blood loss following TURP, this is not practised routinely. The goal of this study is to evaluate the effect of finasteride on intraoperative and postoperative blood loss following TURP, which could resolve some of the controversies over the use of this drug.

**Aims and objectives**

**Aim**

To assess the surgical blood loss in patients who undergo transurethral resection of Prostate for BPH with and without preoperative short course Finasteride therapy

**Objectives**

**Primary objectives**

- To assess the post-operative drop in Haemoglobin and PCV, and intra-operative calculated blood loss in the two groups
- To assess the resected prostatic tissue micro vessel density, resected tissue weight and operative time in the two groups.

**Secondary objectives**

To assess and compare the other postoperative complications like clot retention, need for blood transfusion, failure to void after catheter removal and post-operative urinary tract infection in two groups.

**Methods**

The study was conducted in the Department of Urology, Katuri Medical College, Guntur, Andhra Pradesh. One hundred patients who underwent TURP for symptomatic BPH from September 2015 to December 2019 were included here.

**Group A:** (Test Group): Symptomatic BPH patients received 2 weeks Tab. Finasteride 5 mg OD dose prior to Surgery (TURP).

**Group B:** (Placebo Group); Symptomatic BPH patients received 2 weeks placebo prior to surgery

**Inclusion criteria**

1. Men with enlarged prostate and associated lower urinary tract symptoms
2. Patient’s age should be more than 40 years
3. USG prostate weight should be more than 30 grams
4. Patients with no psychological or clinical contraindications to anaesthesia or surgery
5. Able to understand and give written consent for the study
6. Patients who have comprehension and commitment to follow up.

**Exclusion criteria**

1. Previous history of prostatic surgery
2. Suspected prostatic carcinoma or prostatic diseases other than BPH
3. Patients who already received long term 5 alpha reductase inhibitors or alpha blockers
4. Patients who are on anti-coagulants, aspirin or NSAIDS
5. Patients with bleeding diathesis or liver disease

6. Patients who are high risk for surgery (ASA iv)
7. Patients who refused to consent for the study

**Results**

They were randomized in to group A (received 2 weeks of preoperative tab. Finasteride 5 mg OD) and group B (placebo group), with a total of fifty patients in each group.

**Table 1:** Age Group

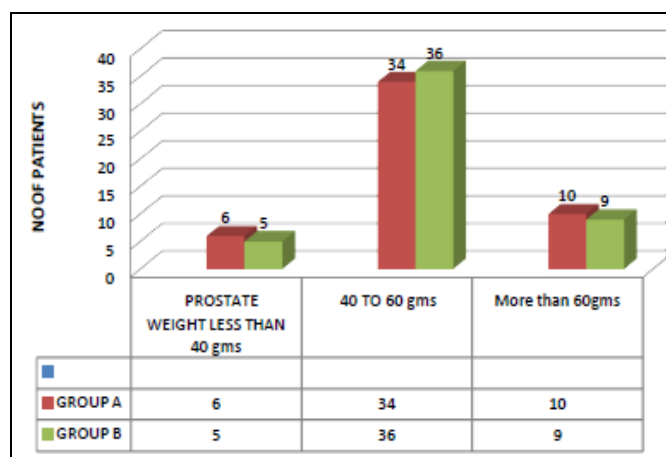
Group	No of Patients	Mean	Age-	Std	Std. error of Mean
		Age (Years)	Range Years	Deviation	
Group A	50	66.	56 to 82	9.	2.
Group B	50	65.	52-80	8.	2.

Mean age in group A & B was 65.74, 65.08 years and minimum and maximum age of the patients in group A was 56 and 82 years, in group B, 52 &80 years respectively. In both the groups more than 40% of the patients belonged to the age group 60 to 70 years. From table no 3, age distributions in both groups were comparable.

**Table 2:** Prostate weight distribution

USG Prostate Weight (Grams)	Less than 40 Gms	40 To 60 Gms	More than 60 Gms	Total patients
Group A (no of patients)	6	34	10	50
Group B (no of patients)	5	36	9	50
Total study group	11	70	19	100

In 70% of the patients in this study group, the prostatic weight was between 40 to 60 grams. 10 out of 50 patients in group A and 9 out of 50 patients in group B had prostatic weight of more than 60 grams.



**Fig 1:** Prostate weight distribution

**Table 3:** Pre-operative Hb

Preoperative Haemoglobin (grams/dl)	Range	Mean	Standard Deviation
Group A(grams/dl)	10 to 12.5	12.	0.3469
Group B((grams/dl)	10.1 to 12.7	12	0.5559
Total Study group (grams/di)	(10 to 12.7)	12.	0.4587

From the above table it can be inferred that the mean haemoglobin for group A was 11.7 grams/dl and the range was 10 to 12.5 grams. The mean haemoglobin for group B was 12.0 grams and the range was 10.1 to 12.7 grams/dl. The p value for this table was 0.114, hence statistically not significant. Therefore both the groups were comparable.

**Table 4:** Post-operative Hb

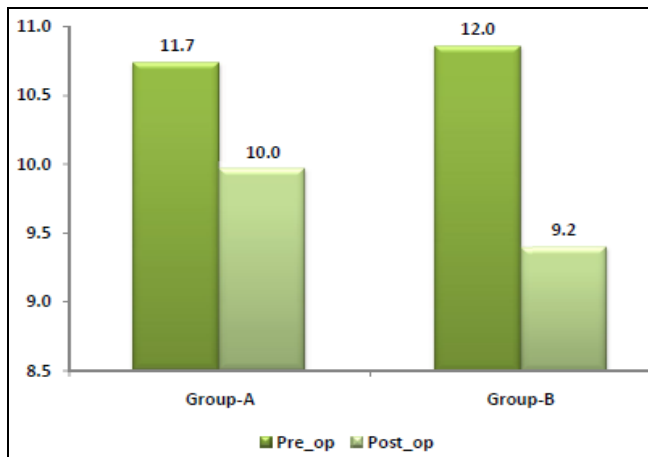
Post-Operative Haemoglobin(gms/dl)	Range	Mean	Standard Deviation
Group A (gms/dl)	8 to 11.0	10	0.5049
Group B (gms/dl)	8.2 to 10.3	9.	0.5148

There is significant haemoglobin drop difference between the groups. p=0.001.it's statistically significant.

**Table 5:** Mean-operative Hb

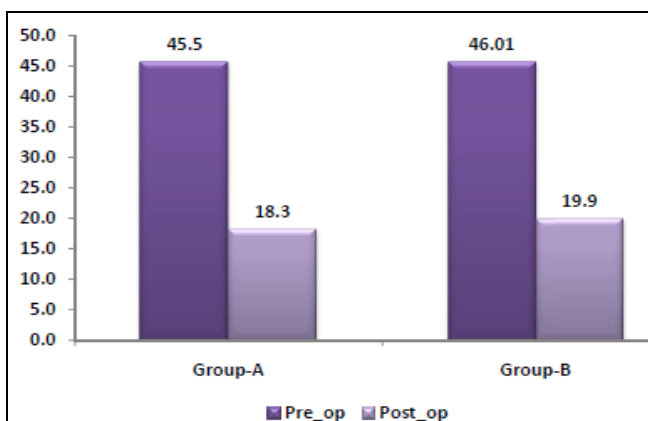
Mean Preoperative Haemoglobin (Gins/dl)	Mean post op a Haemoglobin (Gauss/dl)	Mean HB loss(g/dl)
Group A (gms/dl)	12.	10
Group B (gms/dl)	12	9.
Total Study Group (gins,411)	12.	10.

It can be inferred from the above table pre and postoperative mean haemoglobin in group A were 11.7 & 10 grams and mean haemoglobin loss after TURP in this group was 1.7 grams/dl and p value is 0.112. In group B pre and post-operative haemoglobin were 12.0 & 9.2 grams and mean haemoglobin loss in group B was 2.8 grams and p value is 0.000. So there is significant post-operative haemoglobin drop in group B and that is statistically significant.



**Fig 2:** Pre and post mean HB by group

Pre-operative PCV of our entire study group patients was 31.5%. After TURP there was a fall in PCV seen in both groups. Mean fall in PCV in group A was 1.9% and for GROUP B, 3.5%. Over all for the entire study population, the mean fall in PCV after TURP was 1.028.

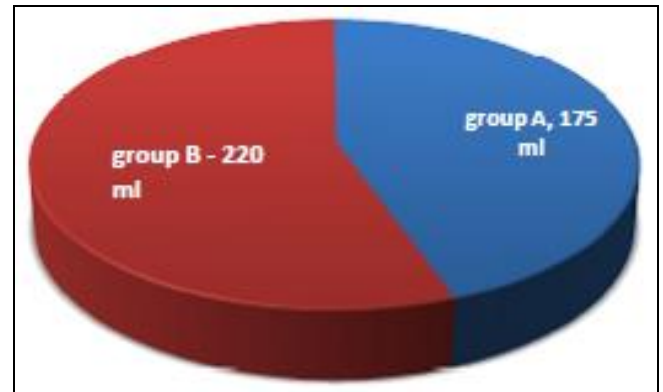


**Fig 3:** Pre and post USG prostate mean weight

The mean postoperative USG residual prostate weight in group A and B were 18.3 and 19.9 grams respectively. The mean reduction in prostatic weight after TURP in group A & B were 27.2gms and 26.1 gms respectively. The p value was calculated to be 0.054. Though group A had more reduction in prostate weight than group B, this difference had no statistical significance.

**Table 6:** Blood Loss

Blood Loss (ml)	Range	Mean	Standard Deviation
Group A	95 to 270	175	95.
Group B	150 to 320	220	125.



**Fig 4:** Blood loss

The estimation of intraoperative blood loss was calculated from the irrigation fluid used for TURP. The method of estimation has been explained in the materials and methods. The calculated blood loss for the patients in group A ranged between 95 to 270 ml and for patients in group B between 150 to 320 ml. The mean blood loss in group A & B were 175 ml and 220 ml respectively. Tables and pie chart show that patients in group A had less intra-operative calculated blood loss than patients in group B. This was statistically significant, and indicates that preoperative short course finasteride therapy in BPH patients is likely to significantly reduce intra-operative blood loss.

**Discussion**

Benign prostatic hyperplasia (BPH)<sup>54</sup> is one of the common urological diseases after fifty years of age. The symptoms can start at any age and may present even in early age group. At 50 years of age, up to 50% of men have symptoms or histological evidence of BPH. The incidence of symptomatic BPH is known to increase with age.

When prostate get enlarged, the prostatic urethra gets compressed between the prostatic lobes. This outflow obstruction produces impedance to urinary flow from the bladder and it may cause storage and voiding symptoms like frequency, urgency, hesitancy, nocturia and decreased stream. These symptoms are collectively known as lower urinary tract symptoms (LUTS). As the disease progresses, the associated complications like recurrent UTI, bladder calculi, diverticulum formation, refractory hematuria and obstructive uropathy also increase. Therefore treatment for symptomatic BPH is the corner stone for avoiding these complications in older age group.

Intraprostatic Dihydrotestosterone (DHT) is the main mediator for BPH progression. 5 α reductase is the main nuclear enzyme which converts testosterone to DHT. Hence 5 α reductase inhibitors have been the main drugs used in the medical management of BPH. Finasteride and dutasteride are the two common 5 α reductase inhibitors (ARI) used in the current

medical management of BPH. Dutasteride inhibits both 5  $\alpha$  reductase Type 1 & 2, but finasteride inhibits only 5  $\alpha$  reductase type. Due to this dual action dutasteride reduce serum DHT up to 90%, whereas finasteride reduces DHT levels by only 70 to 80%. Within the prostate 5  $\alpha$  reductase type 2 is the predominant enzyme, and reduces intraprostatic DHT up to 90%. These drugs mainly induce apoptosis of stromal and glandular components of the prostate. Up to 30% glandular volume reduction is noticed after six months of finasteride therapy.

Our study showed that short course preoperative finasteride therapy (5mg od for two weeks) significantly reduced the intra and post-operative blood loss, operative time and resulted in greater resection of tissue and lessened the complications like post-operative clot retention, voiding failure, requirement of blood transfusion.

### Conclusion

From our study we conclude that preoperative short course of finasteride therapy (Tab. finasteride 5 mg OD) definitely reduces the perioperative complications like intra and postoperative blood loss, persistent hematuria, need for blood transfusions, clot retention and postoperative voiding failure. It also decreases operative time, tissue microvessel density and post-operative UTI. It aids removal of more prostatic tissue and also improves the urinary flow rate (Q max). Hence based on our study we recommend the use of preoperative short course (2 weeks) finasteride therapy prior to TURP in the treatment of BPH, due to its role in effective control of perioperative Blood loss and associated complications.

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