

THE EFFECT OF DUTASTERIDE IN PERI-OPERATIVE BLOOD LOSS DURING TRANSURETHRAL RESECTION OF PROSTATE (TURP)

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Abstract

This prospective double blind comparative study was designed to compare the effect of Dutasteride on the perioperative blood loss in Transurethral Resection of Prostate (TURP). Sixty patients with BPH underwent TURP were divided into 2 groups. Patients belong to the group B (Control) and group A (Experimental). Experimental group patients were given Cap. A (dutasteride 0.5 mg) before two weeks of TURP and group B (control) were given Cap. B (placebo). Postoperative comparison between two groups showed that there were no significant difference between the weight of resected prostatic tissue (control = 22.41±6.83 gm, and experimental = 25.38±7.22 gm; p=0.107). Postoperative hemoglobin level of both group (Control group = 10.78±0.64 gm/dL and experimental group = 10.83±.51 gm/dL) revealed no significant difference (p=0.774). The mean hemoglobin loss per gram of prostate tissue in both groups (control = 1.81±0.81 gm/gm and experimental = 1.79±0.88 gm/gm) did not show any statistical difference (p=0.938). In this the study it was found that if the BPH patients are subjected with dutasteride 0.5mg before 2 weeks of TURP, bleeding decrease slightly (Control group = 20.35±7.99 ml/gm and Experimental groups = 17.41±7.70 ml/gm). However, these data of bleeding loss did not show any statistical significance.

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Introduction:

BPH is the most common urological problem in aging men with its prevalence approaching 70% by age 65 years¹. At age 55, approximately, 25% of men report obstructing voiding symptoms. At age of 75 years 50% complain of decreased urinary flow[2].

Transurethral resection of prostate (TURP) is a standard surgical therapy for BPH. Though TURP is an established procedure, significant intraoperative as well as postoperative bleeding remains a common complication leading to postoperative clot retention and required blood transfusion[3].

Dutasteride inhibits conversion of testosterone to dihydrotestosterone (DHT) and is used for the treatment of benign prostatic hyperplasia (BPH). It belongs to a class of drugs called 5-alpha-reductase inhibitors, which block the action of 5-alpha-reductase enzymes that convert testosterone into dihydrotestosterone. Dutasteride inhibits both two isoform of 5-alpha reductase, I and II. Dutasteride acts by inhibiting androgen induced angiogenesis and mean vascular density of prostate[4].

Studies have found that 5 alpha reductase inhibitors suppress the androgen controlled vascular endothelial growth factor (VEGF), leading to decreased angiogenesis and less prostatic bleeding perioperatively[5]. Dutasteride is effective to reduce preoperative blood loss during TURP with preoperative short course[6].

This study was to measure preoperative prostate volume, measure and postoperative Hb. Concentration of blood, weight of resected prostatic chips after TURP.

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Estimated blood loss per gram of prostatic tissue in group A and group B, and compare blood loss per gm. of prostatic tissue between group A and group B.

Materials and Methods

This was a double blind randomized controlled clinical trial conducted in the Department of Urology, BSMMU, Dhaka, Bangladesh from Jan 2016 to April 2017 with an objective to determine whether pretreatment with dutasteride reduces postoperative blood loss or not in-patient undergoing TURP for benign prostatic hyperplasia (BPH). In urology OPD, all the patients were evaluated preoperatively by history, complete physical examination including DRE with focal neurological examination and relevant investigation, eg. Urine for R/M/E & C/S, CBC with Hb%, PSA, s.creatinine, RBS, HBsAg, Anti HCV and USG of KUB with prostatic volume with MCC & PVR and uroflowmetry, CxR, ECG and echocardiogram. The patient who were aged 45 to 75 yrs, diagnosed as BEP having indication of surgery, PSA- Less than 4 ng/ml, prostate volume is equal or more than 30gm by abdominal USG were selected for this study. Patients with the history or evidence of prostatic disease other than BEP, previous prostate surgery, requirement for treatment with aspirin or other anticoagulants or NSAIDS during the perioperative period, severe medical conditions such as liver disease, bleeding disorders, CKD and unstable cardiorespiratory problem were excluded. There were two groups of study population consisting of 30 subjects in each group, selected randomly. One group was Group A and another was Group B. Group A taking capsule A and while Group B taking capsule B prior to underwent standard TURP. Both the capsules were soft gelatin gel with similar outlook specifically produced for this study for Double Blinding.

Group-A was given Cap. A, and Group B was given, Cap. B on morning for 2weeks before operative procedure. All the patients were underwent standard mono polar TURP. Sample for preoperative Hb was collected 3 days before TURP. Sample for postoperative Hb was collected 1hour after surgery if no blood were transfused preoperatively. If blood were transfused during surgery then sample was collected 1hour after completion of transfusion. Peroperative hemoglobin loss were calculated by deducting postoperative Hb from preoperative value and adding 1gm for each unit of whole blood transfusion. Volume of blood loss was derived by multiplying Hb loss with 450 ml⁷.

After completion of TURP, resected prostatic chips were measured by analytical balance. Blood loss per gm of

prostatic tissue was calculated by dividing volume of blood loss with weight of resected chips of prostate.

Cap. A was containing dutasteride 0.5mg and cap. B placebo. During this time of study it was known that group A was experimental group B was control group.

Data Analysis: Cap A was Dutesteride 0.5 mg and cap B was Placebo. Statistical analysis of the results was done by using computer based statistical software, supplied by BSMMU. Results were expressed as mean \pm SD and compared by student's *t* test. A 'p' value of < 0.05 was considered as significant. A fragmented portion of result was also analyzed by Wilcoxon Sign Ranked Test a level of significance was 0.05.

Results

Mean age of control group was 64.17 \pm 7.88 years and experimental group was 66.23 \pm 6.65 years with a range of 45-75 and 50-75 years, respectively and there was no significant difference between two groups ($p=0.277$). Preoperative prostate size of control group was 50.53 \pm 9.05 gm. and experimental group was 52.60 \pm 7.96 gm. and that was statistically insignificant ($p=0.352$). Preoperative hemoglobin levels in control group and experimental group were 12.06 \pm 0.54 and 11.95 \pm 0.34 gm./dL, respectively which was statistically insignificant ($p=0.363$) (Table 1).

In control group 22.41 \pm 6.83 gm of prostate tissues were resected during TURP and in experimental group it was 25.38 \pm 7.22 gm. and there was no significant difference between group A and B ($p=0.107$). After the surgery postoperative hemoglobin level of both group were measured but the measured data of control group (10.78 \pm 0.64 gm/dL) and experimental group (10.83 \pm .51 gm/dL) revealed no significant difference ($p=0.774$). Hemoglobin loss per gram of prostate tissue in both groups (control = 1.81 \pm 0.81 gm/gm and experimental = 1.79 \pm 0.88 gm/gm) did not show any statistical difference ($p=0.938$) (Table 2).

It was found that the by taking the dutasteride before two weeks of TURP in BPH patients compared with the control group without dutasteride slightly decreased the post-operative blood loss (control group = 20.35 \pm 7.99 ml/gm and experimental groups = 17.41 \pm 7.70 ml/gm). However, statistically significant difference was not found between the two groups ($p=0.152$) (Table 3).

Table-I
Comparison of preoperative baseline variable in both groups (n=60)

Outcomes	Group		P Value
	Control (B) (n=30)	Experimental (A) (n=30)	
Age (Range)	64.17±7.88 44-75	66.23±6.65 50-75	0.277
Preoperative prostate size (gram) (Range)	50.53±9.05 35-68	52.60±7.96 40-72	0.352
Preoperative hemoglobin level (gm/dL) (Range)	12.05±0.54 11.1-13.4	11.95±0.34 11.4-12.6	0.363

Data of age, Preoperative prostate size, serum hemoglobin were analyzed using student's t- test and the level of significance was 0.05.

Table-II
Comparison of weight of resected prostatic tissue, Postoperative hemoglobin level, and hemoglobin loss per gram of prostate tissue (n=60).

Outcomes	Group		P Value
	Control (B) (n=30)	Experimental (A) (n=30)	
Resected prostate volume (gm) (Range)	22.41±6.83 10-36	25.38±7.22 15-38	0.107
Postoperative hemoglobin level (gm/dL) (Range)	10.78±0.64 9.4-12.4	10.83±0.51 10.0-11.8	0.774
Hemoglobin loss/gram of prostate tissues Ranges	0.08±0.032 0.03-0.16	0.07±0.031 0.02-0.14	0.116

Data were analyzed using student's t- test and the levels of significance were 0.05.

Table-III
Comparison of blood loss per gram of prostatic tissue (n=60).

Outcome	Group		P Value
	Control (A) (n=30)	Experimental (B) (n=30)	
Blood loss per gram of prostatic tissue (mL/gm) (Range)	20.35±7.99 4.2-33.8	17.41±7.70 6.25-38.75	0.152

Data were analyzed using student's t- test and the levels of significance were 0.05.

Discussion

In this study the age range was 45-75 years. The mean age of control group was 64.17 ± 7.88 years and experimental group was 66.23 ± 6.65 years; ($p=0.277$). This result coincides with other similar researches⁷ where the mean age of control group was 65.5 years and experimental group was 63.8 years ($p=0.022$). Before the TURP we measured the preoperative prostate size which was 50.53 ± 9.05 gm. in control with range 35-68 gm. and 60 ± 7.96 gm. with range of 40-72 gm. in experimental group ($p=0.352$). It was investigated the effects of dutasteride in TURP by measuring the preoperative prostate size where it was 40.4 ± 9.7 gm. with range of 26-63 gm. in control group and 39.8 ± 10.4 gm. with range 20-69 gm. in experimental group ($p=0.76$). During this study we found the preoperative hemoglobin levels in control group and experimental group were 12.06 ± 0.54 and 11.95 ± 0.34 gm/dL, respectively which was statistically insignificant ($p=0.363$). This results also accordance with the results of other studies where the preoperative hemoglobin level in control and experimental groups were 11.6 and 11.8 gm/dL respectively.⁷

Comparison of postoperative parameters like weight of resected prostatic tissue, hemoglobin level, hemoglobin loss and blood loss per gram of prostatic tissue were considered in this study. In control group 22.41 ± 6.83 gm of prostate tissues were resected during TURP and in experimental group it was 25.38 ± 7.22 gm ($p=0.107$). Similar results were also found by Uchida et al (1999)⁸ where resected prostate tissue 25.9 and 23.3gm in early group and late group respectively. After the surgery postoperative hemoglobin level of both group were measured but the measured data of control group (10.78 ± 0.64 gm/dL) and experimental group (10.83 ± 0.51 gm/dL) which revealed no significant difference ($p=0.774$) between the two groups. Hemoglobin loss per gram of prostate tissue in both groups (control = 1.81 ± 0.81 gm/gm and experimental = 1.79 ± 0.88 gm/gm) did show insignificant difference ($p=0.938$). Uchida et al (1999) and Jamal et al., (2010) did not found any significant difference in hemoglobin loss in both of their groups⁷. Jamal et. al., found that the Hb loss per gram of prostate tissue in control and experimental groups were 1.29 and 1.46gm ($p=0.41$).

It was found that by taking Cap.A (dutasteride 0.5 mg) before two weeks of TURP in BPH patients compared

with the control group taking Cap.B (placebo), slightly decreased the post-operative blood loss (control group= 20.35 ± 7.99 ml/gm and experimental groups= 17.41 ± 7.70 ml/gm). However, statistically significant difference was not found between the two groups ($p=0.152$).

Comparing the findings of the present study it can be concluded that two weeks pretreatment with dutasteride 0.5mg in Benign prostatic hyperplasia (BPH) patients has no statistically significant effects on reduction of blood loss during TURP.

Conclusion

The present study revealed that no significant differences were seen in bleeding during the TURP after dutasteride administration. This study adds little more bulk to the body of conflicting evidence. Further research is necessary to provide sufficient data for meta analysis to comment unequivocally about effect on bleeding during TURP.

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