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Effects of 5-α-Reductase Inhibitor (Finasteride) on Per Operative Blood Loss in Patients with BPH undergoing TURP

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ABSTRACT

Aim of the study: *To assess the effects of 5-α-reductase inhibitor (finasteride) on per operative blood loss in patients with BPH undergoing TURP by measuring preoperative and postoperative Hb by comparison with control cases.* ***Methodology:*** *A total of 50 patients of Benign Prostatic Hyperplasia (BPH) planned for Trans-Urethral Resection of Prostate (TURP) having a prostate size of more than 40 grams on trans-abdominal ultrasonography an\or transrectal ultrasonography with PSA of less than 0.4 ng\dl was randomized into 2 groups, each group having 25 patients. The finasteride group (Group A) was prescribed oral 5 mg of finasteride daily for 2 weeks before surgery. The control group (Group B) did not receive any agent. After 2 weeks, TURP was performed and variables were recorded.* ***Results:*** *There was no significant difference in the mean age of patients, prostate volume, PSA and preoperative hemoglobin level in both groups, however, significant difference was found for postoperative hemoglobin level with highly significant p-value=0.001 in that postoperative hemoglobin was dropped more in control group, and the rate of blood transfusion was more in the control group (7% for the control group while 1% for study group) besides these, amount of irrigation fluid used and duration of irrigation was more in the control group.* ***Conclusion:*** *The 5-α-reductase inhibitors (finasteride) reduces intraoperative and postoperative blood loss in patients with BPH undergoing TURP if given two weeks before surgery as well as decrease rate of blood transfusion, amount of irrigation fluid used and duration of irrigation needed to clear hematuria postoperatively.*

Keywords: 5-α-reductase inhibitor, BPH, TURP

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the leading cause of lower urinary tract symptoms (LUTS) among the aging male population affecting more than 50% of men above 60 years of age [1]. AUA guideline (2003) suggests an increase in the incidence of BPH worldwide and predicts by the age of 60 years, more than 50% of men will have microscopic evidence of the disease and by the age of 85 years, about 90% of men will be affected [2]. Transurethral resection of the prostate (TURP) remains the gold standard for patients with benign prostatic hyperplasia (BPH) that failed medical therapy. Perioperative hemorrhage is one of the major complications of TURP, and prolonged bleeding will lead to blood transfusion and clot retention [3].

Various drugs have been used to decrease prostatic blood flow. Finasteride, an antiandrogen, was the first 5-α-reductase inhibitor approved in the United States in 1992 for the treatment of BPH [4]. Finasteride is a type 2 5-α-reductase inhibitor and reduces prostatic vascularity by interacting with vascular endothelial growth factor (VEGF), which is an androgen-sensitive growth factor stimulating angiogenesis. Microvessel density (MVD) is a histological measurement of angiogenesis and thus a marker of bleeding. Studies have shown that BPH presenting with hematuria have a significantly higher MVD than BPH without hematuria, suggesting that MVD is a marker of vascularity and suburothelial microvessel proliferation may play an important role in mediating hematuria associated with BPH [1,5]. Emerging data have shown that finasteride treatment prior to TURP significantly decreases MVD in the prostate tissue [6-10].

Finasteride is well absorbed orally with an oral bioavailability of 63%. Total 40%-50% is metabolized in the liver, primarily by CYP3A4 to metabolites that are inactive and are eliminated through feces and urine. The half-life of

finasteride is 6-8 hours and it is 90% bound to plasma proteins [11,12]. The 5 mg dose was found to produce a marked improvement in symptom score, urinary flow rate, and prostate volume compared to that of placebo [13,14].

PATIENTS AND METHODS

Between October 2017 and October 2018, 50 patients were included in the study; patients were randomized blindly into 2 groups, control group who did not receive any drugs before TURP and study group who received finasteride 5 mg once daily for two weeks before surgery. Patients on aspirin and other NSAIDs, Clopidogrel, history of previous UTI within last week before surgery, prostate size more than 60 ml, bleeding disorders, on finasteride for the last 3 months and PSA more than 4 ng/dl were excluded from the study.

Patients who fulfilled the criteria of the study were 50 patients, 25 for each group. Patients underwent standard TURP in both Rizgary Teaching Hospital and Zheen International Hospital. Recorded data included were per operative Hb level, amount of irrigation fluid used, hours of wash after TURP and blood transfusion rate. Analysis of the data was performed using SPSS (version 17). Results are expressed as means ± standard error. Independent t-test used for comparison of ages, prostate-specific antigen, prostate volume, preoperative hemoglobin, postoperative hemoglobin, amount of irrigation of fluid used and duration of irrigation of fluid used postoperatively between control and study group. Fisher's chi-square was used for comparison of blood transfusion rates between control and study groups. A $p \leq 0.05$ were considered to be statistically significant.

RESULTS AND DISCUSSION

There was no significant difference in the mean age of patients, prostate volume, PSA and preoperative hemoglobin level in both groups, however, significant difference was found for postoperative hemoglobin level with highly significant p-value=0.001, in that postoperative hemoglobin was dropped more in control group, and the rate of blood transfusion was more in the control group (7% for the control group while 1% for study group) besides these, amount of irrigation fluid used and duration of irrigation was more in the control group.

Despite the minimally invasive nature of TURP, bleeding remains the most common complication of the procedure [9,15,16]. Regarding the perioperative complications of TURP, besides sepsis, shock and post TURP syndrome, hemorrhage is the single most common complication, which may require a blood transfusion, return to operation room if severe, clot retention and prolong hospital stay [9].

Bleeding associated with TURP depends on the preoperative use of finasteride, size of the prostate gland, length of the operation, and experience of the operating surgeon. Clot retention also depends on the quality and number of 3-way Foley's catheter used for irrigation [17]. Finasteride is a selective 5-alpha-reductase type 2 inhibitor, which reduces prostate vascularity by reducing the conversion of testosterone to dihydrotestosterone (DHT), shrinks the prostate size and reduces hormone-dependent neo-vascularity of the gland in BPH patients, thus resulting in reduced bleeding during TURP [18].

Finasteride downregulates VEGF, so has a beneficial role in the treatment of haematuria secondary to benign prostatic hyperplasia. It has also been demonstrated that the short-term preoperative use of finasteride reduces bleeding during and after TURP. Thus, finasteride has been used. In our study, there is no statistically significant difference in baseline age, prostate volume, PSA or preoperative hemoglobin (Table 1). In the study done by Ozdal, et al., the intraoperative blood loss is calculated using the formula:

Blood loss=(Irrigating fluid × Hb in irrigating fluid)/pre-op Hb

It is 142.2 ± 18.7 ml in the finasteride group and 224.3 ± 52.7 ml in the control group. Blood loss per gm of resected prostate is 8.76 ± 0.3 ml in finasteride group and14.68 ± 1.5 ml in the control group and are found to be statistically significant (p=0.001), but in our study we were depended on simple measurement of postoperative Hb 48 hours after operation to eliminate the bias of hem dilution due to fluid transfusion because of lack of facility.

Table 1 Comparison of ages, prostate volume and PSA between control and study groups (means ± Standard errors)

Groups	Ages (years)	Prostate Volume (ml)	PSA (ng/dl)
Control	66.65 ± 1.52	48.39 ± 1.39	2.26 ± 0.12
Study group	69.33 ± 1.68	48.82 ± 1.50	1.95 ± 0.17
p-value	N.S.	N.S.	N.S.
NS: Non-significant			

Table 2 shows a comparison of preoperative Hb and postoperative Hb between control and study groups in which there was a significant difference (p=0.001) between postoperative Hb in both groups, there was a drop of Hb more in the control study. A study by Donohue, et al., compared finasteride 5 mg daily with placebo for 2-weeks prior to TURP and found that there was significantly less mean blood loss in irrigation fluid in the finasteride group than in the control group (43.6 gm versus 69.3 gm hemoglobin, p=0.011) [15]. The mean difference was more significant when blood loss per gm resected prostate was calculated (2.65 gm versus 4.65 gm hemoglobin per gm prostate, p<0.01). This less blood loss in the study group may be explained by the fact that finasteride will decrease microvessel density in the prostate as in the research conducted by Donohue, et al., [15].

Table 2 Comparison of preoperative Hb and postoperative Hb between control and study groups (means ± standard errors)

Groups	Preoperative Hb (gm/dl)	Postoperative Hb (gm/dl)
Control	13.60 ± 0.28	11.52 ± 0.25
Study group	14.00 ± 0.36	13.03 ± 0.31
p-value	N.S.	0.001
NS: Non-significant		

Table 3 shows comparison of the amount of irrigation fluid used and duration of irrigation between control group and the study group which demonstrated significant difference in the amount of fluid used in both groups, for control group was (16843.63 ± 341.26 ml) while for study group was (16162.60 ± 299.77 ml) with (p=0.05), and also the duration of irrigation for control group was shorter (24.73 ± 1.53 hours) and for study group (38.60 ± 1.99 hours) with (p=0.001) and this is explained by better clearance of wash and earlier clearance of it in patients who are pretreated with finasteride.

Table 3 Comparison of the amount of irrigation fluid used and the duration of irrigation between control and study groups (means ± standard errors)

Groups	Irrigation Fluid (ml)	Duration of Irrigation (hrs)
Control	16843.63 ± 341.26	38.60 ± 1.99
Study group	16162.60 ± 299.77	24.73 ± 1.53
p-value	0.05	0.001

Table 4 shows the comparison between blood transfusion rates between both groups with blood transfusion rate being more in the control group with significant p-value level.

Table 4 Chi-square analysis for comparison of blood transfusion rates between control and study groups

Groups	Blood transfusion	No Blood transfusion
Control	7.00(28%)	18.00(72%)
Study group	1.00(4%)	24.00(96%)
Pearson chi-square=5.357; p-value=0.05		

CONCLUSION

The 5-α-reductase inhibitors (finasteride) reduces intraoperative and postoperative blood loss in patients with BPH undergoing TURP if given two weeks before surgery as well as decrease rate of blood transfusion, amount of irrigation fluid used and duration of irrigation needed to clear hematuria postoperatively.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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