

The Effect of Two Weeks Preoperative Finasteride Therapy in Reducing Prostate Vascularity

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ABSTRACT

Objective: To determine the effect of two weeks preoperative finasteride therapy in reducing prostate vascularity in terms of mean microvessel density (MVD) and expression of VEGF in prostate urothelium among patients of BPH by comparing with controls.

Study Design: Randomized controlled trial.

Place and Duration of Study: Shifa International Hospital, Islamabad, from January 2013 to January 2014.

Methodology: A total of 80 patients of Benign Prostatic Hyperplasia (BPH) planned for Trans-Urethral Resection of Prostate (TURP) having prostate size of more than 40 grams on trans-abdominal ultrasonography was randomized into two groups, each group having 40 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 prostate samples were sent for histopathological determination of MVD and expression of VEGF.

Results: The mean age of patients was 66.21 ±10.08 years, ranging from 48 to 86 years. The mean prostate gland size was comparable in both groups (55 ±10.7 vs. 58.1 ±10.8 grams, p=0.21). Mean MVD in finasteride group (20.25 ±10.3) was significantly lower as compared to control group (48.9 ±22.6, p < 0.001). Similarly expression of VEGF was also significantly lower in finasteride group (30%) as compared to control group (65%) [p= 0.0017]. Mean MVD had a significant weak correlation with the size of prostate gland on Pearson correlation test (2-tailed) with r = 0.222.

Conclusion: Finasteride reduces microvessel density and hence prostate vascularity with only 2-week therapy and the mean MVD is clearly correlated with size of prostate.

Key Words: *Finasteride. Microvessel density. Benign prostatic hyperplasia (BPH). Vascular endothelial growth factor (VEGF). Hematuria. Transurethral resection of prostate (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

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.^{2,3}

In a RCT, comparing the impact of finasteride on hematuria due to BPH, Foley *et al.* found that hematuria completely resolved in about 86% of the patients on finasteride compared to only 37% in the control group.⁴ Also, if used preoperatively, finasteride could decrease intraoperative haemorrhage during TURP.^{5,6}

In comparison to control group, treatment with finasteride significantly lowers the mean MVD in the suburethral portion of prostate.⁷⁻⁹ However, the guidelines of American Urological Association's (AUA) show insufficient evidence to recommend perioperative 5-ARI treatment to decrease bleeding.¹⁰

Reducing prostate vascularity will be helpful in decreasing intra-operative prostatic bleeding. The aim of this study was to determine the effect of two weeks preoperative finasteride therapy in reducing prostate vascularity in terms of mean Microvessel Density (MVD) and expression of VEGF in prostate urothelium among patients of BPH by comparing with controls.

METHODOLOGY

This randomized controlled trial was conducted in the Department of Urology in collaboration with the Department of Pathology at Shifa International Hospital, Islamabad, from January 2013 to January 2014 after approval from Institutional Review Board. Patients of

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BPH planned for TURP having prostate sized more than 40 grams on trans-abdominal ultrasonography were randomized into two groups having 40 patients each. Patients with anemia (Hb% < 12 gm/dl), history of urinary tract infection/prostatitis in the last 2 weeks, prostate cancer, patients used 5-alpha reductase inhibitor in the last 1 year, patients using aspirin or clopidogrel or having bleeding disorders were excluded from the study through appropriate clinical evaluation by proper history, physical examination and performance required investigation. Sample size was calculated by using WHO sample size calculator, using level of significance (α): 5%, power of test (%) 1- β : 80%, population standard deviation (O): 5.75 (Pooled SD),⁵ population variance (O2): 33.0, test value of population mean: 9.08⁵ and anticipated populations mean (μ): 13.94⁵, which led to an estimated sample size (n): 40 patients in each group.

The Finasteride group (Group A) was prescribed oral 5mg of finasteride daily for 2 weeks before surgery. The control group (Group B) did not receive any medicine. After 2 weeks, standard TURP was performed and prostatic chips were sent for histopathology. The prostatic urothelium was stained for expression of VEGF and CD-34 and the microvessel density (MVD) were measured by one consultant pathologist. The MVD was measured by counting stained blood vessel in 10 consecutive non-overlapping high power fields (x200). It was measured on two slides in the same day and the mean value was calculated for each specimen.

All collected data was entered into Statistical Package for Social Sciences (SPSS) version 16.0 (Chicago, IL, USA). Continuous variables, like age, was presented as mean \pm SD and categorical variables like expression of VEGF, were presented as proportions (%). The finasteride group was compared with control group for mean MVD, using student's t-test and Pearson correlation test (2-tailed). A p-value of < 0.05 was taken as statistical significant.

RESULTS

Eighty patients with a mean age of 66.21 \pm 10.08 years (48 - 86 years) were included with 40 patients in each group. Mean prostate gland size was compared in both groups (55 \pm 10.7 grams vs. 58.1 \pm 10.8 grams, p=0.21).

Mean MVD in finasteride group was 20.25 \pm 10.3, whereas in control group mean MVD was 48.9 \pm 22.6. When compared the mean MVD in both groups, the mean MVD was significantly low in finasteride group as compared to control group with p < 0.001 (Table I).

Table I: Comparison of mean MVD and Expression of VEGF(%) between two groups.

Group	Number of cases	Mean MVD	Std. deviation	p-value	% Expression of VEGF	Number of cases	p-value
Finasteride	40	20.25	10.3	<0.001	30%	40	0.0017
Control	40	48.9	22.6		65%	40	

Table II: Correlation between prostate size and mean MVD.

	Numbers of cases	Mean	Std. deviation	Pearson Correlation test (2-tailed)
Prostate size	80	58.12	11.16	r=0.222* p= 0.048
Mean MVD	80	34.61	22.68	

* Correlation is significant at 0.05 level (2 tailed)

Similarly, mean expression of VEGF was 30% in finasteride group compared to 65% in control group. This expression of VEGF was also significantly lower in finasteride group as compared to control group (p=0.001).

When the size of prostate gland was compared with mean MVD, the mean MVD had a significant weak correlation with size of prostate gland on Pearson correlation test (r = 0.222, p = 0.048, Table II).

DISCUSSION

Trans-Urethral Resection of Prostate (TURP) is a common operation performed when medical therapy for BPH has failed or is inappropriate.^{11,12} Peri-operative bleeding is one of the major complications of TURP that may lead to clot retention, reoperation and often requires blood transfusion.^{13,14}

Finasteride is a type 2 5 α -reductase inhibitor that inhibits the conversion of testosterone to more active dihydrotestosterone (DHT). Finasteride reduces prostatic vascularity by interacting with Vascular Endothelial Growth Factor (VEGF), which is an androgen-sensitive growth factor stimulating angiogenesis.¹¹ Studies have shown that finasteride reduces prostatic related bleeding-hematuria.¹⁵⁻¹⁸ Finasteride has been used in reducing bleeding during TURP.^{4,5} Preoperative therapy with other 5 α -reductase inhibitor or dutasteride, also significantly reduces bleeding and MVD in patient with BPH underwent TURP.^{19,20}

Hyun reported the effect of finasteride for a minimum 3 weeks before surgery.²¹ Mean prostate size in their study was 66.08 \pm 36.1 grams while mean MVD was 16.02 \pm 4.43 in finasteride group, which are comparable to this study. In this study, the mean MVD in control was lower as compared to our study (25.76 \pm 4.76 vs.20.25 \pm 10.3)

Xiao-dong reported the effect of 2-week finasteride therapy before TURP and found a significant low mean MVD of 21.4 \pm 9.7 in finasteride group compared to 33.4 \pm 11.2 in control group.²² Donohue and associates⁸ also studied the effect of only 2-week finasteride therapy and found a significantly low mean MVD in finasteride group compared to placebo (60 vs. 71).

On the other hand, many authors have reported the effect of 4 weeks preoperative finasteride therapy and found a significant lower MVD in finasteride group.^{3,7,23,24}

When correlated the size of prostate gland with mean MVD, the mean MVD was found higher in larger prostate as compared to smaller gland. On Pearson correlation test, the mean MVD had a significant weak correlation with the size of prostate gland.

CONCLUSION

Finasteride significantly reduces suburothelial microvessel density and prostate vascularity with only 2-week therapy and the mean microvessel density is found correlating with the size of prostate gland.

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