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ORIGINAL RESEARCH

COMPARATIVE STUDY ON EFFECT OF TWO WEEKS OF DUTASTERIDE VS FINESTERIDE ON BLEEDING AFTER TRANSURETHRAL RESECTION OF PROSTATE

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ABSTRACT:

Aims: The aim of the study was to compare the effect of the short term (2-4 weeks) pretreatment of BPH with dutasteride and finasteride on bleeding after TURP. To date no study has been done which has compared 2 weeks of preoperative finasteride and placebo with 2 and 4 weeks of preoperative dutasteride.

Materials and methods: A prospective randomized double blind study was conducted in for a period of 2 years. All patients presenting with lower urinary tract symptoms (LUTS) suggestive of enlarged prostate were evaluated further as required. All cases who were diagnosed to have BPH and were planned for surgery were included in the study.

Results: There was no significant difference in duration of surgery, amount of irrigation fluid used, weight of the resected tissue and duration of postoperative irrigation. Statistically significant differences were seen in total volume of blood loss, blood loss per minute of operating time and blood loss per gram of resected prostatic tissue. When compared to placebo (P2) group, the total volume of blood loss, blood loss per minute of operating time, blood loss per gram of resected tissue, fall in hemoglobin at 24 hours, fall in hematocrit at 24 hours and requirement of blood transfusion was significantly less in D2 and F2 groups.

Conclusion: Short term preoperative dutasteride and finasteride for 2 weeks can significantly reducethe blood loss during the perioperative period. Both the 5-ARIs, dutasteride and finasteride are equally effective in reducing the perioperative blood loss during TURP and they significantly reduce the requirement for blood transfusion.

Keywords: Dutasteride, Finasteride, Blood transfusion, haematocrit.

INTRODUCTION:

Transurethral Resection of Prostate (TURP) is the standard of care for the surgical treatment of patients with Benign Prostatic Hyperplasia (BPH) who do not respond to medical management. Still, this procedure has its own set of complications including perioperative bleeding, urinary incontinence, retrograde ejaculation, transurethral resection (TUR) syndrome, and erectile dysfunction. Combined morbidity rates of around 18% have been reported in studies, of them hemorrhage is one the most prevalent and serious complications. It can lead to clot retention and the need for blood transfusion in the postoperative period which prolongs the hospital stay and may necessitate a repeat surgery. Perioperative blood loss of more than one litre in 13% of patients has been reported in the past.[1,2]

The five alpha reductase inhibitors (5-ARI) along with the alpha blockers have been approved for the medical treatment of BPH. The 5-ARI act by inhibiting the conversation of testosterone (T) to its active form dihydrotestosterone (DTH) by the enzyme five alpha reductase (5-AR). Finasteride and dutasteride are the available 5-ARIs and they suppress the levels of DTH, prostate growth and vascularity. Several studies have showed that pre-treatment with finasteride has resulted in decreased blood loss during TURPwhich is related to the decreased micro vessel density (MVD) in the prostatic urothelium and stroma and vascular endothelial growth factor (VEGF) and some have said it has no effect. But the studies on dutasteride have mixed results, some have shown that pre-treatment with dutasteride reduces the bleeding during TURP with associated decrease in the MVD and some report dutasteride has no effect.[2,3,4]

The mechanism of action of both the 5-ARIs is slightly different as finasteride inhibits only type I 5-AR whereas dutasteride inhibits both type I and II isoenzymes. Dutasteride results in suppression of serum DTH by >90% whereas finasteride suppresses only in around 70% patients. But the intraprostatic DTH suppression by both the drugs is almost the same around 85-90%. The pharmacokinetics of both the drugs are similar except for a very long half-life of dutasteride 4-5 weeks compared to 6 hours of finasteride.[6] So, if the less potent finasteride can decrease bleeding in TURP, dutasteride should do the same. The studies which have reported reduction in blood loss by finasteride but not by dutasteride has not mentioned the reason behind the difference in the outcomes. The aim of the study was to compare the effect of the short term (2-4 weeks) pre-treatment of BPH with dutasteride and finasteride on bleeding after TURP. To date no study has been done which has compared 2 weeks of preoperative finasteride and placebo with 2 and 4 weeks of preoperative dutasteride.

MATERIALS ANE METHODS:

A prospective randomized double blind study was conducted in Osmania General Hospital, a tertiary care centre from January 2018 to December 2019 for a period of 2 years. Ethical committee approval was taken from Osmania Medical College before commencing the study and was conducted in accordance with the Declaration of Helsinki. All patients presenting with lower urinary tract symptoms (LUTS) suggestive of enlarged prostate were evaluated further by International Prostate Symptom Score (IPSS), Digital Rectal Examination (DRE), Uroflowmetry, Serum Prostate Specific Antigen (PSA) and Ultrasonography (USG) abdomen and Transrectal USG for prostate volume. Urodynamic Study (UDS) was done when required. All cases who were diagnosed to have BPH and were planned for surgery were

included in the study. All cases were treated with alpha-blockers before inclusion in the study. A detailed history was taken and physical examination was done. All basic preoperative blood and urine investigations were done.

Patients with history of treatment with 5-ARIs within past one year, previous invasive procedures of the prostate, pelvis malignancy, any other urological malignancy, anticoagulant use, haematological disorders, deranged renal function, severe hepatic dysfunction and unstable cardiac disease were excluded from the study. Cases with prostate volume <30 gm were also excluded. Case with Urinary Tract Infection (UTI) received treatment based on the cultures and those with PSA > 4 ng/ml underwent TRUS biopsy before including them in the study. Non- steroidal Anti-inflammatory Drugs (NSAIDS) and aspirin were discontinued 2 weeks before and till 1 week after the surgery.

After the patients fulfilled the inclusion and exclusion criteria, written and informed consent was taken from them. Patients were randomized into 3 groups using computer generated randomisation chart by a separate investigator who did not take part in analysis of result. The patients were blinded to their study group.

Group 1: D2, Dutasteride 0.5 mg once daily for 14 days before TURP. Group 2: F2, Finasteride 5 mg once daily for 14 days before TURP.
Group 3: P2, Placebo (empty capsules) once daily for 14 days before TURP.

TURP was done for all patients under spinal anaesthesia with 26 F Iglesias continuous irrigation resectoscope sheath (Karl Storz) with bipolar loop working element and normal saline (0.9%) irrigation. The operating surgeons were of equal skills and were blinded to the treatment group. All the irrigation fluid was allowed to collect in the bucket in which 1000 U of heparin was added to prevent the blood from clotting. If the bladder was emptied or when the chips were evacuated, the irrigation fluid collected in other container was returned to the collection bucket. After completion of the procedure, the bucket was stirred manually and two samples of 5 ml were taken from the periphery of the bucket and transferred to a vial for estimation of hemoglobin. A low hemoglobin measuring system (HemoCue AB, Sweden) was used to measure the hemoglobin concentration of the irrigating fluid with high precision. The amount of intraoperative blood loss was calculated by multiplying the hemoglobin concentration (gm/dl) of the collected irrigation fluid by the total volume of the irrigation (dL) used. The obtained result was divided by the value of hemoglobin obtained before surgery to get the amount of total blood loss. Serum hemoglobin levels were measured just before shifting the patient to the operating room and 24 hours after the procedure to calculate the change. Weight of the resected prostatic chips was also taken after the surgery.

A 20 French three way Foleys catheter was placed with bulb inflated to 30 ml, and normal saline irrigation was continued postoperatively till the haematuria subsided. Traction was applied to the catheter in all patients and was released after 6 hours. Foleys catheter was removed on day 2 and a voiding trial was given. Blood transfusion was given only when the hemoglobin was less than 9 gm/dl. Dutasteride or Finasteride and placebo drugs were stopped in the postoperative period.

The outcome parameters were recorded by another surgeon who was also blinded by the study group of the patients. The primary outcomes were duration of surgery, amount of irrigation fluid used, duration of post-operative irrigation, weight of the resected tissue, total volume of blood loss and blood loss per minute of operative time, blood loss per gram of the

resected prostate tissue. The secondary outcomes were fall in serum hemoglobin level at 24 hours, fall in Hematocrit after surgery, blood transfusion requirement and duration of hospital stay. Histopathological analysis of all cases was done and the patients who had a diagnosis other than BPH were excluded from the study.

The sample size was calculated based on the power calculations done by Kim et al[7]showing benefit of preoperative dutasteride in reducing blood loss after TURP. He had sample size of 40 patients in each treatment group with >90% power to detect differences in pair wise comparison for the primary end point (blood loss in TURP) and around > 80% power to detect differences in secondary end points. XLSTAT 2019 was used as statistical software for analysis of results. One way Analysis of Variance (ANOVA) was used for the continuous data and Fischer Exact test was used for categorical data. The post hoc comparison test was used for intergroup comparison with adjustments for multiple comparisons using Bonferroni method. A p value of < 0.05 was considered to be statistically significant.

RESULTS:

Table-1: Demographic data and the baseline parameters of different study groups

Parameters	Dutasteride (D2)	Finasteride (F2)	Placebo (P2)	p-value
Mean Age (years)	62.4±4.9 (52-74)	64.2±4.8 (51-76)	63.6±5.1 (53-75)	0.24
BMI	24.5±3.5 (17-31)	23.9±2.9 (18-29)	24.7±2.9 (17-30)	0.48
Total Prostate Volume (cm^3)	54.8±11.6 (32-80)	51.7±10.8 (34-74)	52.6±11.7 (31-76)	0.45
PSA (ng/dl)	2.7±1.6 (0.4-7.3)	2.5±1.9 (0.6-8.1)	2.9±1.8 (0.8-9.4)	0.59
No of patients requiring Urodynamic study †	4 (6.9%)	5 (8.7%)	5 (8.5%)	0.95
No of patients undergoing TRUS Biopsy †	6 (10.3%)	7 (12.2%)	5 (8.4%)	0.84
Duration of symptoms (months)	16.2±4.8 (6-25)	14.6±4.3 (9-30)	15.8±5.6 (5-32)	0.32
IPSS Score	17.1±5.8 (8-35)	16.4±5.8 (9-34)	15.9±5.2 (7-35)	0.63
Qmax (ml/sec)	10.4±2.3 (6-14)	10.3±2.1 (7-13)	10.2±1.8 (8-14)	0.91
Postvoid Urine Residue (ml)	57.2±21.2 (31-110)	52.7±19.2 (28-107)	54.2±21.9 (24-101)	0.59

All data mentioned as mean ± Standard Deviation (Range) †Data mentioned as number (Percentage) BMI: Body Mass Index, PSA: Prostate Specific Antigen, TRUS: Trans-Rectal Ultra Sonography, Qmax: Maximum urinary flow rate.

Mean age and BMI among the four groups were similar. The baseline variable of total prostatic volume, PSA, no of patients requiring urodynamic study, no of patients undergoing

TRUS biopsy, duration of symptoms, IPSS score, Q_{max}, post void residue and no of patients on catheter were comparable among the groups and the data was statistically not significant.

Table-2: Data comparing the primary outcomes among the various groups

Parameters	Dutasteride (D2)	Finasteride (F2)	Placebo (P2)	p-value
Duration of surgery (min)	48.2± 11.8 (31-87)	47.3± 13.1 (29-85)	49.8±14.5 (28-92)	0.69
Amount of irrigation fluid used (L)	18.3±6.0 (6.5-31)	17.1±7.0 (6- 33)	18.6±6.5 (7-35)	0.26
Weight of the resected tissue (gm)	24.1±8.2 (11-48)	24.9±8.9 (9- 53)	24.8±8.4 (8-46)	0.90
Total volume of blood loss (ml)	183.4±199.8 (36-1223)	172.7±183.4 (32-1187)	288.5±197.0 (87- 1354)	0.01
Blood loss per minute of operating time (ml/min)	3.80±4.0 (1.1-24.95)	3.65±3.6 (0.9-24.2)	5.71±3.5 (2.5-26.5)	0.02
Blood loss per gram of resected prostatic tissue (ml/gm)	7.61±7.3 (2.8-45.2)	7.43±6.6 (2.6-33.9)	11.57±5.8 (5.8-43.6)	0.008
Duration of post-operative irrigation (hours)	9.4±7.2 (4- 46)	10.3±7.1 (4- 48)	11.5±6.9 (4-44)	0.42

There was no significant difference in duration of surgery (48.2 vs 47.3 vs 49.8 minutes , p =0.69), amount of irrigation fluid used (18.3 vs 17.1 vs 18.6 vs 17.7 liters , p=0.26), weight of the resected tissue (24.1 vs 24.9 vs 24.8 vs 24.0 gm, p= 0.90) and duration of postoperative irrigation (9.4 vs 10.3 vs 11.5 hours, p=0.42). Statistically significant differences were seen in total volume of blood loss (183.4 vs 172.7 vs 288.5 ml, p = 0.01), blood loss per minute of operating time (3.80 vs 3.65 vs 5.71 ml/ min, p= 0.02) and blood loss per gram of resected prostatic tissue (7.61 vs 7.43 vs 11.57 ml/gm, p=0.008).

Table-3: Data comparing the secondary outcomes among the various groups

Parameters	Dutasteride (D2)	Finasteride (F2)	Placebo (P2)	p-value
Hb before TURP (gm/dl)	13.6±1.6 (10.2-16.8)	13.7±1.6 (10.1-16.3)	13.8±1.4 (10.0-16.3)	0.83
Hb after TURP (gm/dl)	12.5±2.0 (6.6-16.0)	12.7±1.8 (8.3-15.5)	11.9±1.8 (8.2-15.1)	0.03
Fall in hemoglobin at 24 hrs (gm/dl)	1.10± 0.9 (0.4-3.7)	0.98± 0.6 (0.3-3.8)	1.91±1.1 (0.6-6.7)	0.001
Hematocrit before TURP	41.2±4.6 (32.1-50.2)	41.4±4.6 (30.8-49.2)	41.4±4.3 (30-48.9)	0.97
Hematocrit after TURP	37.8±5.9 (20.5-46.7)	38.1±5.4 (23.6-45.9)	34.9±5.7 (20.9-47.7)	0.02
Fall in Hematocrit at 24 hrs	3.37±2.7 (0.9-12.8)	3.32±2.0 (1.0-12.9)	6.46±3.5 (2.0-22.7)	0.001
Requirement of blood	2 (5%)	1 (2.5%)	6 (15%)	0.03

transfusion (n, %)				
Postoperative hospital stay (days)	2.25±0.6 (2- 4)	2.18±0.5 (2- 4)	2.27±0.6 (2- 4)	0.82

All data mentioned as mean ± Standard Deviation (Range) †Data mentioned as number (Percentage)

Hb: Hemoglobin, TURP: Trans Urethral resection of Prostate

Hemoglobin and Hematocrit before TURP were comparable among the groups with no statistical difference. Statistically significant differences were seen in fall in hemoglobin at 24 hours (1.10 vs 0.98 vs 1.91 gm/dl, p=0.001), fall in hematocrit at 24hours (3.37 vs 3.32 vs 6.46, p = 0.001), Hemoglobin and hematocrit after TURP. Blood transfusion requirement was more in placebo group (11.8%) compared to other groups (5%, 2.5% and 15%) and the difference was statistically significant (p=0.03). The postoperative hospital stay was almost similar in the various groups without any significant differences (p=0.69).

Table-4: Intergroup comparison of significant parameters (t-test)

Parameters	D2 vs P2	F2 vs P2	D2 vs F2
Total volume of blood loss (ml)	0.01	0.004	0.40
Blood loss per minute of operating time (ml/min)	0.01	0.006	0.43
Blood loss per gram of resected prostatic tissue (ml/gm)	0.004	0.001	0.45
Fall in hemoglobin at 24 hrs (gm/dl)	0.001	0.001	0.48
Fall in Hematocrit at 24 hrs	0.001	0.001	0.46
Requirement of blood transfusion (n, %)	0.03	0.005	0.72

All data mentioned as p values.

D2: Dutasteride 2 week group, F2: Finasteride 2 week group, P2: Placebo 2 week group, D4: Dutasteride 4 week group.

When compared to placebo (P2) group, the total volume of blood loss, blood loss per minute of operating time, blood loss per gram of resected tissue, fall in hemoglobin at 24 hours, fall in hematocrit at 24 hours and requirement of blood transfusion was significantly less in D2 and F2 groups. There were no significant statistical differences between D2 and F2 groups when these parameters were compared.

Both the drugs were well tolerated and no severe adverse effects were observed during the study. No major TURP related complications were found in the postoperative period.

DISCUSSION:

The primary aim of this randomized, double blind and placebo controlled study was to access the effect of short term preoperative dutasteride and finasteride on bleeding after TURP in men with BPH. A significant reduction in blood loss during the perioperative period was observed when the patients had 2 weeks of preoperative dutasteride and finasteride compared to the placebo. The secondary aims of the study, the fall in hemoglobin and hematocrit, and the requirement for blood transfusion were also significantly reduced by pre-treatment with dutasteride and finasteride. The current study is the first one to compare 2 weeks of preoperative dutasteride and finasteride with placebo to date.

The rationale of the use of 5-ARIs before TURP comes from their ability to reduce the intraprostatic concentration of DTH which leads to decreased levels of the androgen derived

growth factors required for angiogenesis. This ultimately decreases the blood flow to the prostate by decreasing the number of blood vessels (MVD) resulting in reduced blood loss. Kravchick at al [8]reported decreased vascularity of prostate by counting discrete colour Doppler signal (CD-spot) of the prostate after treatment with 5-ARIs. But the routine preoperative use of the 5-ARIs is not accepted worldwide due to conflicting results from the studies. Few studies support that only finasteride results in decreased bleeding , few studies state both the 5- ARIs reduce the blood loss[9] and few studies are in notion that neither of these drugs has any effect . According to a survey based in the United Kingdom in 2004, 98% of urologists used 5-ARIs for treatment of hematuria of prostatic origin but only 4% used it before TURP.[10]

The duration of preoperative treatment with 5-ARIs to reduce bleeding is very much variable in the conducted studies ranging from 2 weeks to 3 months. No proper rationale for the specified duration has been mentioned in the studies. Donohue et al[11] studied 64 men randomized in two group, placebo and 5 mg finasteride for 2 weeks before TURP and reported significantly lower MVD (60 vs 71) and lower expression of VEGF (47vs 61) in the finasteride group. This provides some evidence that the changes required to reduce bleeding are achieved early after only 2 weeks of exposure. Carlin et al[12] studied 12 men prospectively for gross hematuria due to BPH treated with finasteride and reported that hematuria subsided within 2 weeks. Kearney et al[12] retrospectively studied 53 patients and reported, in the 16 patients who began finasteride while actively bleeding the average time to clear urine was 12 days (range 2 to 45). Prostatic volume correlated with the average time needed for resolution of hematuria, which was 2.7 days or longer for small (less than 40 gm.), 10.3 days or longer for large (40 to 100), 19 days or longer for extra-large (100 to 150) and 45 days or longer for extra-large (greater than 150) glands. It can be observed that the clinical effect of the drug takes place well within 2 weeks even for glands up to 100 gm. So, we decided to keep the duration of the preoperative treatment to 2 weeks only as done in several other studies and added another arm of 4 weeks of dutasteride due to its low efficacy reported in the studies.[13] Long term treatment may also relieve some patients to a level that they do not require surgery and leave only more vascular prostates and comparing them may give erroneous results.

Various methods to quantify blood loss have been used in the studies, fall in hemoglobin, fall in hematocrit and measuring the hemoglobin in the irrigating fluid. Among these measurement of hemoglobin in the irrigating fluid is the most practical way to quantify the blood loss. Due to very low hemoglobin levels present in the irrigating fluid a very sensitive photometer (HemoCue AB, Sweden) gives good results. The speed of resection (depends on the experience of the surgeon) and the amount of resected tissue accounts for the two third of the variability found in the perioperative blood loss. The blood loss per gram of the resected prostatic tissue and per minute of operating time was used in the study to adjust those variables. [4]

The fall in hemoglobin and hematocrit was used in our study as secondary parameters to compare their utility in determining the blood loss. They might not give accurate estimate but are routinely used as guide to monitor and determine the need for blood transfusion and intervention.

In our study, the total volume of blood loss, blood loss per minute of operating time, blood loss per gram of resected prostatic tissue were significantly higher in the P2 group compared to F2 and D2 groups. Fall in hemoglobin and hematocrit at 24 hours and the need for blood transfusion was also significantly higher in the placebo group. When Intergroup comparisons were done there was no significant differences between D2 and F2 groups. Our resultsareconsistentwiththeotherstudiesreportedintheliterature.Bansaletal[4] inhisreport of 450 patients comparing 4 weeks of preoperative finasteride, dutasteride and placebo reported significant reduction in mean blood loss, blood loss/time, and total blood loss per gram of resected tissue in finasteride and dutasteride groups compared with placebo. The blood loss per gram of the resected tissue and blood loss per minute was similar in our studies.

Table-5: comparison with other studies in comparison with other studies

Parameters	**Dutasteride (our study vs Bansal at al[4])**	**Finasteride(our study vs Bansal at al [4])**	**Placebo(our study vs Bansal at al [4])**
Total volume of blood loss (ml)	183.4 vs 162.4	172.7 vs 168.7	288.5 vs 265.3
Blood loss per minute of operating time (ml/min)	3.8 vs 4.3	3.65 vs 4.23	5.71 vs 6.59
Blood loss per gram of resected prostatic tissue (ml/gm)	7.61 vs 7.4	7.43 vs 7.3	11.57 vs 10.74
Parameters	Dutasteride (our study vs Kim at al [7])	Placebo(our study vs Kim at al [7])	
Fall in hemoglobin at 24 hrs (gm/dl)	1.10 vs 1.16	1.9 vs 1.86	
Fall in Hematocrit at 24 hrs (%)	3.37 vs 3.69	6.46 vs 5.39	
Parameters	Finasteride (our study vs Liu et al [14])	Placebo(our study vs Liu et al [14])	
Total volume of blood loss (ml)	135.8 vs 172.7	245.1 vs 288.5	
Parameters	Our study	Bansal et al [4]	Hann et al [15]
Weight of the resected tissue (gm)	24.1	23.1	25
Duration of surgery (min)	48.3	39.9	45
Parameters	Our study	Bansal et al [4]	Hann et al [15]
Amount of irrigation fluid used	17.9	—	18.3

Kim et al[7] reported study of 83 patients in which he used 2 weeks of preoperative dutasteride before TURP. Lower mean blood loss was observed in the dutasteride group than the control

group after 24 hours after surgery (ΔHb=1.16vs. 1.86; ΔHct=3.69% vs. 5.39%). In our study the fall in hemoglobin at 24 hours in D2 vs P2 group was 1.10 vs 1.91 gm and the fall in hematocrit at 24 hours was 5.8% vs 7.8%. Liu et al[8] in his report of 100 patients in which he used 2 weeks of preoperative finasteride concluded that VEGF expression and angiogenesis in the prostate tissue are suppressed and blood loss during TURP decreased by the used of preoperative finasteride, mean operative bleeding was 135.8 and 245.1 ml in finasteride and placebo groups respectively. Our study reports a similar amount of blood loss 172.7 and 288.5 ml in the F2 and P2 groups respectively.

Various other studies have reported no significant benefit of preoperative use of 5-ARIs[12]. Hann et al[15] in his randomized double blind placebo controlled trial of 2-4 weeks of dutasteride in 214 patients, reported no significant differences when compared to the placebo group. Tuncel et al[16] (75 patients) concluded that 5 weeks of dutasteride had no effect on the blood loss and the MVD of prostatic tissue. Lund et al[17] (35 patients) and Sandfeldt el al[18] (60 patients) concluded that 3 months of preoperative finasteride does not reduce bleeding compared to placebo. The power of the study was very low to make any conclusions. Of these, the study by Hann et al[15] is only a large multi-centric, randomized study with good power. They did not find a reduction in the MVD of prostatic tissue even after 4 months of dutasteride therapy despite achieving ~90% reduction in serum and DTH concentrations which is contradictory to a large study of 450 patients by Bansal et al[4].

The weight of the resected gland was comparable among the three groups with mean of all the groups being 24.1 gm which was similar to 23.1 gm as reported by Bansal et al[4] and 25 gm as reported by Hann et al[15]. The mean duration of surgery was similar in all groups in our study and the pre-treatment with 5-ARIs has no effect on it, rather it was dependent on the skill of operating surgeon. It was 48.3 minutes in our study which was similar to 45 minutes as reported by Hann et al[15] and slightly higher than 39.3 minutes in the study of Bansal et al[13]. These variations depict the role of institution and surgeon in the speed of resection, there also might be differences in defining the duration of surgery in different institutions. The amount of irrigation fluid used is directly dependent on the duration of surgery and it was similar in all three groups with mean of 17.9 L which was similar to 18.3 L as reported by Hann et al[15].

MVD of the prostatic stroma and suburothelium has been studied along with the blood loss estimation as an indirect evidence of a reduction in vascularity of the prostate. A strong positive correlation between the MVD and blood loss has been established and almost all studies reporting reduction in blood loss after preoperative 5-ARIs have reported reduced MVD counts in the resected tissue . Haggstorm el al[19] did not find any reduction in the human prostate MVD even after treatment with finasteride for 3 months in his study. This might be due to the simultaneous shrinking of the gland and despite the drug reduced the number of vessels in the prostate, the density was unaffected. This leaves few unanswered questions about the use of MVD. So, we did not go for measurements of MVD and evaluated only the direct clinical effect of the 5-ARIs. Several other studies have also reported VEGF and other markers of angiogenesis to evaluate the effect of 5-ARIs on prostate vascularity as an indirect measure of blood loss. They have also correlated positively with the blood loss during surgery. We did not measure these markers in our study. Measurements of DTH (serum/prostatic) is also included by some studies and >90% suppression has been reported

within a few weeks .[5,6] We measured only the clinical and direct outcome parameters for the effect of 5-ARIs in our study.

We tried to answer the role of short term 5-ARIs in reducing bleeding in TURP by a well-designed randomised, placebo controlled study with clinical effect as the main outcome criteria and included a relatively large number of patients. This is the first study comparing 2 weeks of preoperative dutasteride and finasteride with placebo in preventing blood loss with an additional comparison arm of 4 weeks of dutasteride. Limitations of the study were that indirect methods to predict blood loss like MVD, VEGF and Colour Doppler sonography were not used.

CONCLUSION:

Short term preoperative dutasteride and finasteride for 2 weeks can significantly reduce the blood loss during the perioperative period. Both the 5-ARIs, dutasteride and finasteride are equally effective in reducing the perioperative blood loss during TURP and they significantly reduce the requirement for blood transfusion. So, a short course (2 weeks) administration 5-ARIs before TURP may reduce the blood loss in the perioperative period and thus reduce the blood loss related complications and need for transfusion.

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