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The Effect Of 04 Weeks Dutasteride Use On Perioperative Blood Loss In Patients Undergoing Transurethral Resection Of Prostate.

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ABSTRACT:

Background: Among old men, BPH is the most common urological illness. Medicinal and surgical treatments can be used. In medication, both 5-alpha reductase inhibitors and alpha-blockers are used. TURP, or transurethral resection of the prostate, serves sufferers new to conventional therapy. They are 5-ARI aims to reduce the size and vascularity of the prostate in the meantime. The aim of this study was to investigate whether 5-ARI Dutasteride might reduce blood loss during TURP for BPH by drugs that block 5-ARI.

Objectives :The goal of this research was to see if preTURPitterside, a 5-alpha reeducates inhibitor (5-ARI), can reduce the amount of blood lost during surgery–TURP for benign prostatic hyperplasia (BPH)- in contrast and comparison. The postoperative hemoglobin levels for Dutasteride and non-Dutasteride groups having TURP were compared to determine if Dutasteride can reduce blood loss in TURP.

Study design: This Study is a prospective observational study.

Place and duration of the study: A prospective observational study was conducted from field the Institute of Kidney Diseases to December, 2019 at Hayatabad Medical Complex in Peshawar.

Methodology: A prospective observational study was conducted at the Institute of Kidney Diseases at Hayatabad Medical Complex, Peshawar, from field June to December 2019. Patients with TURP who met the inclusion criteria were divided into two groups according to whether they were taking drugs for BPH. The Dutasteride group took 0.5 mg/day of Dutasteride plus alpha-blocker(s), while the non-dutasteride group took alpha-blocker(s) only. A comparison was made of the difference between preoperative and postoperative haemoglobin levels in individuals taking TURP. A subsequent analysis was carried out using SPSS v23.0 to deduce the data.

Results: Postoperative haemoglobin levels were less likely to fall in those individuals who took Dutasteride for TURP than in the non-dutasteride group (0.75 mg/dl ± 0.4 VS where is the proof ? 1.3 mg/dl ± 0.4.)

Conclusion: Our research concludes that there is less haemoglobin decline when 5-ARI dutasteride 0.5 mg/day is used four weeks prior to surgery than when no dutasteride is used.

Keywords: Transurethral resection of the prostate, benign prostatic hyperplasia, 5-alpha reductase inhibitor, Dutasteride.

Authors Contribution

JJK. Concept & Design of Study WHS DraftingLA. Data Analysis AS. Critical Review , JJK,SR.Final Approval of version

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Among older men, benign prostatic hyperplasia (BPH) is one of the most prevalent urological conditions¹. It is linked to the peaceful development of the prostate gland, which surrounds the urethra and is located underneath the bladder. This causes the urethral canal to gradually narrow, which causes symptoms related to the lower urinary system.² The symptoms of the lower urinary tract (LUTS) may be further classified as voiding and storage symptoms. The voiding symptoms include urgency, nocturia, incomplete micturition, and poor stream. Surgery may be indicated for patients with moderate to severe LUTS.³ Patients with LUTS who are not responsive to medication therapy because of benign prostatic hyperplasia and still undergo transurethral resection of the prostate (TURP), which is still the gold standard surgical procedure. Even though TURP is considered the gold standard, there are some risks associated with it, such as transfusion-needed bleeding, clot retention, and urinary tract infection, urethral stricture, and bladder neck contracture. Technological advances, such as the miniaturization of resectoscopes, which reduces the resection time and improves eyesight, are being used to try to minimize the number of issues related to total upper limb replacement procedures (TURP)⁵. Nonetheless, transfusion-related bleeding has continued to be the most frequent surgical complication, occurring up to 7% of the time⁶. Dihydrotestosterone (DHT), an androgen, is responsible for the increased vascularity of the prostate in older men because it promotes the growth of new blood vessels and smooth muscles within the prostate⁶. 5- α - reductase enzymes (5-AR)⁸ of types 1 and 2 synthesize DHT from testosterone. Numerous pharmacological medicines aim to restrict the conversion of testosterone to its more powerful form, DHT, by blocking the enzyme 5- α -reductase inhibitor (5-ARI), which in turn reduces the development and vascularity of the prostate gland⁷. 5-ARI is utilized as a therapy for BPH in bigger prostates since shrinking the prostate gland significantly improves the LUTS. It is hypothesized that if 5-ARI is given in patients having TURP, there may be less blood loss in the perioperative phase compared to the patients who are not taking 5-ARI because of its influence on vascularity⁸. A powerful 5-ARI called Dutasteride is used to treat BPH in cases with enlarged prostates. Dutasteride has been investigated by a number of writers in relation to bleeding after TURP, and the findings are encouraging since they have led to less blood loss⁹. Our research aims to compare the mean haemoglobin decrease before and after TURP for BPH with the non-dutasteride group and ascertain the function of Dutasteride in this regard. This research will provide us

with the most recent and updated information on the mean decrease in haemoglobin between the Dutasteride and non-dutasteride groups in patients having TURP since no similar study has been carried out in our community in the previous five years. When individuals receiving TURP for BPH are given Dutasteride post-operatively, their mean drop in haemoglobin is much lower than that of a placebo¹⁰.

Materials and methods

This prospective observational research was done from June to December 2019 at the Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar. The trial lasted six months following ethical review committee clearance. Patients who needed BPH surgery and satisfied the inclusion criteria might participate in the trial in the outpatient clinic. The study's goal and advantages were communicated to consenting participants, who gave informed written permission. Patients who took alpha-blockers and Dutasteride

0.5 mg/day for at least four weeks before surgery were assigned to the dutasteride group, whereas those who just used alpha-blockers as part of their medical therapy were assigned to the non-dutasteride group. The trial included all interested patients having TURP with a prostate size of 35-60 gm between ages 50-75. Patients with bleeding problems, PSA

> 4 ng/ml, creatinine \geq 1.5 mg/dl, or current UTI were excluded. Each patient's haemoglobin, age, and prostate volume were documented before the surgery. One skilled urologist with at least five years of experience performed transurethral prostate excision on all patients. Before TURP, regular cystoscopy employed Cluttons dilators up to 24fr before resectoscope entry into the urethra. All patients used monopolar diathermy and glycine for irrigation. After surgery, all patients received bladder irrigation with normal saline via a 22Fr 3-way catheter for 24 hours. On the first postoperative day, all

Patients' haemoglobin was measured. After surgery, each patient's haemoglobin was compared to their preoperative. Data was entered and analyzed in SPSS v23.0. To protect secrecy, the primary investigator (PI) collected medical record data on his laptop. The mean and standard deviation were computed for continuous characteristics such as age, prostate size, operation time, and preoperative and postoperative haemoglobin¹¹.

Results

There were a total of 120 patients who underwent TURP for BPH. Of those 120 patients, 60 patients had taken 0.5mg of Dutasteride along with an alpha-blocker, while 60 patients had only been on an alpha-

blocker as part of their BPH medical management. The mean age of patients in the dutasteride group was 59.9 years \pm 5.9, while for the non-dutasteride group was 61.0 years \pm 6.5. The mean preoperative size of the prostate was 52.1gm \pm 6.6 for the Dutasteride group and 51.5gm \pm 6.8 for the non-dutasteride group (table 1). There was no significant difference in the operative Time for each group, 44.8 minutes \pm 18.2 vs 42.2 minutes \pm 16.8 in the Dutasteride vs non-dutasteride group. There was, however, a statistically significant difference in haemoglobin seen in patients with the Dutasteride vs. the Dutasteride group. The mean drop in haemoglobin in the dutasteride group was 0.75 gm/dl \pm 0.4, while in the non-dutasteride group was 1.3 gm/dl \pm 0.4 (p < 0.05).

Table 1: Demographics and clinical parameters of patients.

Variables	Non-Dutasteride group	Dutasteride group	P-value
	Mean \pm SD	----	
Age (Years)	61.0 \pm 6.5	59.9 \pm 5.9	0.032
Prostate Size (gm)	51.5 \pm 6.8	52.1 \pm 6.6	0.589
Operative Time (min)	42.2 \pm 16.8	44.8 \pm 18.2	0.546
Preoperative Hemoglobin (gm/dl)	13.9 \pm 1.2	13.7 \pm 1.1	0.424
Postoperative Hemoglobin (gm/dl)	12.6 \pm 1.1	13.0 \pm 1.1	0.072
Difference of Hemoglobin (gm/dl)	1.3 \pm 0.4	0.75 \pm 0.4	< 0.05

Discussion

Most men above 40 years of age are affected by symptoms of the lower urinary tract due to an enlarged prostate. There are many treatment options available, including conservative and minimally invasive, but TURP remains the gold standard surgical treatment option¹². Despite being the gold standard, there are several complications associated with TURP¹²; one such complication is bleeding. If the bleeding persists, a blood transfusion is required. The complications of TURP include bleeding, urinary incontinence, retrograde ejaculation, urinary tract infection and TUR syndrome¹³. Severe blood loss during TURP is rare, but mild to moderate blood loss can occur even in this modern age, which can significantly affect the outcome of the procedure. Intraoperative bleeding can result in impaired vision and can cause difficulty in doing the procedure. As a result, serious complications such as capsule perforation, prolonged duration of surgery, and excessive use of fluids resulting in TUR syndrome and sepsis can occur¹⁴. This can also result in a long hospital stay, more use of irrigation fluids and an increased economic burden on the hospital and its

resources. It can even result in clot retention and blockage of a catheter, which is bothersome for the patient and may require clot evacuation under anaesthesia. The growth of the prostate gland is dependent upon one key hormone, dihydrotestosterone (DHT), which is converted from testosterone by the 5-alpha reductase enzyme¹⁵. DHT causes the proliferation of stromal and acinar cells in the prostate gland, resulting in increased vascularity of the prostate¹⁵. DHT is three to five times more potent in the proliferation of the prostate gland compared to testosterone. By suppressing the production of DHT from testosterone using a 5-alpha reductase inhibitor, the proliferation of stromal and acinar cells in the glands is hampered. This results in the decreased vascularity of the prostate gland, and if the use of the 5-alpha reductase inhibitor is continued for 6-12 months, there is around a 30% reduction in the prostate volume¹⁶. It is also noted that the vascular endothelial growth factor (VEGF), which is responsible for neo-vascularization within the prostate gland, is dependent on DHT; thus, by blocking the conversion to DHT, 5-alpha reductase inhibitors decrease the vascularity of the prostate gland¹⁷. Several authors have investigated the Effect of 5-ARI on postoperative haemoglobin after TURP, but the results have been somewhat conflicting. Although one might agree with the logical explanation as the decrease in vascularity in the gland should result in a decreased blood loss during prostate surgery, a large multicentric randomized controlled trial by Boccon-Gibod et al.¹⁸ reported that no significant difference was seen in haemoglobin between the groups that were given Dutasteride 4 weeks before surgery and placebo group. There are, however, several other studies which concluded that the use of 5-ARI can result in a decrease in perioperative bleeding. Gökçe et al. did a retrospective study on 218 patients undergoing TURP for BPH. They found that the dutasteride group had significantly lower bleeding compared to the dutasteride naïve group (1.93g/dl vs 2.72g/dl) respectively¹⁹.

Furthermore, Kravchick et al. concluded from their study that if the patient is pretreated with six weeks of Dutasteride 0.5mg once daily, there is a significant reduction in blood loss during TURP and reduced operative Time as it minimizes the vascularity of the prostate gland, especially in the periurethral zone²⁰. In a study from Bangladesh, MM Rehman et al. studied the Effect of preoperative use of Dutasteride on blood loss and the total operative Time. His study also had two groups: Group

A had TURP done without the use of Dutasteride, and Group

B had TURP with Dutasteride. There was a statistically significant difference seen between the groups for

postoperative haemoglobin, and the non-dutasteride group had more blood loss compared to the dutasteride group. Also, the operative Time was higher in the non-dutasteride group compared to the dutasteride group ²¹. In our study, only those patients who had been taking Dutasteride for at least four weeks were enrolled. There was, however, a study by S Hina which studied the Effect of shorter two-week administration of Dutasteride on postoperative blood loss. There was a significant decrease in blood loss even with a two-week administration of dutasteride²². The use of Dutasteride preoperatively in patients undergoing TURP for BPH seems logical, and the result from our study adds to the body of conflicting evidence. It is, therefore, imperative that further large-scale trials be conducted on the subject that can give better insight and the true representation of data²³.

Conclusion

Dutasteride reduces the amount of blood loss during TURP if given to patients at least four weeks before surgery. However, since our study was a single-centre and on a small sample size, We recommend RCTs on larger sample sizes that involve multicenter to bring up a conclusion about the efficacy of Dutasteride in the reduction of blood loss during TURP for BPH.

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