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# USE OF TRANEXEMIC ACID AS A TOPICAL AGENT TO REDUCE BLEEDING DURING TURP: A NOVEL TECHNIQUE!

Anaesthesiology

**Dr Rashmi Rani** — Assistant Professor- Department of Anesthesia, St Johns Medical College And Hospital Bangalore 560034 Karntaka India

**Dr Saurabh Mittal*** — Mch Resident – Urology – Second Year, Department Of Urology St Johns Medical College And Hospital Bangalore, Karnataka India *Corresponding Author

**Dr Surya Kant Choubey** — Head of Department – Urology St Johns Medical College And Hospital Bangalore 560034 Karntaka India

**Dr Gotam Pipara** — Mch Resident – Urology – Final Year Department Of Urology St Johns Medical College And Hospital Bangalore, Karnataka India

## ABSTRACT

**INTRODUCTION:** Benign prostatic hyperplasia (BPH) is a common condition affecting the males with age group of more than 50 years. The gold standard of treatment for BPH is transurethral resection of the prostate (TURP). However, complications like bleeding and TURP syndrome are well known with TURP. Tranexamic acid (TNXA) is synthetic antifibrinolytic helps in reducing blood loss. Its use has been done intravenously in the various urological procedures till date. However, concerns about the safety of systemic administration of tranexamic acid and the risk of thromboembolic events such as deep-vein thrombosis or pulmonary embolism restrict its usage. In our study we have, used TNXA as a topical agent with the irrigation fluid during TURP. This study is the first of its kind in literature.

**MATERIALS AND METHODS:** A prospective randomized control trial was conducted by the department of Urology and Anesthesiology with 60 men in the age group of 50-75yrs who underwent TURP at St Johns medical college and hospital, Bangalore, Karnataka, India from Oct 2016 - July 2017. They were randomized into 2 groups of 30 each as study (group A) and control( group B).In the study group, TNXA was added in irrigation fluid and control group included patients in which irrigation fluid without TNXA was used . Serum hemoglobin was measured preoperatively and 2 hours after surgery, the volume and hemoglobin concentration of irrigation fluid, resected prostate weight and duration of resection was noted.

**RESULTS:** Mean hemoglobin in group A was 12.7gm/dl whereas in group B was 12.5. In group A, the average blood loss intraoperatively was 145.4 ml while in Group B was 197.5 ml, P value < 0.05 – statistically significant. The amount of hemoglobin lost per gram of resected tissue was 0.032grams in group A and 0.062grams in Group B (P value < 0.05 – statistically significant). Operative time was almost same in both the groups. However intraoperative vision was better with Group A owing to less intraoperative bleeding.

**CONCLUSION:** TNXA when used as a topical agent during TURP with the irrigation fluid decreases the blood loss and hemoglobin fall per gram of prostatic tissue resected. Although there was no effect on the operative time or fluid volume used, it definitely led to better vision during surgery.

## KEYWORDS

TURP, BLEEDING, TRANEXEMIC ACID, BPH

## INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition affecting the males with age group of more than 50 years[1]. The gold standard of treatment for BPH is transurethral resection of the prostate (TURP). However, complications associated with TURP like bleeding and TURP syndrome are well known with TURP. Bleeding during TURP needing transfusion accounts to 3.9 % [2]. Prostate size, , weight of resected prostate , operative time , preoperative 5 alpha reductase inhibitor treatment(5 ARI), any coagulation abnormality, hypertension are the few major factors affecting blood loss[3]. TURP results in activation of coagulation and a consequent hypercoaguable state[4]. Post op blood loss is thought to be associated with increase in urinary fibrinolytic activity. Urine and urothelium contains high concentration plasminogen activators that facilitate lysis of clots. Tranexamic acid (TNXA) is potent inhibitor of plasminogen activator and urokinase, thereby preventing clot lysis. It is thought to be more effective than epsilon amino caproic acid (EACA) in reducing blood loss. TNXA is synthetic antifibrinolytic drug that prevents the breakdown of fibrin, thereby stabilizing blood clots and reducing blood loss in conditions that promote fibrinolysis. Recent studies have proven the role of intravenous tranexamic acid in reducing the blood loss after orthopedic, urological and dental surgeries[5-7]. However, concerns about the safety of systemic administration of tranexamic acid and the risk of thromboembolic events such as deep-vein thrombosis or pulmonary embolism in this patient population have hindered the wide adoption of this medication in the setting TURP. Topical application of tranexamic acid in the surgical field is a cost-effective and simple route of administration that has been shown to reduce bleeding associated with dental[8], cardiac[9,10], and spine procedures [11]. We have used TNXA in a topical form by adding it to the irrigation fluid while performing the TURP that will reduce bleeding yet will not increase the risk of a hypercoagulable state. The role of topical application of tranexamic acid in decreasing blood loss during TURP through irrigation fluid has not been studied so far and our study is the first of its kind in literature.

We hypothesized that topical application of TNXA during TURP decreases postoperative bleeding as reflected by the maximum drop in hemoglobin level during the postoperative period.

In this study, we have evaluated the use of intraoperative TNXA added to the irrigation fluid for patients undergoing TURP for assessment of intraoperative blood loss, operative time, clarity of vision and amount of irrigation fluid needed.

## MATERIALAND METHODS

A prospective randomized control trial was conducted by Department of Urology and Anesthesiology with 60 men in the age group of 50-75yrs who underwent TURP for BPH with lower urinary tract symptoms at our center .from Oct 2016 - July 2017.

Patients with IPSS (International prostate symptom score) score of 15 and above with sonologically assessed prostate size between 40 and 70 gm were included in the study. Patients having bleeding disorders, hypertension, history of IHD(ischemic heart disease) and CVA( cerebrovascular accident) prostatic carcinoma, previous prostate surgery, bladder stones, on anticoagulation therapy, on 5 ARI during the last 1 year, patients on NSAID / aspirin, having renal impairment (serum creatinine of > 1.5 mg/dl), history of deep venous thrombosis and pulmonary embolism were excluded from the study.

They were randomized into 2 groups of 30 each as study (group A) and control (group B). Patients with outpatient numbers ending with even numbers were taken as study group and those with odd numbers were taken as control group. In the study group, TNXA was added in irrigation fluid and control group included patients in which irrigation fluid without TNXA was used. TURP was done using a continuous flow 26 Fr resectoscope and all the surgeries were performed by the same surgeon under spinal anesthesia. 1.5% glycine (prewarmed) was used as irrigation fluid. Cautery setting was used as 110 watt (W) and

40 W for cutting and coagulation respectively. Serum hemoglobin was measured preoperatively and 2 hours after surgery, the volume and hemoglobin concentration of irrigation fluid, resected prostate weight and duration of resection was noted.

The doses of tranexamic acid chosen for the current investigation were based on previous studies of intravenous tranexamic acid in patients undergoing open surgeries showing efficacy with doses of 15 to 20 mg/kg (i.e.,1.5 g) and a meta-analysis suggesting that doses of >30 mg/kg(i.e., 3 g) were more effective for reducing bleeding[5].Hence in our study , as a protocol we choose to add 1 gm of TNXA in 5 liters of glycine .On an average 5 to up to 15 liters of glycine was used for each surgery making it a variable of TNXA between 1 to 3 gm .

**Blood loss was calculated as follows**

Suppose the pre-operative hemoglobin of the patient was X gm/dl – which means 10X gm of hemoglobin is present in one liter of blood , hence 1 gm of hemoglobin is present in 1/10X liter of blood.

Considering the hemoglobin concentration of the irrigation fluid at the end of the procedure to be Y gm/dl – implies 10 Y gm of hemoglobin is present in 1Liter of irrigation fluid , now if total Z liters of fluid has been used for irrigation 10ZY grams of hemoglobin is present in the total irrigation fluid used.

Hence if 1 gm of hemoglobin is present in 1/10X L of blood, then 10ZY grams of hemoglobin will be present in Z Y / X liters of blood.
Hence, (TBL) total blood loss (in liters) =

Total irrigation used (L) * Hemoglobin concentration of irrigation fluid (gm/dl)
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Total body Hemoglobin concentration (gm/dl)

The amount of hemoglobin lost per gram of prostatic tissue resected can be calculated by dividing the hemoglobin lost in gm i.e. decrease in hemoglobin level (Preop. – Postop.) divided by prostatic tissue resected in grams (that was measured at the end of the procedure by using a weighing machine.)

The results were analyzed using unpaired t test. SPSS software version 16 was used.

## RESULTS

In our study, total of 60 patients were taken out of which 30 belonged to study and 30 to control group. The mean age was 66.7years in group A and 64.3 years in group B. Mean prostate weight measured by abdominal ultrasound was found to be 54.27gm in Group A and 54.03 in Group B. No statistically significant difference was found in both the groups in relation to age and prostate size. (TABLE 1)

Mean hemoglobin in group A was 12.7gm/dl whereas in group B was 12.5. In group A, the average blood loss intraoperatively was 145.4 ml while in Group B was 197.5 ml, P value < 0.05 – statistically significant. (FIGURE 1)

Irrigation fluid used was approximately 12.8 L per case and weight of resected prostate was 25.1gms in Group A, whereas 13.0 of irrigation fluid was used in group B and weight of prostate resected was 24.1 gm . There was no statistically significant difference.

The amount of hemoglobin lost per gram of resected tissue was 0.032grams in group A and 0.062grams in Group B (P value < 0.05 – statistically significant). Operative time was almost same in both the groups. However intraoperative vision was better with Group A owing to less intraoperative bleeding. (FIGURE 2)

None of the patients in either of the groups needed any blood transfusion or post-operative clot evacuation. Recovery / discharge time from hospital was the same for both the groups on POD3.

## DISCUSSION

TURP is the gold standard method for relieving bladder outlet obstruction in men due to BPH. Intraoperative complications like bleeding and TUR syndrome are associated with TURP especially in large prostates (>40 gm). In one study, perioperative blood loss was >1 L in 13% of the patients, leading to an increased risk of hemodynamic instability and the need for blood transfusion [2]. Hematuria and clot retention after TURP might prolong hospitalization and may even necessitate cystoscopy.

Several techniques have been devised to reduce bleeding during TURP including intravenous administration of estrogens, catheter traction, intraprostatic vasopressin, per os etamsylate, fibrin adhesive, phenol solution, and, more recently, finasteride[12-14]. However, none of these techniques are used in routine except for catheter traction .Though finasteride is implicated to reduce blood loss when started pre operatively, not many studies support the same. There have been a few reports where intravenous tranexamic acid has been used to reduce bleeding during TURP. TNXA is a synthetic antifibrinolytic drug that prevents the breakdown of fibrin, thereby stabilizing blood clots and reducing blood loss in conditions that promote fibrinolysis. However, concerns about the safety of systemic administration of tranexamic acid and the risk of thromboembolic events such as deep-vein thrombosis or pulmonary embolism in this patient population have hindered the wide adoption of this medication in the setting of TURP. Hence we used TNXA as a topical application by putting it into the irrigation fluid being used during TURP. The potential mechanism and advantage of topical application of tranexamic acid into the surgical field is to directly target the site of bleeding. The advantage of topical application of tranexamic acid is minimal systemic absorption. To our surprise, we noted that the intraoperative blood loss and hemoglobin fall per gram of prostate tissue resected was ***much lower*** in the study group.

Our findings of reduced postoperative bleeding are consistent and comparable with the findings of previous individual studies of intravenous Tranexamic acid administration in patients undergoing TURP, which demonstrated a reduction of blood loss[15].

Although intraoperative vision was better in the study group, no difference in operative times was noted in both the groups. The amount of irrigation fluid (glycine 1.5 %) used was also almost the same with a difference of about 1 liter that was not statistically significant. None of the patients needed post-operative blood transfusion, clot evacuation, re cystoscopy or had TUR syndrome. By using TNXA topically we also avoided any systemic complications of the same including thromboembolic complications.

The present study had a few limitations in as much as that none of the study or control subjects needed blood transfusion. Hence the study could not assess whether the use of TNXA can actually decrease the frequency of blood transfusions. Also the catheter was removed on post-operative day 3 in both study and control subjects, hence the effect of reduced bleeding with TNXA did not manifest as an outcome on duration of hospitalization.

## CONCLUSION

TNXA when used as a topical agent during TURP with the irrigation fluid decreases the blood loss and hemoglobin fall per gram of prostatic tissue resected. Although there was no effect on the operative time or fluid volume used, it definitely led to better vision during surgery. This form of TNXA usage combines its benefits as a fibrinolytic agent minimizing bleeding and reducing its systemic complications like thromboembolism especially in our elderly patients undergoing TURP.

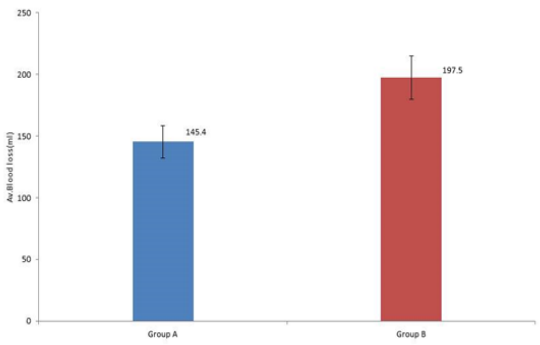


Figure 1 : comparison of blood loss in both the groups

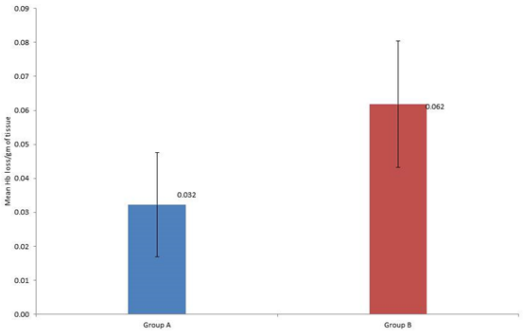


Figure 2 : hemoglobin lost per gram of resected tissue

**Table 1**

| Variable | Group A | | Group B | | t value^ | P value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| age | 66.7 | 5.3 | 64.3 | 4.7 | 1.89 | 0.06, ns |
| preop hb | 12.67 | 1.14 | 12.53 | 1.12 | 0.48 | 0.64, ns |
| p size | 54.27 | 7.81 | 54.03 | 6.42 | 0.13 | 0.90, ns |
| fluid | 12.78 | 1.37 | 12.99 | 1.41 | 0.59 | 0.56, ns |
| blood loss | 145.4 | 13.0 | 197.5 | 17.8 | 12.91 | 0.00** |
| wt pr tissue | 25.07 | 2.88 | 24.07 | 3.71 | 1.17 | 0.25, ns |
| fall in hb | 0.81 | 0.40 | 1.46 | 0.37 | 6.48 | 0.00** |
| time | 49.50 | 5.31 | 50.10 | 4.21 | 0.48 | 0.63, ns |
| hb loss/gm of tissue | 0.032 | 0.015 | 0.062 | 0.019 | 6.72 | 0.00** |
| ^ Unpaired t test | | | | | | |
| * P < 0.05, Sig | | | | | | |
| ** P < 0.001, HS | | | | | | |
| P > 0.05, Not Sig | | | | | | |

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