

Tranexamic acid decreases blood loss during transurethral resection of the prostate (TUR-P)

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KEY WORDS

prostate ► prostatic hyperplasia ► transurethral resection of the prostate ► tranexamic acid

ABSTRACT

Introduction. Postoperative blood loss after prostate surgery is thought to be associated with an increase in urinary fibrinolytic activity. Tranexamic acid (TXA) is both a potent inhibitor of plasminogen and urokinase activators and a low molecular weight substance that is excreted unchanged in the urinary tract and can be administered both orally and intravenously. We investigated the effect of TXA on the amount of blood loss during transurethral resection of the prostate (TURP). **Materials and methods.** Forty patients with registry numbers ending in even numbers were allocated to the treatment group; those ending in odd numbers were used as controls and received no treatment. The treatment group received 10 mg/kg TXA by intravenous infusion during the first half hour of the operation, while the control group of patients received no medication. Serum hemoglobin was measured before and after surgery. The volume and hemoglobin concentration of the irrigation fluid, resected prostate weight, and duration of resection were recorded.

Results. The mean loss of hemoglobin per gram of resected prostate tissue was 1.25 g in the TXA group and 2.84 g in the control group. Total hemoglobin loss in the irrigating fluid and hemoglobin loss per 1 gram of prostate tissue was lower in the group of patients given TXA than in the control group ($p = 0.018$ and $p < 0.001$).

Conclusion. Reduced bleeding during TURP as a result of TXA treatment may lead to better surgical conditions and, as a consequence, shorter operative times and lower irrigating fluid volumes.

shown to be 8-times more effective than epsilon aminocaproic acid (EACA). Urine and urothelium contain high concentrations of plasminogen activators that facilitate the lysis of clots [4]. Therefore, administration of antifibrinolytic agents might be beneficial in reducing the amount of postoperative blood loss resulting from TURP.

TXA is a synthetic antifibrinolytic drug that prevents the breakdown of fibrin, thereby stabilizing blood clots and reducing blood loss in conditions that promote fibrinolysis [5].

Previous studies investigating the beneficial effects of these compounds on TURP-associated bleeding have resulted in conflicting conclusions [6, 7]. Recently, a growing body of evidence has indicated that TXA is an effective agent for reducing blood loss in cardiac, orthopedic, and hepatic surgery. TXA has also been shown to be of benefit in the treatment of secondary hemorrhage associated with TURP [8, 9].

In this report we investigated the effect of tranexamic acid on the amount of blood lost during TUR-P. Its impact on operative time as well as duration of catheterization and hospitalization was also investigated.

MATERIAL AND METHODS

A prospective and randomized trial was conducted with 40 men requiring TURP for obstructive urinary symptoms. The ethics committee of the hospital approved this study and the patients signed their consent on a written form of information. Exclusion criteria included a history or evidence of prostate disease other than BPH, previous prostate surgery, treatment with any 5ARI within 12-months, requirement for treatment with aspirin or NSAIDs during the restricted periods, and severe medical conditions such as liver disease, bleeding disorders (e.g. hemophilia, von Willebrand's disease, etc.), and unstable cardiovascular problems.

Therefore, 40 patients were eligible for participation in our study. All patients had both clinical and laboratory evidence of prostatic enlargement caused by benign prostatic hyperplasia. Prostate size was determined by abdominal ultrasonography. The patients with even registry numbers were allocated to the treatment group, while those with odd numbers were used as controls and received no treatment. The treatment group received 10 mg/kg TXA by intravenous infusion during the first half hour of the operation.

The control group of patients received no medication. Patients taking acetylsalicylic acid or warfarin discontinued their treatment seven and two days before surgery, respectively. Serum hemoglobin was measured before and after the surgery. The volume and hemoglobin concentration of the irrigation fluid, resected prostate weight, and duration of resection were recorded.

All TURPs were performed under spinal anesthesia and by the same surgeon. We used a 26F resectoscope and warm irrigating fluid. Surgical blood loss was determined by the amount of hemoglobin in the irrigating fluid using a photometer as described previously.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition affecting men older than 50 years of age [1]. The historical gold standard has been transurethral resection of prostate (TURP), which is an effective procedure but is still associated with risk of bleeding. Factors that influence perioperative and postoperative blood loss include: prostate weight, weight of the resected tissue, operating time, preoperative urine culture, preoperative finasteride treatment, use of acetylsalicylic acid, type of anesthesia, as well as patient age and blood pressure, although some of these associations remain controversial [2].

Tranexamic acid (TXA) is a potent inhibitor of plasminogen activators and urokinase, thereby preventing clot lysis, and has been

Table 1. Patient characteristics

Variable	TXA (n = 20)	Control (n = 20)	P value
Age (yrs.)	67 (61-76)	65 (63-75)	0.085
Prostate size	52.5 (36.0-85.0)	49.5 (36.0-80.0)	0.098

The loss of the hemoglobin per gram of resected tissue at operation time was calculated by dividing the total resected prostate tissue by total hemoglobin loss. We defined the operating time as the start of resection until hemostasis was complete. All resected tissue was weighed and underwent pathological evaluation.

The statistical analyses were performed with NCSS 2000 statistical software. Correlations between the parameters were analyzed by using the Spearman's rank order test. Differences between groups were analyzed with the two-tailed two-sample t test, Mann-Whitney U test, or chi-square test, as needed. Finally, correlations were ranked by multiple regression analyses.

RESULTS

Data of 20 patients treated with TXA and 20 control patients were available. In the TXA given group, of whom the average age was 67, median prostate weight measured by abdominal ultrasound was found to be 52.5 g (36.0-85.0 g). The average age of the control group was 65 and median prostate weight was 43 g (36.0-80.0 g). No statistically significant difference of age and prostate weight were detected between groups (Table 1).

The mean serum hemoglobin loss on the first postoperative day in the TXA group was found to be 0.71 g/dl and was 0.98 g/dl in the control group. Even if there was a difference in hemoglobin decrease between the two groups, it was not statistically significant ($p = 0.086$) (Table 2). According to the hemoglobin in irrigating fluid, the mean hemoglobin loss in the TXA group was 16.18 g and it was 24.83 g in the control group. The mean hemoglobin loss per gram of resected prostate tissue was 1.25 g in the TXA group and 2.84 g in the control group. According to this, total hemoglobin loss in the irrigating fluid and hemoglobin loss per 1 gram of prostate tissue was lower in TXA given patients than in the control group ($p = 0.018$ and $p < 0.001$) (Table 2).

The total amount of irrigation fluid used, operation time, and the amount of resected prostate tissue were compared in TXA and control groups. Average irrigation fluid used during TUR-P was 16.34 L in TXA and 20.05 L ($p = 0.027$) in control groups.

The duration of operation was 46.75 minutes in the TXA given and 63.5 minutes in the control group ($p < 0.001$). The mean resected prostate tissue was found to be 24.33 g in the TXA given group and 16.68 g in the control group ($p < 0.038$). The duration of catheterization and hospitalization are the same in both groups ($p = 0.415$, $p = 0.218$) (Table 2).

According to multiple regression analyses, only the resected weight and operating time were independent variables. Age was not associated with the other variables. According to these findings, the irrigation fluid was less and operation time was shorter ($p = 0.027$, $p < 0.001$); resected prostate tissue was statistically more ($p = 0.038$) in the TXA group than the control group. However TXA treatment had no effect on the duration of catheterization and hospitalization.

DISCUSSION

TURP is the standard method for relieving bladder outlet obstruction in men with BPH, but the operation still requires in-hospital management due to a relatively high incidence of complications

Table 2. Comparisons of treatment group and control group

Variable	TXA (n = 20)	Control (n = 20)	P value
Mean serum hemoglobin loss on first postoperative day (g/dl)	0.71	0.98	0.086
Mean hemoglobin loss in irrigating fluid (g)	16.18	24.83	0.018
Hemoglobin loss per gram of resected tissue (g)	1.25	2.84	<0.001
Volume of irrigation fluid (L)	16.34	20.05	0.027
Operating time (min)	46.75	63.5	<0.001
Weight of resected tissue (g)	24.33	16.68	0.038
Length of catheterization (days)	3 [3, 4]	3 [3, 4]	0.415
Length of hospitalization (days)	3 [3, 5]	3 [3, 4]	0.218

during and afterward, particularly in patients with large prostates. In one study, perioperative blood loss was >1 L in 13% of the patients, leading an increased the risk of hemodynamic instability and the need for erythrocyte transfusions [10]. Hematuria and clot retention after TURP might prolong the hospital time and may even necessitate re-operation.

To reduce the perioperative and postoperative bleeding, several different approaches have been tried, including intravenous administration of estrogens, catheter traction, intraprostatic vasopressin, per os etamsylate, fibrin adhesive, phenol solution, and, more recently, finasteride [11, 12, 13]. Although these approaches have yielded some promising results, no one technique has gained widespread acceptance and incorporation into surgical routine.

Treatment with finasteride or other antiandrogens before TURP was reported to reduce surgical blood loss, but not all studies showed a consistent effect. Finasteride is thought to act by mediating androgen-dependent growth factors that regulate angiogenesis in the prostate. TXA, in contrast, accumulates in the extracellular space of tissues where it inhibits tissue fibrinolysis [12, 14].

Postoperative TURP-associated blood loss has been correlated with an increase in urinary fibrinolytic activity. Administration of antifibrinolytic drugs may be beneficial in reducing postoperative bleeding. There have been studies related to TXA usage before TURP [8, 9]. In these studies, TXA was used pre- and postoperatively per os. We used TXA treatment by intravenous infusion during the first half hour of the operation.

During TURP, similar results were obtained according to total hemoglobin decrease in the studies of oral TXA use.

In addition to reduced operative blood loss, we were surprised to observe a statistically significant decrease in the operative time and volume of irrigating fluid required.

Reduced bleeding during TURP as a result of TXA treatment may lead to better surgical conditions and, as a consequence, shorter operative times and lower irrigating fluid volumes. This is an intriguing finding, because absorption of irrigating fluid is another concern with TURP and is associated with increased operative time and blood loss. Therefore, TXA treatment may have the additional benefit of reducing irrigating fluid absorption. None of our 40 patients had clinical signs of irrigating fluid absorption [transurethral resection syndrome]. The frequency of transurethral resection syndrome varied from 0.18% to 10.9% [15]; therefore, we would have had a much larger pool of patients to detect any statistically significant differences.

Several studies have demonstrated that TXA treatment does not predispose a patient to thromboembolic complications [16, 17]. Similarly, we did not observe any thromboembolic complications.

CONCLUSION

TXA treatment reduced operative blood loss and decreased the operative time and volume of irrigating fluid required. Reduced bleeding during TURP as a result of TXA treatment could lead to better surgical conditions and, as a consequence, shorter operative times and lower irrigating fluid volumes.

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