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TRANEXAMIC ACID TO REDUCE SURGICAL BLOOD LOSS FOR TURP

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Introduction :
Benign prostatic hyperplasia (BPH) is a common condition affecting men older than 50 years of age.The historical gold standard for treatment has been trans Urethral resection of prostrate, which is effective procedure but is still associated with risk of bleeding. Factors that influence perioperative blood loss include prostate weight, weight of resected tissue, operating time (resection time), type of anesthesia, skill of the surgeon vascularity of the gland.

Tranexamic Acid (TXA) is a synthetic antifibrinolytic agent. A potent inhibitor of plasminogen and Urokinase activator (plasmin leads to breakdown of fibrin) Due to the anti fibrinolytic effect, the clots are stabilized blood loss is reduced.

Recently studies have shown that TXA is an effective agent for reducing blood loss during operative procedures.

In this study we are trying to investigate the efficacy of tranexamic acid in reducing the amount of blood loss during TURP.

AIM
- To estimate the amount of blood loss during TURP.
- To determine the correlation of volume of irrigating fluid used weight of tissue resected and duration of surgery on amount of blood loss.
- To determine if use of antifibrinolytic, tranexamic acid helps in reduction of blood loss.

Hypothesis :
The intraoperative administration of Tranexamic acid (TXA) reduces blood loss associated during TURP.

Materials and methods:
A Pilot study will be done in forty patients with twenty patients in each group. The final sample size will be decided after power analysis.

Selection of patients :
Patients undergoing TURP for Benign Prostrate Hypertrophy at ACS Medical College and Hospital, Velapanchavadi.

This study was carried out after ethical comitee approval.

Inclusion Criteria
Age of patients undergoing TURP for BPH under sub-arachnoid block above 50 years.

Exclusion Criteria
- Patients having history of allergy to any other medications and previous history of allergy to tranexamic acid.
- Patients suffering from bleeding disorders.
- Patients on anticoagulant therapy.
- Patients having renal impairment.
- Local anesthetic allergy.
- Ulcer or infection at skin puncture.

A prospective and randomized single blind, trial will be conducted for forty patients requiring TURP for obstructive urinary symptoms.

The patients will be allocated in two groups.
Data of 30 patients treated with TXA and 30 control patients were available. In the TXA given group, of whom the average age was 75, 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 .

Group C patients received 10mg/kg Tranexamic Acid intravenous infusion during first half an hour of operation followed by 1mg /hr infusion.

Group P : Patients received 10mg/kg normal saline during 1st hour of operation followed by 1mg /kg infusion.

Pre Anesthetic evaluation
(Patients included in this study underwent thorough pre-operative evaluation).

History :
History of underlying bleeding disorders, on anticoagulants, having renal impairment.

Physical examination :
General condition of the patient.
Systemic examination
PulseRate
Bloodpressure
METS

Investigations :
- Complete haemogram
- Blood sugar
- Blood Urea, serum creatinine
- Serum electrolytes
- Bleeding time, clotting time
- Electro cardiogram
- Chest x-ray
- Body Weight
- Pulmonary function test

ECG, Chest X Ray and Echocardiography
Patients who satisfied inclusion criteria will be explained about nature of study and anesthetic procedure. Written informed consent will be obtained from all patients included in the study. Starvation will be checked.
On the day of surgery,after checking consent and adequate starvation, patient will be brought into the theatre. Monitors (Non invasive blood pressure,Electrocardiogram,Pulse oximeter) will be attached.

Intravenous access will be done and with 500 ml Ringer lactate will be started at the rate of 20 ml/kg/hour as preloading for spinal anaesthesia.

Patient in sitting position the standardized anesthesia technique of sub arachnoid block is given using 3 cc of injection Bupivacaine 0.5% Heavy under aseptic precautions.

Patient will be positioned in lithotomy. Throughout the procedure, continous intraoperative monitoring will be done.

After the procedure the patient will be shifted to Post operative room and monitoring will be continued, till he is sent to the ward.

INTRAOP MONITORING

Time (min)	Heart Rate	Blood Pressure	Spo_2 Oxygen Saturation	Intravenous Fluid	Volume of Irrigation Fluid (Glycine)	Resection Time

Most important consideration during surgery were

Total resection time
Total volume of glycine used (In our hospital the irrigation fluid used is Glycine Solution 3liters bottle, each 100 ml containing 1.5gms.)

Total volume of irrigation fluid returned.

Mass of tissue resected.

Statistical analysis
The parameters recorded will be subjected to statistical analysis to find whether, addition of tranexamic acid is beneficial in reducing blood loss after TURP.

Perioperative analysis
1.Haematocrit of irrigation fluid returned.
2.Hemoglobin of the patient at the end of surgery
3.Hemoglobin of the patient after 24 hours.
4.Total intravenous fluid received in 24 hours
5.Mean serum hemoglobin loss on first
6.postoperative day (g/dl)
7.Mean hemoglobin loss in irrigating fluid (g)
8.Hemoglobin loss per gram of resected tissue (g)
9.Volume of irrigation fluid (L)
10.Operating time (min)
11.Weight of resected tissue (g)
12.Length of catheterization (days)
13.Length of hospitalization (days)

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 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. 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.. 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 .

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. 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%; 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 . Similarly, we did not observe any thromboembolic complications.

RESULTS:

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 ($p = 0.086$) . 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 $p <0.001$)).

Short-term TXA treatment significantly reduced the operative blood loss associated with TURP (128 mL versus 250 mL, $P = 0.018$), and this difference was not a result of the amount of tissue resected between the two groups (16 g versus 16 g, $P = 0.415$). In addition, TXA treatment reduced the amount of blood loss per gram of resected tissue (8 mL/g versus 13 mL/g, $P = 0.020$). Furthermore, the volume of irrigating fluid required (15 L versus 18 L, $P = 0.004$) and operating time (36 minutes versus 48 minutes, $P = 0.001$) were also reduced. However, TXA treatment did not influence the number of patients requiring a blood transfusion. Six patients in the treatment group (7.2%) and five in the control group (6.8%) required a transfusion ($P = 0.709$). Moreover, TXA treatment did not affect the duration of catheterization (1 day versus 1 day, $P = 0.342$) or hospitalization (3 days versus 3 days, $P = 0.218$).

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. 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.

REFERENCES

1. Meigs JB, Mohr B, Barry MJ, et al: Risk factors for clinical benign prostatic hyperplasia in a community-based population of healthy aging men. J Clinical Epidemiology 2011; 54: 935-944.
2. Borboroglu PG, Kane CJ, Ward JF, et al: Immediate and postoperative complications of transurethral prostatectomy in the 1990s. J Urol 1999; 162: 1307-1310.
3. Erstad BL: Systemic hemostatic medications for reducing surgical blood loss. Ann Pharmacother 2001; 35: 925-934.
4. Nielsen JD, Gram J, Fabrin A, et al: Lack of correlation between blood fibrinolysis and the immediate or post-operative blood loss in transurethral resection of the prostate. Br J Urol 1997; 80: 105-110.
5. Mannucci PM: Hemostatic drugs. N Engl J Med 1998; 339: 245-253.
6. Madsen PO, Strauch AE: The effect of aminocaproic acid on bleeding following tran-

surethral prostatectomy. J Urol 1966; 96: 255-256.
7. Sharifi R, Lee M, Ray P, et al: Safety and efficacy of intravesical aminocaproic acid for bleeding after transurethral resection of prostate. Urology 1986; 27: 214-219.
8. Miller RA, May MW, Hendry WF, et al: The prevention of secondary haemorrhage after prostatectomy: the value of antifibrinolytic therapy. Br J Urol 1980; 52: 26-28.
9. Rannikko A, Petas A, Taari K: Tranexamic acid in control of primary hemorrhage during transurethral prostatectomy. Urology 2004; 64: 955-958.
10. Ekengren JC, Hohn RG: Blood loss during transurethral resection of the prostate as measured with the Hemocue photometer. Scand J Urol Neph 1993; 27: 501-507.
11. Donohue JF, Sharma H, Abraham R, et al: Transurethral prostate resection and bleeding: a randomized, placebo controlled trial of the role of finasteride for decreasing operative blood loss. J Urol 2002; 168: 2024-2026.
12. Hagerty JA, Ginsberg JD, Harmon JD, et al: Pretreatment with finasteride decreases perioperative bleeding associated with transurethral resection of the prostate. Urology 2000; 55: 684-689.
13. Sandfeldt L, Bailey DM, Hahn RG: Blood loss during transurethral resection of the prostate after 3 months of treatment with finasteride. Urology 2001; 58: 972-976.
14. Puchner PJ, Miller MI: The effects of finasteride on hematuria associated with benign prostatic hyperplasia: a preliminary report. J Urol 1995; 154: 1779-1782.
15. Hahn RG, and Ekengren JC: Patterns of irrigating fluid absorption during transurethral resection of the prostate as indicated by ethanol. J Urol 1993; 149: 502-506.
16. Berntorp E, Follrud C, Lethagen S: No increased risk of venous thrombosis in women taking tranexamic acid. Thromb Haemost 2001; 86: 714-715.
17. Ruel MA, Wang F, Bourke ME, et al: Is tranexamic acid safe in patients undergoing coronary endarterectomy? Ann Thorac Surg 2001; 71: 1508-1511