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RESEARCH ARTICLE

IS TRANEXAMIC ACID EFFECTIVE IN REDUCING TURP RELATED BLOOD LOSS? – A PROSPECTIVE STUDY

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ABSTRACT

Blood loss related to transurethral resection of the prostate (TURP) is a significant cause of morbidity, especially in larger glands.
Aim: To determine the effectiveness of short-term treatment with Tranexamic acid (TXA), a potent antifibrinolytic, in reducing the blood loss related to TURP.
Materials and Methods: One hundred patients with benign prostatic hyperplasia requiring TURP were randomly allocated into treatment and control groups (50 patients in each). Based on prostate volume, patients were categorized into groups A (40-49cc) (n=30), B (50-69cc) (n=58), C (70-75cc) (n=12). Each group had Treatment (received TXA) and Control subgroups. The selected patients were given 10mg/kg TXA intravenously, 1 hour prior to surgery and two doses post operatively, eighth hourly. Serum hemoglobin on the 1st post operative day, volume and hemoglobin concentration of the irrigation fluid, amount of tissue resected, duration of surgery were compared between the test and control groups. Also the number of patients presenting with delayed hematuria, clot retention and requiring transfusion were compared.
Results: Mean blood loss 323ml vs 527 ml (p= 0.000) in test and control subgroups respectively, in Group B. Blood loss/gram (ml/g) of resected tissue was 9.7 vs 13.5 (p= 0.000) in Group A, 11.3 vs 21.5 (p= 0.000) in Group B, 17.3 vs 21.5 (p =0.002) in Group C. The hemoglobin loss in the irrigating fluid was significantly lower in the group of patients given TXA than in the control group (p<0.01).
Conclusion: Short-term TXA treatment is effective in reducing the blood loss related to TURP and also improving surgical outcomes.

Key words: Tranexamic acid, Trans urethral resection of prostate, blood loss.

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INTRODUCTION

TURP is believed to be the gold standard for surgical management of BPH (Benign prostatic hyperplasia). Blood loss related to TURP is presumed to be due to an increased urinary fibrinolytic activity (Şükrü Kumsar *et al.,* 2011). Urine and urothelium contain high concentrations of plasminogen activators that enhance clot lysis (Nielsen *et al.,* 1997). An increase in blood loss during prostate resection is due to the release of urokinase from prostatic tissue. Tranexamic acid (TXA), a synthetic derivative of the amino acid lysine, exerts its antifibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules. It is a potent inhibitor of plasminogen and urokinase activators, thereby preventing clot lysis, and is 8 times more potent than its predecessor, Epsilon amino caproic acid (Mannucci *et al.,* 1998).

Aim

- To estimate amount of blood loss during TURP.
- To assess whether short term use of Tranexamic acid decreases the associated blood loss.

MATERIALS AND METHODS

Prospective study was done from May 2016 – Dec 2016. A cohort of 100 patients requiring TURP were randomly allocated into treatment and control groups (n=50) each. Pre operative work up included a thorough history, International Prostate Symptom Score (IPSS), clinical examination, ultrasound KUB, uroflow, post void residue, complete hemogram, renal function tests, coagulation profile, urine c/s, serum PSA (prostate specific antigen), echocardiography, chest X ray. Patients with positive urine culture were treated with appropriate antibiotics prior to surgery. Patients on anticoagulants, treatment with 5 alpha reductase inhibitors, severe medical comorbidities (renal/ cardiac/ hepatic failure), previous prostate surgery, prostatitis, elevated total PSA, free PSA/tPSA < 0.25, and associated vesical calculus were excluded. Based on prostate volume, Patients were categorized into groups A (40-49cc) (n=30), B(50-69cc)(n=58), C (70-

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75cc) (n=12). Each group had Test (T) and Control (C) subgroups. Group A (T- 16, C- 14), Group B (T - 32, C - 26), Group C (T-6, C- 6). Test subgroup received Tranexamic acid 10mg/kg, intravenous, 3doses on the day of surgery. 1st dose one hour prior to surgery, two other doses post operatively (8th hourly). TURP was done with conventional 26Fr resectoscope. Irrigation fluid used was 1.5% glycine.

Blood loss estimation

Blood loss in irrigation fluid was estimated by Drabkin's (cyanmethhemoglobin) method. To 0.02 ml of sample, 5ml of Drabkin's reagent was added and read against spectrophotometer at 540nm. Blood loss(ml) = Volume of fluid(ml) x % blood in sample x normal Hb/ Patient Hb. Efflux collected and Injection Heparin 1500 IU was added to every 8 litres of irrigation fluid.

Parameters analysed

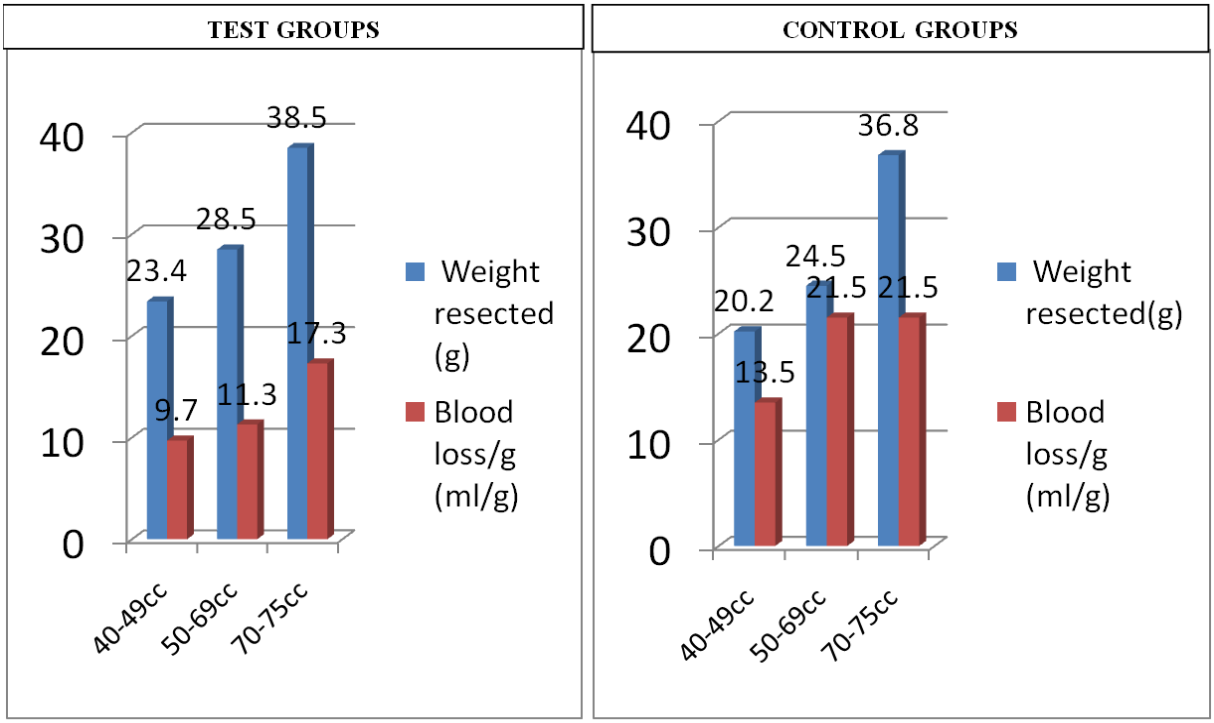
- Blood Hb on first post operative day
- Blood loss in irrigation fluid and its volume
- Weight of resected prostatic tissue
- Blood loss/g of resected tissue
- Duration of resection
- Requirement of post op transfusion

Statistical analysis was done by Student't' test. Data from test and control subgroups compared and analysed in each group (A, B, C).

RESULTS

The mean Hemoglobin loss on the first post op day was 0.71 g% vs 1.5 g% (test vs control respectively) (p= 0.000) in group B. Mean blood loss 323ml vs 527 ml (p= 0.000) in Group B and 668ml vs 974 ml (p = 0.012) in Group C. Blood loss/gram (ml/g) of resected tissue was 9.7 vs 13.5 (p= 0.000) in Group A, 11.3 vs 21.5 (p= 0.000) in Group B, 17.3 vs 21.5 (p =0.002) in Group C. Blood loss (ml) and blood loss/gram of resected prostate were significantly lower in test subgroups of Groups B and C and this was not as a result of difference in weight of the tissue resected in Group C (38.5g vs 36.8g, P = 0.084) and in Group B, the resected weight was significantly higher in Test subgroup (28.5g vs 24.5g, p= 0.01) with a significantly reduced amount of blood loss. Volume of irrigation fluid utilized was 16.5L vs 18.48 L (p = 0.000) in Group B. Duration of surgery was 42 min vs 48 min (p = 0.000) in Group A and 65min vs 88min (p= 0.000) in Group B. Requirement of transfusion post operatively was in 1patient in control group (3.8%) and 1 in test sub group (3.1%) (50-69cc)(Group B). Delayed hemorrhage and clot evacuation was done in 1 patient in test subgroup and 2 in control subgroup (70 –75cc) (Group C). Thus the use of Tranexamic acid was associated with lower blood loss, improved resection, shorter operative times and lesser amount of irrigation fluid consumed and thereby decreasing the chance of TUR syndrome in moderately large glands. However, the use of Tranexamic acid did not significantly reduce the number of patients requiring transfusion (3.8% vs 3.1%) (p= 0.50), delayed hemorrhage and clot retention.

Volume of Prostate	40-49 cc			50-69cc			70-75cc		
	TEST	C		TEST	C		TEST	C	
Hb loss on 1st POD (g %)	0.63	0.81	p=0.09	0.71	1.5	p=0.00	1.7	1.73	p=0.83
Blood loss(ml)	227	273	p=0.38	323	527	p=0.00	668	794	p=0.012
Resected weight(g)	23.4	20.24	p=0.53	28.52	24.5	p=0.01	38.5	36.8	p=0.084
Blood loss/g (ml/g)	9.7	13.5	p=0.00	11.3	21.5	p=0.00	17.3	21.5	p=0.002
Volume of irrigation fluid(L)	14	15	p=0.31	16.5	18.48	p=0.00	21.2	22.5	p =0.23
Duration of surgery (min)	42	48	p=0.00	65	88	p=0.00	92	95	p=0.06



Comparison between test and control groups of - blood loss/gram of resected tissue and weight of gland resected

DISCUSSION

TURP has been the gold standard for surgical management of BPH. Even with the advent of LASER prostatectomy, Bipolar TURP, Enucleation, Microwave therapy, Monopolar TURP continues to be widely practised, especially in developing countries. Perioperative bleeding continues to be a significant event, with estimated transfusion rates around 4.4% (Mayer et al, 2012). Factors influencing perioperative blood loss are size and vascularity of the gland, weight of resected tissue, resection time, presence of UTI, preoperative use of anticoagulants and the type of anesthesia (Şükrü Kumsar *et al.,* 2011). To reduce perioperative bleeding, several approaches have been tried, including intravenous estrogen, catheter traction, intraprostatic vasopressin, per os ethamsylate, fibrin adhesive, phenol solution, 5alpha reductase inhibitors and also single dose of Goserelin acetate (Erstad *et al.,* 2001). Finasteride 5 mg for 4 weeks before TURP was tried and found to decrease transfusion rate in cases with >30 g of resected tissue (Hagerty *et al.,* 2000) (Hagerty *et al.,* 2000; Sandfeldt *et al.,* 2001). Also pretreatment with dutasteride 0.5mg for 2 weeks has been tried (Kravchick *et al.,* 2009), but due to conflicting results in different studies, 2010 AUA guidelines for BPH does not recommend perioperative 5 alpha reductase inhibitors (ARIs) to decrease bleeding. Also the anti - angiogenic effect of 5 ARIs proposed was controversial and some studies denying such a role (Shanmugasundaram *et al.,* 2007). Goserelin acetate 3.6mg, s.c, single dose, 4 wks before TURP was shown to reduce bleeding by reducing testosterone and DHT levels. (Mohamed *et al.,* 2016) But further RCTs are needed to provide concrete evidence to its use. TXA, in contrast, is given for a short period and acts by accumulating in extracellular space of tissues, where it inhibits fibrinolysis. TXA needs dose reduction in renal failure and such patients were excluded from our study. Also, short term TXA perioperatively, does not appear to increase the risk of thromboembolic events (Ruel *et al.,* 2001). We used short term TXA perioperatively and found to have a significant reduction in mean blood loss, blood loss/gram of resected tissue and also statistically significant reduction in operative times and the amount of irrigation fluid used. However, there was no significant difference in the incidence of delayed hemorrhage and clot retention.

Conclusion

Short term TXA is effective in reducing TURP related blood loss, as there's a much

- Shorter duration of treatment
- Improved compliance
- Cost effective
- Lesser side effects
- Decreases duration of surgery and hence chance of TUR syndrome.

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