Original Article

Single Dose of IV Tranexamic Acid Preoperatively Reduces the Incidence of Post-Operative Scrotal Edema Following Lichtenstein Hernioplasty. A Randomized Prospective Cohort Analysis

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ABSTRACT

Objective: to determine the single Dose of IV Tranexamic acid perioperatively reduces the incidence of post-operative scrotal oedema following Lichtenstein hernioplasty.

Study Design: A randomized prospective analysis

Place and Duration of Study: This study was conducted at the Civil Hospital Karachi, Pakistan from June, 2019 to December, 2020 for a period of six months.

Materials and Methods: All patients operated for inguinal hernia repair on elective basis at Surgical Unit of a tertiary care hospital was done after taking the approval from the hospital ethics committee. 40 patients in each group. All the patients aged between 18 and 65 years who underwent elective repair of inguinal hernia were a part of this study. Patients who were excluded from the study were the ones classified as ASA class III or IV by anaesthesiologist, patients with chronic end-organ diseases including CLD, CKD, CHF, history of intracranial haemorrhage, connective tissue disease or hypoalbuminemia, Patients with a history of convulsions, patients previously on anticoagulants and antiaggregant and patients having hypersensitivity to tranexamic acid.

Results: A total of 80 patients undergoing inguinal hernia repair were divided into 2 groups. The mean age for the control group was 39.33 ± 11.72, while for the intervention group was 41.53 ± 11.76 [$p<0.05$]. The most common complication apart from scrotal edema was urinary retention in both the groups. [27.5% in control vs 10% in TXA group], the rate of complications was more significant in control group [$p=0.02$]. The mean operating time for the intervention group was significantly reduced in the intervention group [68.25 ± 22.60 min vs 85.62 ± 31.78 min, $p=0.006$]. Edema resolved in 1.57 ± 1.44 days in intervention group while it took 4.85 ± 3.20 days for edema to resolve in the control group $p<0.001$. The patients who received TXA returned to work earlier than the ones without administration [$p<0.001$] along with a significantly reduced rate of complication [$p<0.001$].

Conclusion: A single dose of intravenous tranexamic acid 1gm can be safely administered to reduce scrotal edema following Lichtenstein hernioplasty with no demonstrable side effects.

Key Words: Lichtenstein hernioplasty; Tranexamic Acid; Scrotal edema; SERG score

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INTRODUCTION

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Around the globe, millions of people undergo hernia surgery annually[1]. Lichtenstein hernioplasty is considered a gold standard approach for inguinal hernia repair. Though a very safe and effective procedure, one of the troublesome postoperative problems is the development of scrotal swelling which includes seroma as well as hematoma. Despite being a benign complication, it's very irritating to the patients with an incidence rate approaching 1.4 to 12% [2,3].

Different approaches have been devised to avoid this problem. The use of intramuscular hydrocortisone has been shown to reduce the immediate post-operative scrotal edema after an inguinal varicocelectomy [4]. Scrotal compressions have been widely used to avoid scrotal edema after inguinal hernia surgeries [5]. However, the use of per-operative intravenous [IV]

Tranexamic acid [TXA] has not been explored in this regard. Tranexamic acid being an anti-fibrinolytic agent has been used on various occasions both intra and postoperatively. Zaman et al reported a single dose of IV TXA can result in less postoperative nasal bleed following a septoplasty [7]. Similarly, Goldstein et al showed that intravenous tranexamic acid can result in decreased bleeding in end prosthesis knee and hip surgeries [8]. Its role in the management of coagulopathy of trauma showed in the CRASH trial has proven revolutionary [9].

The prime focus of our study was to assess the role of IV TXA, given intraoperatively at doses of 10mg/kg [up to 1000mg] in preventing the development of immediate [1st postoperative day] and latent [within 7-8 operative days] scrotal edema.

MATERIALS AND METHODS

A randomized prospective analysis was conducted from June 2019 to December, 2020 at Civil Hospital Karachi, Pakistan. All patients operated for inguinal hernia repair on elective basis at Surgical Unit of a tertiary care hospital was done after taking the approval from the hospital ethics committee. 40 patients in each group. The participation in the study was voluntary and all the patients enrolled in the study were thoroughly briefed about the study methodology**.** Informed consent was then obtained from every participant in the native language 'Urdu'. Each participant was administered prophylactic antibiotics at the time of incision, as per the protocol.

All the patients aged between 18 and 65 years who underwent elective repair of inguinal hernia were a part of this study. Patients who were excluded from the study were the ones classified as ASA class III or IV by anesthesiologist, patients with chronic end-organ diseases including CLD, CKD, CHF, history of intracranial hemorrhage, connective tissue disease or hypoalbuminemia, Patients with a history of convulsions, patients previously on anticoagulants and antiaggregant and patients having hypersensitivity to tranexamic acid.

The factors examined included age, comorbidities, complications other than scrotal edema, scrotal edema on 2nd and 7th postoperative day, and duration of edema. The quantification and grade of scrotal edema was measured using scrotal edema Rating Grade [SERG] score as a statistically significant difference in SERG score among the two groups implies increased prevalence/ incidence of scrotal edema in group with increased SERG score as compare to the group with lower SERG score. It is calculated by asking the patient to be in standing position and measuring the widest scrotal circumference using a numbered tape. The SERG score was measured preoperatively, on 2nd post-op, and 7th post-op day for every patient. The score ranged from 0 to 3 as follows:

0 = no edema = the pre-operative scrotal circumference
1 = mild edema = < 2 folds increase in the widest scrotal circumference
2 = moderate edema = 2 - 3 folds increase in the widest scrotal circumference
3 = severe edema = > 3 folds increase in the widest scrotal circumference.

RESULTS

A total of 80 patients undergoing inguinal hernia repair met the inclusion criterion and were selected for analysis. The patients were divided into 2 groups. After matching for age, co-morbidities, and BMI, both the groups contain 40 patients.

Table No.1: Comparison of Demographics and Co-morbidities in two groups

	TXA given (n=40)	**TXA not given (n=40)**
Demographics		
Mean Age	41.53 SD 11.76	39.33 SD 11.72
Gender	Man	Man
Co-morbidities		
Chronic Kidney Disease (CKD)	1	2
Diabetes Miletus (DM)	3	5
Chronic Liver Disease (CLD)	0	0
Hypertension (HTN)	5	6
Ischemic Heart Disease (IHD)	2	5
DM + CKD	1	0
DM + CLD	0	1
DM + HTN	2	2
HTN + IHD	1	0
IHD + DM + HTN	0	1
None	25	18

Table No.2: Rate of complications in two groups

Complication	**TXA given (n=40)**	**TXA not given (n=40)**
Ileus	0	3
Urinary Retention (UR)	3	9
Wound Infections	2	5
Post-Operative Pain	1	3
Ileus + UR	1	0
Wound Infection + UR	0	1
Thrombotic complication	0	0

The mean age for the control group was 39.33 ± 11.72, while for the intervention group was 41.53 ± 11.76 [p<0.05]. Hypertension [Htn] was the most common abnormality found amongst the two groups [22.5% in the control group vs 20.5% in the intervention group]. However, no statistically significant difference was found among the co-morbidities of the two groups [p=0.60], See Table 1. The most common complication apart from scrotal edema was urinary retention in both the groups. [27.5% in control vs 10% in TXA group], the rate of complications was more significant in control group [p=0.02]. See Table 2 for further detail.

Table 3 shows the multivariate logistic regression analysis for pre-op and post-operative characteristics among the 2 groups. The mean operating time for the intervention group was significantly reduced in the intervention group [68.25 ± 22.60 min vs 85.62 ± 31.78 min, p=0.006]. There was a remarkable difference in the SERG score at 2nd postoperative day among the two categories [0.62 + 0.92 vs 1.45 ± 1.01, p=0.005], showing a distinguishable reduction in edema in the patients receiving TXA per-operatively. However, no statistically significant difference in SERG score at 7th operative day was found [0.10± 0.30 vs 0.27 ± 0.55, p=0.09]. Edema resolved in 1.57 ± 1.44 days in intervention group while it took 4.85 ± 3.20 days for edema to resolve in the control group p<0.001. The patients who received TXA returned to work earlier than the ones without administration [p<0.001] along with a significantly reduced rate of complication [p<0.001]. See Table 3 for further details.

Table No.3: Multivariate logistic regression among the two groups for per-operative and post-operative factors

	TXA group	No TXA group	OR	p-value
Duration of Surgery, (min, mean± SD)	68.25 ± 22.60	85.62 ± 31.78	0.977[0.961-0.994]	0.009
SERG at 2nd Post op Day, (mean ± SD)	0.62 + 0.92	1.45 ± 1.01	0.429[0.262-0.703]	0.001
SERG at 7th Post op Day, (mean ± SD)	0.10± 0.30	0.27 ± 0.55	0.381[0.121-0.197]	0.09
Duration of Edema Resolvement, (days, mean ± SD)	1.57 ± 1.44	4.85 ± 3.20	0.690[0.577-0.824]	<0.001
Days of Return to work, (days, mean ± SD)	4.32 ± 1.84	6.67 ± 2.53	0.590[0.452-0.770]	<0.001
Incidence of complications other than scrotal edema (n)	33	18	0.174[0.062-0.484]	<0.001

DISCUSSION

Post-operative scrotal edema is one of the most significant complications diagnosed post inguinal hernioplasty. The pathogenesis behind its development involves multiple factors. One of the widely acknowledged mechanisms is that damage to the tissue causes the release of inflammatory mediators [Ca, nitric oxide, VEGF, EGF, and PDGF] which cause the contraction of endothelial cells and increase the permeation between capillaries and interstitial fluid. Iatrogenic trauma to the tissue is further augmented by poor tissue handling causing damage to the capillary membrane which in turn leads to extravasation of fluid from vessels into interstitial space [6]. TXA being an anti-fibrinolytic agent has proven to be a useful adjunct to reduce this edema. TXA reversibly binds to plasminogen and blocks its conversion to plasmin which in turn halts the fibrin degradation which is an essential step in blood leaking out from the capillaries[10]. Furthermore, the role of TXA as an anti-inflammatory has also been described as it has been shown to decrease the levels of interleukins and acute phase reactants which are essential factors in inflammatory cascades following surgeries [11].

In our study, we reported a decreased incidence of postoperative scrotal edema following IV administration of 1gm TXA during the procedure as compared to the control group. The literature regarding the use of TXA in inguinal hernia surgery is very limited. However, its use in different operative procedures to reduce post-operative edema/seroma is not unpopular. Orteli D et:al reported a decreased rate of post-op seroma following TXA administration in patients with breast cancer undergoing mastectomy or lumpectomy with axillary clearance [12]. Similar results were demonstrated after topical TXA application following reduction mammoplasty [13]. An extensive meta-analysis concerning nasal operative procedures such as septoplasty and rhinoplasty, also demonstrated the efficacy of intravenous TXA in reducing the post-operative eyelid edema, a complication of such procedures [14]. Sara et al also described the decreased incidence of post-op complication eyelid edema, following rhinoplasty when intravenous TXA was used intraoperatively [15].

Our study also reports that there was a significant reduction in intraoperative time in patients in whom TXA was administered. Also, the hospital length of stay in the TXA group was found out to be significantly less

than the control group. These findings are concordant with Goobie et al who also demonstrated that TXA use reduces the intraoperative bleeding in adolescent scoliosis surgery leading to a decrease in hospital stay hence an earlier return to work[16]. Goyal et al also concluded that the use of intraarticular TXA can reduce the length of hospital stay in patients undergoing total knee arthroplasty [17].

Considering the rate of complications between the two groups, the TXA group revealed a decreased incidence than the control group. This differs from Zhou et al who showed no significant difference in complications after inter-trochanteric fracture surgeries between TXA and placebo group [18]. TXA administration is considered a risk factor for venous thromboembolic events [19]. We reported no incidence of such an event similar to findings described by Nishida et al [20]. However, we relied on the demonstration of symptoms to diagnose this complication and didn't perform any radiological investigation which can be considered a limitation of our study

Henceforth, the benefits offered by TXA far outshine the risks associated with its use. Very few side effects have been reported when TXA is given in a single dose of 500 mg to 1gm. The patient in this study stated no adverse reaction that is known to be associated with TXA use [21]. Considering the benefits, the TXA group in our study was superior in all aspects of a surgical procedure be it decreased duration of surgery, decreased incidence of postoperative scrotal edema, earlier return to work, and reduced complication rate. This completely shifts the equilibrium in favour of TXA. However, more extensive trials are recommended to enhance the precision and validity which is limited by the limited sample size of our study.

CONCLUSION

A single dose of intravenous tranexamic acid 1gm can be safely administered to reduce scrotal edema following Lichtenstein hernioplasty with no demonstrable side effects, but with additional benefits of the decreased duration of operative procedures, earlier return to normal life and reduced complication rate. However, more extensive prospective clinical trials are required to increase the validation regarding its use.

Author's Contribution:

Concept & Design of Study:	Farhan Zaheer
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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