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COMPARISON OF HEMOSTASIS BY INTRAVENOUS TRANSAMIN ADMINISTRATION ALONE VERSUS TRANSAMIN-SOAKED PACKING IN THE GALLBLADDER BED ALONG WITH INTRAVENOUS TRANSAMIN IN CHOLECYSTECTOMY

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Abstract

Objective: *To compare the hemostatic efficacy of intravenous transamin alone versus combined intravenous and transamin-soaked re-packing in the gallbladder bed during cholecystectomy.*

Study Design: *Quasi-experimental study*

Place and Duration: *Department of General, Thoracic and Paediatric Surgery, and Department of Anesthesiology at a Tertiary Care Hospital in Kharian, Kharian, Pakistan.*

Methodology: *This quasi-experimental study was carried out on 110 patients undergoing elective laparoscopic cholecystectomy. The patients were randomly divided into two equal groups in the study. Group A received intravenous transamine (10 mg/kg) only, Group B received intravenous transamin and topical transamin soaked packing (500 mg poured over the gauze) applied for three minutes to the gallbladder bed. Intraoperative blood loss, output of postoperative drainage, surgery time, hospital stay, and postoperative complications were recorded.*

Results: *The two groups were also similar with respect to age and gender. There was a significant difference in mean intraoperative blood loss between group B (34.83 ± 7.7 mL) and A (49.47 ± 11.55 mL; $p < 0.05$). Also, surgical drain output was significantly less in group B (47.98 ± 12.56 mL) than for group A (72.69 ± 14.14 mL; $P < 0.05$).*

Conclusion: *Combined intravenous and topical TXA significantly improved hemostasis, decreased blood loss and reduced hospital stay compared to intravenous TXA alone during cholecystectomy.*

INTRODUCTION

Gallstone disease (cholelithiasis) is a common hepatobiliary disease worldwide and one of the factors that significantly affects surgical workload and cost. Its prevalence ranges from 10% to 15% in Western populations and up to 20% in certain areas of Asia, with significant influence by diet, lifestyle, and genetics.[1] Gallstone disease in Pakistan affects 6-20% of the adult population; the prevalence of this condition is higher in females, and it is associated with obesity and age.[2] Laparoscopic cholecystectomy is the standard of care for symptomatic cholelithiasis; it offers advantages compared to open cholecystectomy, including lesser postoperative pain levels, faster recovery, and shorter hospital stay. However, intraoperative bleeding from the cystic artery or the gallbladder bed may present major challenges, such as compromising visualisation, increasing the operative time, and an increase in postoperative morbidity.[3-4]

Hemostasis is a critical physiological mechanism for stopping blood loss following vascular injury, and includes vasoconstriction, platelet activation, and the coagulation cascade. Surgical hemostasis is essential in minimizing blood loss and reducing transfusion requirements, and it improves the clarity of the surgical field during the operation.[5-6] Hemostatic techniques include mechanical methods (such as suturing and ligation), thermal methods (e.g., electrocautery, argon plasma coagulation), and chemical or biological adjuncts (for example, hemostatic powders, fibrin sealants, oxidised cellulose). Anti-fibrinolytics, such as tranexamic acid (TXA), are effective in limiting perioperative bleeding in numerous surgical specialties.[7]

Tranexamic acid, a lysine derivative, inhibits plasminogen to plasmin conversion, stabilizing fibrin clots and preventing fibrinolysis. Its intravenous use in orthopedic, thoracic, and hepatic surgeries has shown a significant reduction in intraoperative blood loss and transfusion needs. Topical TXA administration via gauze, packing, or irrigation enhances localized hemostasis with minimal systemic absorption.[8] In hepatobiliary procedures like cholecystectomy, diffuse oozing from the gallbladder or liver bed can be difficult to control with electrocautery alone.[9] Combined TXA-soaked packing with intravenous administration may provide additive benefits by merging systemic antifibrinolytic effects with localized clot reinforcement.

To date, no well-designed randomized trial has directly compared intravenous TXA alone versus intravenous TXA plus local TXA-soaked packing of the gallbladder bed in cholecystectomy. This gap gives rationale for the present study: to assess whether the addition of local TXA-soaked packing confers measurable additional benefit over IV TXA alone in achieving hemostasis during cholecystectomy, particularly in resource-limited settings like Pakistan, where resource constraints make minimizing blood loss and complications extremely valuable.

METHODOLOGY

The study was designed as a quasi-experimental study and conducted in the Department of General, Thoracic and Paediatric Surgery and Department of Anaesthesiology at a Tertiary care Hospital in the Kharian, after approval from the ethical board committee, ERB-No. A/24/24 dated 10th October 2024.

Inclusion Criteria: All patients diagnosed with symptomatic gallstone disease and scheduled for elective laparoscopic cholecystectomy were considered for inclusion. Patients of both genders, aged between 18 and 65 years, were eligible.

Exclusion criteria: Patients with known hypersensitivity to tranexamic acid, history of thromboembolic disorders, renal impairment, pregnancy, ongoing anticoagulant therapy, acute cholecystitis requiring conversion to open surgery, or intraoperative bile duct injury were excluded.

The sample size was calculated using the OpenEpi sample size calculator (version 3.01) for comparing two means, with a 95% confidence level and 80% statistical power. The calculation was based on a pilot study done in our hospital by the same team, in which the mean intraoperative blood loss during laparoscopic cholecystectomy using intravenous tranexamic acid alone was reported as 47.5 ± 8.6 ml, while the combined use of intravenous and topical tranexamic acid resulted in a mean

blood loss of 35.6 ± 9.13 ml. The pilot study was done after permission from ethical review board, before the approval of this study, so that we could get data for our primary variable, intraoperative blood loss, on the basis of which we calculated the sample size. The minimum sample size needed was calculated to be 9 patients per group using these values. The pilot study consisted of two groups having 20 participants in each group, the primary variable, intraoperative blood loss, was normally distributed in both groups. It is also important to mention that pilot study data were collected using the same variables as were used for the study, moreover, pilot study data weren't entered into this study for calculations. To better the result, provide room for subgroup analysis, and better external validity, the sample size was expanded to 110 patients overall, with 55 patients in each group. This larger sample size also took into account an expected dropout rate of 10-15% due to conversion to open surgery, intraoperative complications, or incomplete data. Informed written consent was obtained from each participant prior to inclusion in the study. Patients were randomly assigned to two groups by computer-generated randomization sequence (Figure 1):-

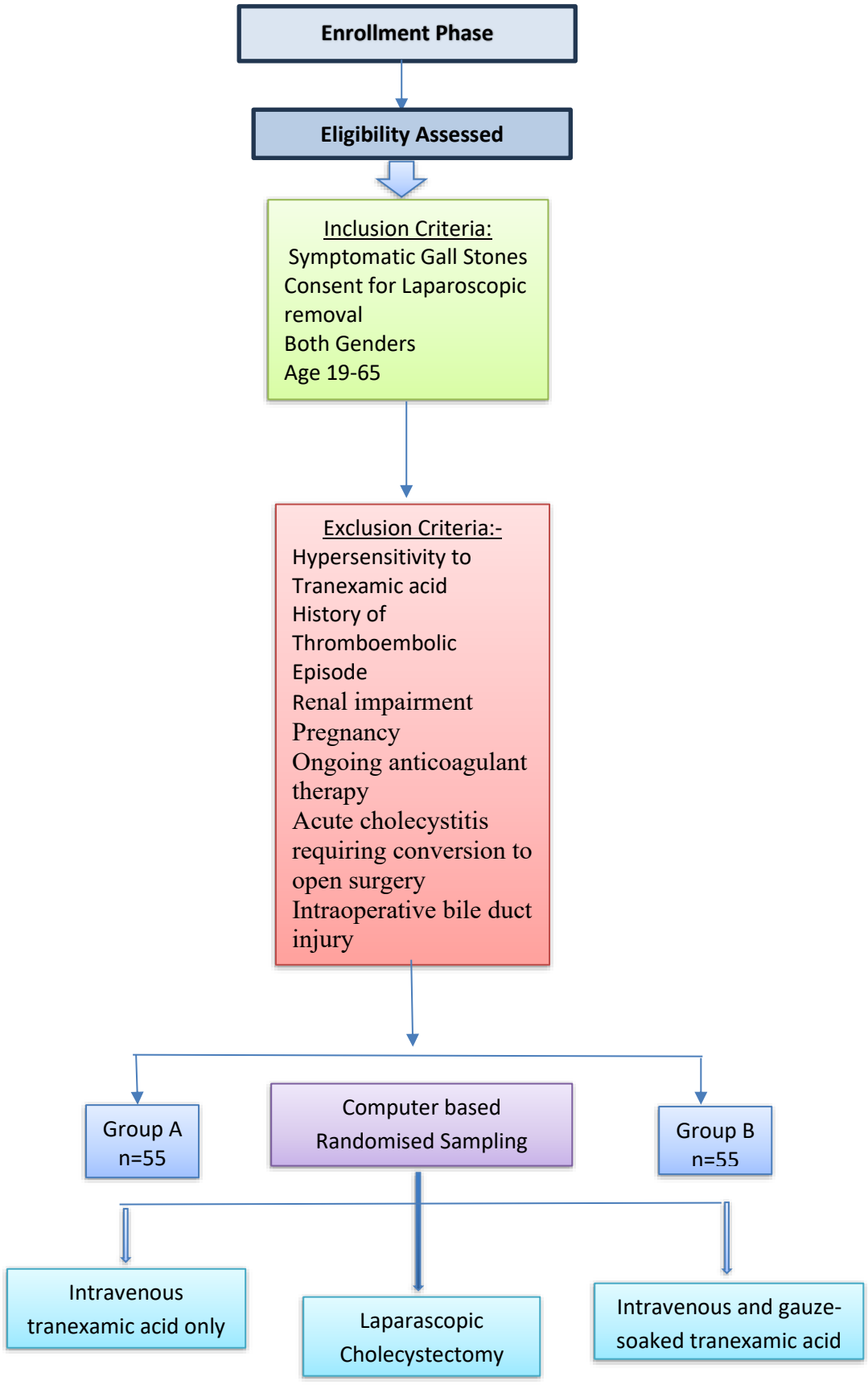

Figure 1: Patient Flow Diagram n=110

Group A received intravenous administration of tranexamic acid alone, whereas Group B, for whom both the intravenous administration of tranexamic acid and transamin-soaked packing in the gallbladder bed was performed. Allocation concealment was ensured by keeping allocation in sealed randomisation envelopes, which were opened at the time of surgery. Both groups underwent standard laparoscopic cholecystectomy under general anesthesia by consultant surgeons with at least 5 years post-specialization experience as the action to avoid operator bias.

For both groups, intravenous administration of tranexamic acid (10 mg/kg, diluted in 100 mL intravenous normal saline) was given slowly (over 10 min) after the induction of anaesthesia. In Group B, an additional 5 mL of solution of tranexamic acid (100 mg/mL) was used to soak a sterile gauze piece, and this was applied directly over the bed of the gallbladder for three minutes (after removal of the gallbladder). The gauze was taken out before the final irrigation and suctioning of the operative field. Hemostasis was then checked to be sure of complete control of bleeding prior to the port sites' closure. Standard surgical procedures were followed between the two groups, and no extra hemostatic agents were added.

The primary outcome measure was intraoperative blood loss, which was measured by calculating the difference between the total volume of blood in the suction bottle (subtracting irrigation fluid) and the weight of pieces of used gauze pieces before and after use. Secondary outcomes of the study were postoperative drain output, duration of surgery, need for blood transfusion, and postoperative complications such as bile leakage, hematoma, or wound infection. Postoperative drain production was measured by using a standard graduated cylinder. All patients were followed regularly till discharge after surgery and seen at the seventh postoperative day for complications and tenth postoperative day for removal of stitches.

Data were collected with the help of a structured proforma and analysed with the help of Spss software version 23. Normality of the data was checked. Age in years and Hospital stay in days were non-normal. Operative time in minutes, intraoperative blood loss in milliliters, and post-operative drain output in milliliters were normal. Quantitative variables, including age, operative time, intraoperative blood loss, and drain output, were expressed as mean plus standard deviation, or median and interquartile range. Categorical variables, including gender, age groups, and presence of complications, were expressed as frequencies and percentages. Independent sample t-test, Mann-Whitney U Test and (Pearson) chi-square test were used to compare continuous and categorical variables, respectively. A p-value of < 0.05 was considered statistically significant.

All surgeries, data recovery, and synonym generator analysis of data followed ethical research attributes with confidentiality of patients and integrity of data preserved. This methodology allowed for a standardised and reproducible comparison of the hemostatic effectiveness of intravenous tranexamic acid alone and combined intravenous plus topical transamin-soaked packing in the gallbladder bed in cholecystectomy.

RESULTS

In Group A (intravenous tranexamic acid only), 28 patients (50.9%) were male and 27 (49.1%) were female, while in Group B (intravenous plus topical tranexamic acid), 32 (58.2%) were male and 23 (41.8%) were female. Regarding age distribution, the majority of patients in both groups belonged to the 31–50 years age range, 36 (65.5%) in Group A and 37 (67.3%) in Group B; followed by 18–30 years (9.1% vs. 12.7%) and 51–65 years (25.5% vs. 20.0%). The mean age of patients in Group A was 43.55 ± 9.70 years, while in Group B it was 42.13 ± 8.23 years, showing no statistically significant difference.

The mean operative time was slightly shorter in the IV + Topical TXA group (58.56 ± 7.07 minutes) compared to the IV TXA only group (62.56 ± 7.95 minutes), and the difference was statistically significant ($p = 0.006$). A highly significant reduction in intraoperative blood loss was observed in the IV + Topical TXA group (34.83 ± 7.7 mL) compared to the IV TXA only group (49.47 ± 11.554 mL, $p < 0.05$).

Similarly, the postoperative drain output volume was significantly lower in Group B (47.98 ± 12.56 mL) compared to Group A (72.69 ± 14.14 mL, $p < 0.05$), indicating improved hemostasis with combined topical and intravenous administration. The mean hospital stay was also shorter among patients in the IV + Topical TXA group (2.47 ± 0.54 days) compared to the IV TXA only group (2.82 ± 0.64 days, $p < 0.05$), suggesting faster recovery and reduced postoperative morbidity. Postoperative complications such as wound infection or hematoma formation were slightly lower in Group B (2 cases, 3.6%) than in Group A (3 cases, 5.5%), though this difference was not statistically significant ($p = 0.647$).

Table-I: Comparison of distribution of different variables between groups

Variables		Groups		p-value
		Group A (IV TXA Only)	Group B (IV + Topical TXA)	
Gender	Male	28(50.9%)	32(58.2%)	0.444
	Female	27(49.1%)	23(41.8%)	
Age (Years)	Mean ± Standard Deviation	43.55 ± 9.70	42.13 ± 8.23	
	Median ± Interquartile Range	44 ±13[a]	44 ± 11[b]	0.487
Age Groups	18 – 30 years	5(9.1%)	7(12.7%)	0.702
	31-50 years	36(65.5%)	37(67.3%)	
	51 – 65 years	14(25.5%)	11(20.0%)	

a: Range is 45 {Minimum:18 to maximum:63}
b: Range is 33 {Minimum:21 to maximum:54}

Table-II: Comparison of outcomes between groups

Outcomes		Groups		p-value
		Group A (IV TXA Only)	Group B (IV + Topical TXA)	
Operation time (minutes)[*1]		62.56±7.95	58.56±7.07	0.006
Intra-operative blood loss (ml)[*1]		49.47±11.55	34.83±7.7	<0.05
Post-operative drain output volume (ml)[*1]		72.69±14.14	47.98±12.56	<0.05
Hospital stay (days)[**1]		2.82±0.641	2.47±0.54	
Hospital stay (days)[*2]		3.00±1[c]	2.00±1[d]	0.006
Post-operative complications	Yes	3(5.5%)	2(3.6%)	0.647
	No	52(94.5%)	53(96.4%)	

*1: Values compared are in Mean ± Standard deviation
**1: Values compared in Mean ± Standard deviation, but p-value not calculated as data was not normal.
*2: Values compared in median ± Interquartile Range
c: Range is 2, minimum is 2, and maximum is 4
d: Range is 2, minimum is 1, and maximum is 3

DISCUSSION

The present study proved that combined use of intravenous and topical tranexamic acid (TXA) was significantly able to improve hemostatic control in cholecystectomy in comparison to intravenous only. The dual approach resulted in lower intraoperative blood loss, lower postoperative drain output and shorter hospital stay, although the complication rates were low and similar between the groups.

These results have shown the additive effect of topical TXA when administered with the systemic administration. Parmeshwar Jha et al. found a significant decline in hematoma formation in patients receiving any form of transamine either intravenous or topical.[10] In our study, the drain output was significantly different between the groups; however, Abrol et al evaluated 100 patients undergoing laparoscopic cholecystectomy and found that combined TXA (IV + topical) led to a drain output of 34.8 ± 25.87 ml when compared with 41.6 ± 19.4 ml in the TXA IV-only group, which in terms of volume is quite a small difference.[11]

Hamedani et al. demonstrated the efficacy of topical TXA in inguinal hernia surgery by having 212.5ml blood loss in TXA group vs 395.ml blood loss in control. Although the hospital stay was almost same in both groups, which contradict our findings, where hospital stay is also significantly shortened by adding topical TXA to intravenous TXA.[12] This variable difference between the hospital stay in both studies might be attributable more to the type of surgery being performed where in one surgery, TXA might not be having significant impact as drain placement might not be needed and near skin wound bed generally have added on benefit of pressure application on the wound secondary to the dressing. Moreover, the stay is usually short in elective hernia procedure in comparison to laparoscopic cholecystectomy.

The hemostatic effect of TXA mainly stems from its capacity to compete with plasminogen activation, thereby enhancing the stability of fibrin clots at the surgical location.[13] The topical application of the drug permits localised high concentration of the drug and minimal systemic absorption, leading to reduced bleeding with minimal risk of thromboembolic complications.[14] In the current study, no major adverse effects were noted, in line with previous reports of safety.[15-16]

Hamedani et al. found that operative time was signficantly reduced by utilisation of TXA. But in our study, it was found that there was no difference in the operative times between groups (p = 0.118) suggesting that the addition of TXA does not interfere with surgical workflow.[12]

In addition, our study is in disagreement with the meta-analysis taken from Xie et al. where TXA administration were compared in intravenous vs combined topical and intravenous forms in spine surgeries. It was found that the perioperative blood loss difference wasn't significant in both groups.[17]

This study was performed at one centre and with a moderate sample size which could be a limitation to generalizability. The analysis was mainly addressed to immediate outcomes after surgery without a long-term follow-up to evaluate delayed complications or thromboembolic events. Inter-surgeon variation, with all the standardization attempts, may also have impacted intraoperative results. Larger multicenter prospective trials are needed to bolster the evidence.

The results provide evidence in favour of the use of combined intravenous and topical tranexamic acid (TXA) therapy as a routine additive in elective cholecystectomy. Wider implementation could help to reduce intraoperative bleeding and recovery time. Further studies are needed that will investigate optimal dose, long duration of safety use, and cost effectiveness. Pharmacokinetic monitoring

would also help to improve the understanding of systemic absorption and safety.

CONCLUSION

Combined intravenous and topical tranexamic acid had a beneficial effect on intraoperative and postoperative hemostasis compared with intravenous administration alone. This approach was effective in controlling the amount of blood lost, the output of the drain, and the hospital stay without increasing complications. The method is simple, safe, and cost-effective for use in the cholecystectomy protocol.

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