Original Article

Role of Tranexamic Acid (Topical and Intravenous) on blood loss in uncomplicated laparoscopic cholecystectomy- Prospective Study

Surbhi Abrol, Inakshi Chrungoo, RK Chrungoo, Nandita Mehta , K.S Mehta, H.S Bali

Abstract:

Backgroud and Purpose: Despite advances in surgical technique, excess bleeding remains a major complication associated with surgery and contributes to poor clinical outcomes. A haemostatic agent with broad applicability and minimal adverse effects such as TXA is attractive as a way to control pathologic haemorrhage.Data for its use in L.C is limited. A study to review the use of TXA in controlling bleeding in uncomplicated L.C, measured in terms of drain output, preoperative and postoperative hemoglobin and hematocrit and hospital stay related to bleeding.

Materials and Method: Patients were randomly divided into 4 groups of 25 patients each by Group A : receiving 10 ml I/v TXA, 30 min prior to surgery and 10ml Topical NS ,Group B : receiving I.v dose of 10ml of NS, 30 min prior to surgery and 10ml TXA topically,Group C: receiving 10 ml i.v TXA, 30 min prior to surgery and 10mlof topical TXA intraoperatively, Group D : receiving 10 ml i.v NS, 30min. prior to surgery and 10ml topical NS intraoperatively.

Results: The drain output and the hospital stay of the patients has significantly reduced. Group C (34.8±25.87) as compared to other TXA groups. Whereas in group- D: drain output was found to be significantly higher (81.08±31.61) and the hospital stay of the patient prolonged for a day as well. Thus use of TXA in uncomplicated L.C is recommended.

Conclusion: We concluded from our study that the groups where TXA was used in either intravenous or topical or in both the forms.

JK-Practitioner2023;28(1-2):42-46

INTRODUCTION

"Blood saving is better than blood transfusion". Despite advances in surgical technique, excess bleeding remains a major complication associated with surgery and contributes to poor clinical outcomes. Surgical variables are prime determinants of the risk of intraoperative and perioperative bleeding[1]

Knowing what to use for what level of bleeding is key to surgical success. [2] Endoscopic surgeons must be trained to recognise, avoid and, if necessary, manage bleeding complications. Over the last decade, novel techniques have been developed to make haemostasis in minimal access surgery as efficient and reliable as in open surgery.[3]

In the beginning of the 1950s it was found that the amino acid lysine inhibits activation of plasminogen, but the effect was too weak to be used in the treatment of fibrinolytic hemorrhagic conditions. Systematic investigations in 1953 by a group in Japan led by Shosuke Okamoto showed that several mercapto and aminocarbonic acids had an antiplasminic effect. The incentive of their industrious work was to reduce the thousands of maternal deaths each year from postpartum haemorrhage. They found that epsilon-aminocaproic acid (Epsilon Amino Caproic Acid), a synthetic derivative of the lysine, had a strong inhibiting effect on plasminogen. [4] but due to its GI side effects and large dose requirement ,search for a more potent antiplasminic substance started. At the research department of the pharmaceutical plant Kabi, Stockholm discovered that only the trans form was antifibrinolytic (trans-4-aminomethyl-cyclohexanecarboxylic acid), and thus trans-AMCHA or tranexamic acid was born. [5,6]

Author Affiliations

Surbhi Abrol, Post graduate ,Department o Surgery, ASCOMS Hospital India, **Inakshi Chrungoo** Registrar , Department of Surgery ,GMC Jammu, **RK Chrungoo**, Professor Emiratus, Depatment of Surgery,ASCOMS Hospital India, **Nandita Mehta,** HOD , Department of Anesthesia, ASCOMS Hospital India, K.S Mehta,HOD, Department of Surgery, ASCOMS Hospital India, **H.S Bali,** Associate professor, Department of Surgery, ASCOMS Hospital India

Correspondence

Dr Surbhi Abrol, Post Graduate, ASCOMS Hospital sidhra Jammu and Kashmir,180019

surbhiabrol@icloud.com

Indexed

EMBASE ,SCOPUS, IndMED ,ESBCO, Google Scholar besides other national and International Databases

Cite This Article as

Abrol Surbhi, Chrungoo I, Chrungoo RK, Mehta Nandita, Bali HS, Role of Tranexamic Acid (Topical and Intravenous) on blood loss in uncomplicated laparoscopic cholecystectomy- Prospective Study. JK Pract2023;28(1-2):42-46

Full length article available at **jkpractitioner.com** one month after publication

Keywords

Blood loss, laparoscopic cholecystectomy, tranexamic acid

TXAis a synthetic derivative of lysine that inhibits fibrinolysis by blocking the lysine binding sites on plasminogen . Onset of action is 5-15 minutes, duration of action is 3 hours, binds 3% primarily to Plasminogen and has a half-life of 2-11 hours. Excretion is via urine (>95% as unchanged drug) [7]

Existing literature has focused most exclusively on the biliary complications of this procedure, but other complications such as significant haemorrhage during laparoscopic cholecystectomy have not been documented. [8]

Since the prevalence of gallstones in adult population is high in Jammu and Kashmir.[9] The study shall be undertaken in the patients undergoing laparoscopic cholecystectomy.

Encouraged by these studies we therefore sought to review the use of Tranexamic Acid (TXA) in controlling bleeding in uncomplicated laparoscopic cholecystectomy.

MATERIAL AND METHODS

- **SOURCE OF DATA**: The study will be conducted on patients admitted in Department of Surgery, ACHARYA SHRI CHANDER COLLEGE OF MEDICAL SCIENCES AND HOSPITAL, SIDHRA JAMMU (ASCOMS) for elective laparoscopic cholecystectomy(L.C).
- **SAMPLE SIZE**: 100 adult patients of either sex in age group of 19 years to 80 years, posted for laparoscopic cholecystectomy.
- **STUDY UNIT**: All patients with USG documented cholelithiasis.
- **STUDY DESIGN**- Hospital based computer generated randomized, double-blind, placebo-controlled trial
- **STUDY PERIOD**: The study was done on patients from 1st November 2019 for a period of one year.
- **STUDY SETTING**-Patients will be randomly divided into four groups of 25 patients each by computer generated randomization.
  1. Group A : receiving 10 ml(1g) intravenous Tranexamic acid, 30 min prior to surgery and 10ml Topical NS
  2. Group B : receiving Intravenous dose of 10ml of NS, 30 min prior to surgery and 10ml (1g) Tranexamic acid topically
  3. Group C: receiving 10 ml (1g) intravenous Tranexamic acid, 30 min prior to surgery and 10ml(1g) of topical Tranexamic acid intraoperatively.
  4. Group D : receiving 10 ml intravenous of Normal saline (NS), 30min. prior to surgery and 10ml topical NS intraoperatively.

After the patient's eligibility had been confirmed and the consent procedures completed, we randomly allocated patients to the intervention or placebo group by assigning them the sequentially numbered envelope. Patients, all members of surgical team, nursing staff and the anaestheist were unaware of allocation. Surgeon and data collectors were blinded . A nurse who was not involved in the study or in the care of patients, opened the sealed envelope in a room away from the operating theatre and prepared the treatment . The bottle with the decided dose of tranexamic acid and syringe were labelled with patient's randomization number. Bottles and syringe containing Tranexamic acid were indistinguishable from those containing placebo (as Tranexamic acid is colorless substance). At the end of each surgery, the envelope was resealed and kept in patient's folder and seal was opened and checked after the patient is discharged.

The results were reported as adjusted odds ratios (AORs) and 95% confidence intervals (CIs). *P* values < .05 were considered to indicate statistically significant results. SPSS software (version 21.0; SPSS) was used for the data analysis.

The data obtained will be statistically analyzed in terms of:

- Drain output on POD1
- Preoperative and Postoperative hemoglobin and hematocrit.
- Hospital stay related to bleeding.

INCLUSION CRITERIA

All patients with USG documented cholelithiasis of either sex in age group of 17 years to 80 years, posted for laparoscopic cholecystectomy.

EXCLUSION CRITERIA

- Patients with acute cholecystitis or acute calcular pancreatitis.
- Patients with bleeding disorders, clotting abnormalities, or those on anticoagulants.
- Patients with Portal hypertension and cirrhosis
- Patients with Renal Impairment.
- Pregnant females.
- Patients with history of Thromboembolism.
- Patients with intra-operative and post-operative bile spillage.
- Patients who had bleeding due to trocar injury to major blood vessels.
- Suspected allergy to Tranexamic acid.
- Any other bleeding mishaps per-operatively, for example-sinus and other bed bleed controlled by various other methods such as spongistorm packing.

DISCUSSION-

Cholecystectomy is the commonest operation of the biliary tract and the second most common operative procedure performed today Karam J, Roslyn JR.(1997).

Laparoscopic cholecystectomy is now considered as the "gold standard" treatment for symptomatic gallstone disease [10]

Although the utility of topical thrombin products is undeniable, questions remain regarding the risks

associated with each formulation[1] Various pharmacological adjuncts have been developed which when applied either systemically or topically , can promote haemostasis. Tranexamic acid is one of them which exerts its antifibrinolytic effect by blocking lysine-binding locus of plasminogen and plasmin molecules, thereby preventing the binding of plasminogen and plasmin to the fibrin substrate.[11]

Hence, our experience regarding the role of tranexamic acid in preventing blood loss in uncomplicated laparoscopic cholecystectomy has been discussed, taking into account the various parameters.

Different dosage regimens exist for adults. Most often an initial IV bolus of 1 g or 10-15 mg/kg body weight with/without repetition after 6 h or continuous infusions over 8 h is administered. Increased rates of thromboembolic events were not noted.[12]

However, the majority of the patients in our study were females that is 61% , which is comparable with the findings of ([13]) on laparoscopic cholecystectomy in 1973, in which the percentage of female patients was 72.6%.

The mean hemoglobin of the patient preoperatively in each group were Group A (12.16±1.60) , Group B (11.85±1.70) ,Group C (11.32±1.43), Group D (12.17±1.84).

The mean post-operative haemoglobin decreased by 1 g/dl in control group. Whereas there were insignificant loss of blood in other 2 groups where tranexamic acid was given topical or intravenous or through both routes.

When pre and post-operative haematocrit were compared in all the four groups , the findings were consistent as with the hemoglobin loss, i.e. in Group A (Tranexamic acid was given intravenous) and Group D (where PLACEBO given I/v and topical) ,a drop of 1% haematocrit were observed.

These observations were consistent with Gohel , et al. (2007) and Pandove, et al.(2017)[8,14] both concluded that patients in the control group bled more as compared to the patients who received tranexamic acid in their papers which studied the efficacy of Tranexamic acid in decreasing blood loss in caesarean section and uncomplicated laparoscopic cholecystectomy. Pandove PK , et al. (2017)[8] concluded that the use of tranexamic acid decreased the intraoperative and postoperative bleeding in laparoscopic cholecystectomy, but it was not statistically significant. This may be due to minimal blood loss in the laparoscopic procedures. There is no active role of tranexamic acid in limiting blood loss in elective laparoscopic cholecystectomy.

In our study the mean change in preop and post op hemoglobin and haematocrit value when compared with Group C and Group D were found significant i.e. the blood loss and drop in haematocrit was statistically significant , a group where both intravenous and topical Tranexamic acid was given and group where intravenous and topical placebo was given. The blood loss was less in group C.

There was no significant alteration in mean pulse of the patients in the groups where Tranexamic acid was given but there were surely significant intraoperative and postoperative heart rate changes in case of placebo group (group D) when compared to other 3 groups in which Tranexamic acid was given either intravenous , topical or both.

A 14 F suction drain was kept in all the patient who underwent laparoscopic cholecystectomy and output was assessed over a period of 24 hours and drain were taken out accordingly. Only 10 patients had their drain removed after 24 hrs. Amongst them only one patient had their drain removed on 3rd POD, rest other 9 patients had their drain removal on 2nd POD.

The drain output was assessed and measured by emptying the contents of the suction drain in the measuring cylinder in 1st 24 hours , the mean output in group A (41.6±19.40), Group B(44.4±22.23), Group C(34.8±25.87), Group D (81.08±31.61. It was also found that out of 10 patients whose drain was removed on 2nd and 3rd POD, 9 patients belonged to group D(control group) indicating increase in hospital stay of the patients who did not receive Tranexamic acid. Which is significant when compared to other 3 groups.

The mean hospital stay of the patients in our study in Group A was 2.12 days, Group B was 2.24 days , Group C - 2.2 days and Group D - 2.76 days. When all the 4 groups were compared, the comparison between group A and D, were found significant i.e the hospital stay increased in patients who belonged to Group-D.

Similar findings were found in study conducted by Pandove, et al. (2017)[8]) where the mean days of hospitalisation for Tranexamic acid group were 2.4 days which was less as compared to placebo group i.e. 2.63 days.

In another the study conducted by Choi, et al. (2009)[15] (on the effect of Tranexamic acid on blood loss during orthognathic surgery (bimaxillary osteotomy) the hospitalisation days between Tranexamic acid group and placebo had no significant difference.

CONCLUSION

1. The dose of Tranexamic acid used in our study both intravenous and topically was 1gram and none of the cases were given any dose postoperatively.
2. When preoperative and post-operative hemoglobin of the patients were compared in all the 4 groups , it was found that there was no statistically significant dip in hemoglobin when the placebo group was compared to Tranexamic acid group.
3. Likewise , there was no statistically significant drop in post -operative hematocrit when compared to preoperative hematocrit when all the groups were compared and assessed.

4. Mean Drain output when measured over 24 hours in each group came out to be significantly increased in group D patients where intravenous and topical normal saline was given .
5. Group A in which intravenous Tranexamic acid was given showed lesser mean drain output i.e., 41.6 ml when compared to group B- where only topical Tranexamic acid was given i.e., 44.4 ml.
6. Group C in which both I/V and topical Tranexamic acid was given, mean drain output was 34.8 lowest when compared to all the other 3 groups.
7. The mean hospital stays of patients in Group A – 2.12 days , Group-B -2.24 days , Group C-2.2days , and Group D- 2.76 days.
8. In 90% patients drain was removed on 1st post-operative day belonging from all the 4 groups.
9. It was also found that out of 10 patients (10%) whose drain was removed on 2nd and 3rd POD, 9 (9%) patients belonged to group D(control group) indicating increase in hospital stay of the patients who did not receive Tranexamic acid.
10. When all the 4 groups were compared, the comparison between group A and D, Group B and D and group C and D were found significant. The hospital stay was prolonged by a day in patients who were given placebo.

We conclude from our study that the groups where tranexamic acid was used in either intravenous or topical or in both the forms. The drain output and the hospital stay of the patients has significantly reduced. Amongst the three groups where Tranexamic acid was given : Group C i.e where Tranexamic acid was given both intravenously and topically the drain output was lesser than other two Tranexamic acid groups. Whereas in the placebo group : intravenous normal saline and topical normal saline was given the drain output was found to be significantly higher and the hospital stay of the patient prolonged for a day as well.

Though, similar previous study did not report significant effect of Tranexamic acid on drain output in laparoscopic cholecystectomy. But various urological , neurosurgical and trauma trials reported the use of Tranexamic acid helpful in bleeding control.

Being an economical and widely used drug with low side effect profile. We do reccomend use of Tranexamic acid both intravenous and topically in uncomplicated laparoscopic cholecystectomy.

REFERENCES

1. Boucher, B.A. and Traub, O. (2009), Achieving Hemostasis in the Surgical Field. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 29: 2S-7S. https://doi.org/10.1592/phco.29.pt2.2S
2. Sileshi B, Achneck HE & Lawson JH. Management of Surgical Hemostasis: Topical Agents. Vascular. 2008 Mar-Apr;16 Suppl 1:S22-8
3. Harrell G, Kercher K, Heniford B: Energy sources in laparoscopy. Semin LaparoscSurg 2004; 11: 201-209
4. Tengborn L, Blombäck M, Berntorp E. Tranexamic acid--an old drug still going strong and making a revival. *Thromb Res*. 2015;135(2):231-242. doi:10.1016/j.thromres.2014.11.012
5. Okamoto S, Sato S, Takada Y, Okamoto U. An active stereo isomer (trans-form) of AMCHA and its fibrinolytic (antiplasminic) action *in vitro* and *in vivo*. Keio J Med 1964; 13: 177–85
6. Melander B, Gliniecki G, Granstrand B, Hanshoff G. Biochemistry and toxicology of amikapron; the antifibrinolytically active isomer of AMCHA. (A comparative study with epsilon-aminocaproic acid). Acta Pharmacol Toxicol (Copenh) 1965;22(4):340–352.[PubMed] [Google Scholar]
7. Rappold JF & Pusateri AE. Tranexamic Acid in Control Resuscitation. Transfusion(2013), 53: 96S-99S.
8. Pandove PK, Singla RL, Mittal P, Mahajan N, Kumar A. Role of Tranexamic Acid on Blood Loss in Laparoscopic Cholecystectomy. Niger J Surg. 2017 Jul-Dec;23(2):111-114. doi: 10.4103/njs.NJS_53_16. PMID: 29089735; PMCID: PMC5649425
9. Khuroo MS, Mahajan R, Zargar SA, Javid G, Sapru S. Prevalence of biliary tract disease in India: a sonographic study in adult population in Kashmir. Gut. 1989 Feb;30(2):201-5. doi: 10.1136/gut.30.2.201. PMID: 2649414; PMCID: PMC1378302.
10. Hardy JF, Desroches J. Natural and synthetic antifibrinolytics in cardiac surgery. Can J Anaesth. 1992 Apr;39(4):353-65. doi: 10.1007/BF03009046. PMID: 1373346.
11. Eriksson O, Kjellman H, Pilbrant Å , Margareta Schannong Pharmacokinetics of Tranexamic Acid after Intravenous Administration to Normal Volunteers Eur J Clin Pharmacol (1974); 7: 375
12. Waskowski J, Schefold JC, Stueber F. Prophylaktische Anwendung von Tranexamsäure in der nichtkardialen Chirurgie : Update 2017 [Prophylactic use of tranexamic acid in noncardiac surgery : Update 2017]. *Med Klin Intensivmed Notfmed*. 2019;114(7):642-649. doi:10.1007/s00063-018-0402-5
13. Kambouris AA, Carpenter WS, Allaben RD. Cholecystectomy without drainage. Surg Gynecol Obstet 1973;137:613-7.
14. Gohel Mayur, Patel Purvi, Gupta Ashoo, Desai Pankaj, Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: A randomized case controlled prospective study, J Obstet Gynecol India Vol. 57, No. 3 : May/June 2007 ; 227-230
15. Choi WS, Irwin MG, Samman N. The effect of tranexamic acid on blood loss during

orthognathic surgery: a randomized controlled trial. J Oral Maxillofac Surg. 2009 Jan;67(1):125-33. doi: 10.1016/j.joms.2008.08.015. PMID: 19070758.