Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2904-2910 | ISSN:2251-6727

Efficacy Of Tranexamic Acid on Recent Internal Haemorrhoid Bleeding as Singe Agent and in Combination with Calcium Dobesilate

Dr P B Thrishuli[1], Dr Munnangi Jagadish Reddy[2*], Dr Pankaja SS[3]

[1]Professor, Department of General Surgery, JSS Academy of Higher Education and Research, Mysuru, Karnataka, India

[2]Postgraduate, Department of General Surgery, JSS Academy of Higher Education and Research, Mysuru, Karnataka, India (Corresponding author)

[3]Associate Professor, Department of General Surgery, JSS Academy of Higher Education and Research, Mysuru, Karnataka, India

(Received: 16 June 2025 Revised: 20 July 2025 Accepted: 19 August 2025)

KEYWORDS

Tranexamic acid, Calcium dobesilate, Haemorrhoidal bleeding, Conservative management, Randomized controlled trial, Rectal bleeding cessation

ABSTRACT:

Background: Haemorrhoidal disease is a common anorectal condition characterized by bleeding, pain, and discomfort, particularly in early stages. Conservative pharmacological treatments aim to reduce symptoms and avoid invasive interventions in patients with Grade 1 and 2 haemorrhoids.

Objective: To determine the efficacy of tranexamic acid as a single agent and in combination with calcium dobesilate in reducing bleeding among patients with recent haemorrhoidal bleeding.

Methods: This randomized controlled trial was conducted at JSS Medical College, Mysuru, involving 60 patients with Grade 1 or 2 haemorrhoids and recent bleeding. Participants were allocated into two groups receiving either tranexamic acid alone or in combination with calcium dobesilate and were assessed for bleeding cessation on day 3 and day 5.

Results: In this study involving 60 patients with recent haemorrhoidal bleeding, both groups – those receiving tranexamic acid (TXA) alone and those receiving TXA with calcium dobesilate (CaD) – were comparable in baseline characteristics including age (mean: 39.6 vs. 38.7 years; $p = 0.648$), gender distribution ($p = 0.301$), symptom profile, anthropometric parameters (BMI: 26.1 vs. 25.7 kg/m²; $p = 0.653$), and haemorrhoid grade and position ($p > 0.05$). The mean duration from symptom onset to treatment was similar between the groups (9.9 vs. 10.8 days; $p = 0.251$). All participants presented with bleeding per rectum. By day 3 of treatment, 60.0% of the TXA group still had bleeding, compared to only 20.0% in the TXA + CaD group ($p = 0.002$). By day 5, bleeding persisted in 33.3% of the TXA group and only 6.7% of the TXA + CaD group ($p = 0.010$).

Conclusion: The combination of tranexamic acid and calcium dobesilate was significantly more effective than tranexamic acid alone in achieving early cessation of bleeding in recent haemorrhoidal cases. This supports the use of combination therapy as a superior conservative management strategy for early-grade haemorrhoids.

Introduction

Haemorrhoidal disease is one of the most common anorectal conditions, affecting approximately 4.4% of the global population, with prevalence rates higher in individuals aged 45–65 years.(1) It occurs due to abnormal enlargement and displacement of vascular cushions in the anal canal, leading to symptoms such as bleeding, pain, and prolapse.(2) Haemorrhoidal bleeding, characterized by bright red blood during or after defecation, is a hallmark symptom and a significant source of morbidity among patients.(3) Effective management of bleeding and associated pain remains a cornerstone in the treatment of haemorrhoids, particularly in cases where conservative therapy is the primary intervention.(4, 5)

Tranexamic acid, a synthetic antifibrinolytic agent, has gained attention for its role in controlling bleeding in various clinical settings, including trauma, surgery, and obstetrics.(6) Its mechanism of action involves inhibiting plasminogen activation, thereby reducing fibrinolysis

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2904-2910 | ISSN:2251-6727

and stabilizing blood clots at the site of injury.(7) The application of tranexamic acid in managing haemorrhoidal bleeding is emerging, with studies suggesting its potential to reduce bleeding episodes effectively.(8) However, the evidence base remains limited, necessitating further research to validate its efficacy in this context. Calcium dobesilate, another therapeutic agent of interest, is a vasoactive drug with anti-inflammatory, antioxidant, and capillary-protective properties.(9, 10) It has been widely used in managing vascular conditions such as chronic venous insufficiency and diabetic retinopathy. Calcium dobesilate's ability to reduce capillary permeability and improve microcirculation makes it a plausible candidate for adjunctive therapy in haemorrhoidal disease.(11, 12)

Combining tranexamic acid with calcium dobesilate may offer synergistic benefits in controlling haemorrhoidal bleeding and alleviating associated pain. While tranexamic acid directly addresses bleeding through antifibrinolytic mechanisms, calcium dobesilate targets the underlying vascular pathology, potentially enhancing treatment outcomes. Against this background, the objective of the present study was to determine the efficacy of tranexamic acid as a single agent and in combination with calcium dobesilate in reducing bleeding among patients with recent haemorrhoidal bleeding.

Materials and Methods

This was a single centre, hospital based comparative experimental study – randomised controlled design – conducted in the outpatient department and/or inpatient wards of the Department of General Surgery, JSS Medical College, Mysuru, India for a duration of 18 months (between June 2023 and December 2024). The study was approved by the Institutional Human Ethics Committee (IHEC) with reference number JSS/MC/PG/2046/123/2023-24 dated 23/06/2023. The participants (and their attenders) were given the Participant Information Sheet (PIS) in their native language, and its contents were verbally explained to ensure their understanding and satisfaction. Enrolment into the study proceeded upon receipt of written informed consent. Patients between 25 and 50 years of age, of both gender, with grade 1 or grade 2 haemorrhoids with recent bleed were included. However, patients with deep vein thrombosis, ischemic heart disease, chronic liver disease, lower gastrointestinal bleeding other than haemorrhoids, history of cerebrovascular attack; taking oral contraceptive pills; pregnant and lactating mothers were excluded.

An a priori sample-size calculation for two independent groups (difference in means) used α=0.05 ($Z\alpha$=1.96), 80% power ($Z\beta$=0.84), SD=5.76, and a clinically important difference of 3. The estimated minimum required sample size was rounded off to 30 per group. We used nonprobability sampling – convenience/purposive sampling technique – complete enumeration of patients in accordance with prespecified inclusion and exclusion criteria. The patients were divided into two groups – Group TXA, received tranexamic acid 500 mg orally three times a day; Group TXA + CaD, received tranexamic acid 500 mg orally three times a day along with calcium dobesilate 500 mg orally twice a day. All participants were assessed for cessation of rectal bleeding on day 3 and day 5 of treatment.

Statistical analysis: The data obtained was manually entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) v23. All the categorical variables were summarised using frequencies and percentages. Continuous variables were summarized using mean (standard deviation). To test for statistical significance, Chi square test (for categorical variables) and independent 't' test (for continuous variables) was used. Statistical significance was considered at p value less than 0.05.

Results

A total of 92 patients were assessed for eligibility, of whom 32 were excluded – 26 did not meet the inclusion criteria and 6 declined to participate. Sixty eligible participants were randomly assigned to two equal groups: Group TXA (n = 30) received tranexamic acid 500 mg orally thrice daily, and Group TXA + CaD (n = 30) received the same dose of tranexamic acid along with calcium dobesilate 500 mg orally twice daily. All participants in both groups received their allocated interventions, and there were no losses to follow-up. Analysis was completed for all 60 participants, with 30 in each group, ensuring full data inclusion in the final statistical evaluation.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2904-2910 | ISSN:2251-6727

Baseline characteristics were well balanced between groups, with no statistically significant differences (all p>0.05). Mean age was similar (TXA 39.6±7.2 vs TXA+CaD 38.7±7.9 years), as were male proportions (46.7% vs 60.0%) and BMI (26.1±3.9 vs 25.7±3.4 kg/m²). Bleeding per rectum was universal in both arms (100%), anal irritation was comparable (46.7% vs 40.0%), grade 2 haemorrhoids predominated (66.7% vs 53.3%), the left lateral position was equally frequent (36.7% each), and the time from symptom onset to drug intake was similar (9.9±3.3 vs 10.8±3.2 days).

At the time of presentation, all participants in both the TXA and TXA + CaD groups reported bleeding per rectum (100% in each group; p = 1.000). By day 3 of treatment, bleeding persisted in 60.0% (n = 18) of the TXA group compared to only 20.0% (n = 6) in the TXA + CaD group, and this difference was statistically significant (p = 0.002). By day 5, bleeding continued in 33.3% (n = 10) of the TXA group, whereas it was observed in just 6.7% (n = 2) of the TXA + CaD group, also showing a significant difference (p = 0.010). These results indicate that the combination of tranexamic acid and calcium dobesilate was more effective in achieving early cessation of bleeding compared to tranexamic acid alone.

Discussion

The baseline characteristics of the study population revealed no statistically significant differences between the TXA and TXA + CaD groups, indicating a well-balanced randomization process and ensuring internal validity for subsequent comparative analyses. The mean age was similar across both groups, with the TXA group averaging 39.6 years and the TXA + CaD group averaging 38.7 years. The age stratification further confirmed comparability, as the proportion of participants aged below and above 40 years did not significantly differ. These findings align with existing literature suggesting that the prevalence of symptomatic haemorrhoids, particularly in grades 1 and 2, is commonly observed among middle-aged adults, as noted by Al-Masoudi et al. in 2024.(13) Similarly, the gender distribution did not differ significantly between the two groups, with a slight predominance of females in the TXA group and males in the TXA + CaD group. Although previous studies have indicated a slightly higher prevalence of haemorrhoids in males,(1, 14) gender was not expected to significantly influence the response to pharmacological treatment in this context.

In terms of clinical presentation, all patients in both groups reported bleeding per rectum, confirming recent haemorrhoidal bleeding as a consistent inclusion criterion. Secondary symptoms such as anal irritation were reported in comparable proportions in both groups, with no statistically significant difference. These findings reflect typical symptomatology of early-grade internal haemorrhoids, as described in previous clinical reviews including Chand et al. (2008) and Margetis (2019).(15, 16) Anthropometric parameters, including height, weight, and BMI, were also comparable between the two groups. This uniformity in baseline physical characteristics reduces the risk of confounding and enhances the credibility of treatment effect comparisons. BMI values in both groups fell within the overweight range, consistent with studies linking increased intra-abdominal pressure and obesity to the development and persistence of haemorrhoidal symptoms.(17, 18)

Regarding disease classification, the distribution of haemorrhoid grades (Grade 1 and 2) and their anatomical positions (left lateral, right posterior, and right anterior) did not significantly differ between the groups. This homogeneity supports unbiased comparison of outcomes between groups, as the severity and anatomical presentation can influence treatment response.(19) The mean duration between symptom onset and treatment initiation was marginally higher in the TXA + CaD group (10.8 days) compared to the TXA group (9.9 days), but this difference was not statistically significant. Delay in presentation and initiation of treatment is a common issue in proctologic disorders and may affect symptom severity at baseline; however, the similarity here reinforces the comparability of groups.(20, 21)

The results of the present study demonstrate a statistically significant benefit of combining tranexamic acid with calcium dobesilate in achieving earlier cessation of haemorrhoidal bleeding compared to tranexamic acid alone. At baseline, all participants in both groups presented with active bleeding per rectum, ensuring uniformity in initial clinical presentation. However, marked differences emerged in bleeding status at subsequent follow-ups. By the third day of treatment,

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2904-2910 | ISSN:2251-6727

a substantial reduction in bleeding was observed in the TXA + CaD group, where only 20.0% (n = 6) continued to experience bleeding, compared to 60.0% (n = 18) in the TXA group. This difference was statistically significant, indicating that the addition of calcium dobesilate potentiated the hemostatic effect of tranexamic acid. By the fifth day, bleeding persisted in only 6.7% (n = 2) of the TXA + CaD group, while 33.3% (n = 10) in the TXA group still had bleeding, further reinforcing the superior efficacy of the combination regimen. Tranexamic acid, an antifibrinolytic agent, promotes haemostasis by inhibiting the activation of plasminogen to plasmin, thereby stabilizing fibrin clots and preventing ongoing bleeding.(6) While effective in controlling capillary bleeding, its action is largely confined to modulating fibrinolysis. Calcium dobesilate, in contrast, is a vasoprotective agent that improves capillary resistance, reduces capillary permeability, and possesses anti-inflammatory properties.(22-24) It has been widely used in conditions characterized by microvascular fragility, including chronic venous insufficiency and diabetic retinopathy. Its mechanism of action complements tranexamic acid by improving vascular integrity and reducing local inflammation, thus providing a synergistic effect when used concurrently. The significantly improved outcomes in the TXA + CaD group suggest a dual mechanism of benefit—while tranexamic acid halts fibrinolysis and stabilizes existing clots, calcium dobesilate may prevent further vascular insult and facilitate mucosal healing. These findings are supported by earlier reports demonstrating the clinical benefit of calcium dobesilate in reducing rectal bleeding in haemorrhoidal disease.(25) Furthermore, a randomized trial by Misra & Parshad (2000) also highlighted that combination therapy involving calcium dobesilate resulted in faster symptom resolution compared to monotherapy in patients with Grade 1 and 2 haemorrhoids.(12)

Briefly, the combination of tranexamic acid and calcium dobesilate led to a significantly earlier cessation of bleeding among patients with recent haemorrhoidal bleeding. The findings emphasize the clinical utility of combining agents with complementary mechanisms of action for enhanced therapeutic outcomes in the conservative management of haemorrhoids.

The present study has certain limitations that should be acknowledged. Firstly, the study was conducted at a single center, potentially introducing location-specific biases and limiting external validity. The use of a convenience sampling method may have introduced selection bias, as participants who presented during the study period and met the inclusion criteria were enrolled without random sampling from the wider patient population. Additionally, the short duration of follow-up, restricted to five days, may not fully capture long-term recurrence or delayed complications associated with haemorrhoidal disease. Subjective outcomes such as symptom relief were not quantified using validated scales beyond bleeding cessation, which may underestimate other relevant clinical improvements. Finally, the absence of blinding in the administration of interventions could introduce performance and detection biases, potentially influencing both patient-reported outcomes and assessor evaluations.

Conclusion

The present study demonstrated that the combination therapy of tranexamic acid and calcium dobesilate was significantly more effective than tranexamic acid alone in achieving early cessation of bleeding in patients with recent haemorrhoidal bleeding. Both treatment groups were comparable in terms of baseline demographic, clinical, and anthropometric characteristics, ensuring a valid comparison. The addition of calcium dobesilate enhanced the therapeutic effect, likely due to its vasoprotective and anti-inflammatory properties. These findings suggest that the combined use of tranexamic acid and calcium dobesilate offers a superior conservative treatment approach for managing early-grade haemorrhoidal bleeding.

References

1. Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. Gastroenterology. 1990;98(2):380-6.
2. Riss S, Weiser FA, Riss T, Schwameis K, Mittlböck M, Stift A. Haemorrhoids and quality of life. Colorectal Dis. 2011;13(4):e48-52.
3. Alonso-Coello P, Zhou Q, Martinez-Zapata MJ, Mills E, Heels-Ansdell D, Johanson JF, et al. Meta-analysis

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2904-2910 | ISSN:2251-6727

of flavonoids for the treatment of haemorrhoids. Br J Surg. 2006;93(8):909-20.

4. Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. World J Gastroenterol. 2012;18(17):2009-17.
5. Villalba H, Abbas MA. Hemorrhoids: modern remedies for an ancient disease. Perm J. 2007;11(2):74-6.
6. Ker K, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. Bmj. 2012;344:e3054.
7. McCormack PL. Tranexamic acid: a review of its use in the treatment of hyperfibrinolysis. Drugs. 2012;72(5):585-617.
8. Hunt BJ. The current place of tranexamic acid in the management of bleeding. Anaesthesia. 2015;70 Suppl 1:50-3, e18.
9. Rabe E, Jaeger KA, Bulitta M, Pannier F. Calcium dobesilate in patients suffering from chronic venous insufficiency: a double-blind, placebo-controlled, clinical trial. Phlebology. 2011;26(4):162-8.
10. Casley-Smith JR. A double-blind trial of calcium dobesilate in chronic venous insufficiency. Angiology. 1988;39(10):853-7.
11. Misra MC, Imlitemsu. Drug treatment of haemorrhoids. Drugs. 2005;65(11):1481-91.
12. Misra MC, Parshad R. Randomized clinical trial of micronized flavonoids in the early control of bleeding from acute internal haemorrhoids. Br J Surg. 2000;87(7):868-72.
13. Al-Masoudi RO, Shosho R, Alquhra D, Alzahrani M, Hemdi M, Alshareef L. Prevalence of Hemorrhoids and the Associated Risk Factors Among the General Adult Population in Makkah, Saudi Arabia. Cureus. 2024;16(1):e51612.
14. Kibret AA, Oumer M, Moges AM. Prevalence and associated factors of hemorrhoids among adult patients visiting the surgical outpatient department in the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. PLoS One. 2021;16(4):e0249736.
15. Chand M, Nash GF, Dabbas N. The management of haemorrhoids. Br J Hosp Med (Lond). 2008;69(1):35-40.
16. Margetis N. Pathophysiology of internal hemorrhoids. Ann Gastroenterol. 2019;32(3):264-72.
17. De Marco S, Tiso D. Lifestyle and Risk Factors in Hemorrhoidal Disease. Front Surg. 2021;8:729166.
18. Peery AF, Sandler RS, Galanko JA, Bresalier RS, Figueiredo JC, Ahnen DJ, et al. Risk Factors for Hemorrhoids on Screening Colonoscopy. PLoS One. 2015;10(9):e0139100.
19. Shanmugam V, Thaha MA, Rabindranath KS, Campbell KL, Steele RJ, Loudon MA. Rubber band ligation versus excisional haemorrhoidectomy for haemorrhoids. Cochrane Database Syst Rev. 2005;2005(3):Cd005034.
20. Sun Z, Migaly J. Review of Hemorrhoid Disease: Presentation and Management. Clin Colon Rectal Surg. 2016;29(1):22-9.
21. Riss S, Weiser FA, Schwameis K, Riss T, Mittlböck M, Steiner G, et al. The prevalence of hemorrhoids in adults. Int J Colorectal Dis. 2012;27(2):215-20.
22. Adank C, Koerner F. Calcium dobesilate in diabetic retinopathy. A retrospective controlled study. Ophthalmologica. 1985;190(2):102-11.
23. Menteş BB, Görgül A, Tatlicioğlu E, Ayoğlu F, Unal S. Efficacy of calcium dobesilate in treating acute attacks of hemorrhoidal disease. Dis Colon Rectum. 2001;44(10):1489-95.
24. Changazi SH, Bhatti S, Choudary A, Sr., Rajput MNA, Iqbal Z, Ahmed QA. Calcium Dobesilate Versus Flavonoids for the Treatment of Early Hemorrhoidal Disease: A Randomized Controlled Trial. Cureus. 2020;12(8):e9845.
25. Patel HD, Bhedi AN, Chauhan AP. CALCIUM DOBESILATE IN SYMPTOMATIC TREATMENT OF HEMORRHOIDAL DISEASE: AN INTERVENTIONAL STUDY. National Journal of Medical Research. 2013;3(01):42-4.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2904-2910 | ISSN:2251-6727

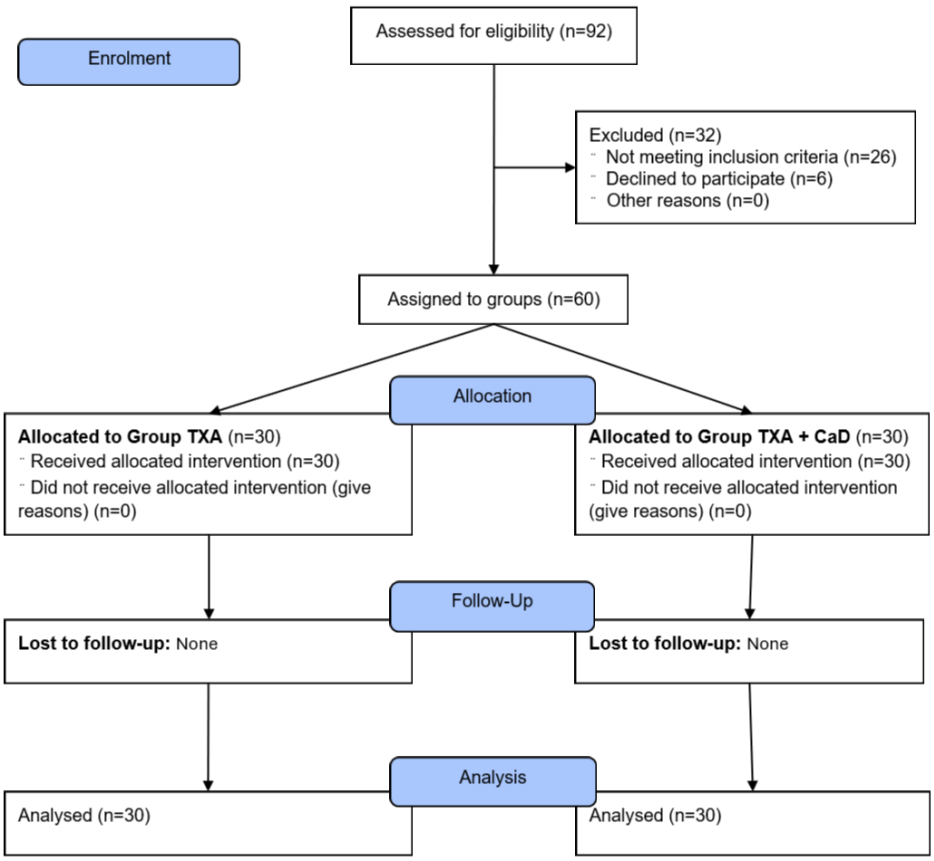

Figure 1: CONSORT flowchart

Table 1: Baseline Demographic and Clinical Characteristics by Treatment Arm (TXA vs TXA + CaD; N=60)

		TXA N = 30	**TXA + CaD N = 30**	**P value**
		n (%)	**n (%)**	
Age (in years), Mean (SD)		39.6 (7.2)	38.7 (7.9)	0.648
Age (in years)	≤40	13 (43.3)	14 (46.7)	0.795
	>40	17 (56.7)	16 (53.3)	
Gender	Male	14 (46.7)	18 (60.0)	0.301
	Female	16 (53.3)	12 (40.0)	
Presenting symptoms *(numbers are not mutually exclusive)*	Bleeding per rectum	30 (100)	30 (100)	0.793
	Anal irritation	14 (46.7)	12 (40.0)	
Height (in cm), Mean (SD)		159.2 (7.2)	159.5 (6.4)	0.725
Weight (in kg), Mean (SD)		65.7 (6.9)	65.0 (7.0)	0.850
Body mass index (in kg/m2), Mean (SD)		26.1 (3.9)	25.7 (3.4)	0.653
Grade	1	10 (33.3)	14 (46.7)	0.292
	2	20 (66.7)	16 (53.3)	
Position	Left lateral	11 (36.7)	11 (36.7)	0.798

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2904-2910 | ISSN:2251-6727

	Right posterior	6 (20.0)	8 (26.7)	
	Right anterior	13 (43.3)	11 (36.7)	
Time between symptom onset and drug intake (in days), Mean (SD)		9.9 (3.3)	10.8 (3.2)	0.251
*Statistically significant at p<0.05 SD, Standard deviation				

Table 2: Comparison of study groups, by bleeding

		TXA N = 30	**TXA + CaD N = 30**	**P value**
		n (%)	**n (%)**	
Bleeding	At the time of presentation	30 (100)	30 (100)	1.000
	At 3 days	18 (60.0)	6 (20.0)	0.002*
	At 5 days	10 (33.3)	2 (6.7)	0.010*
*Statistically significant at p<0.05 SD, Standard deviation				

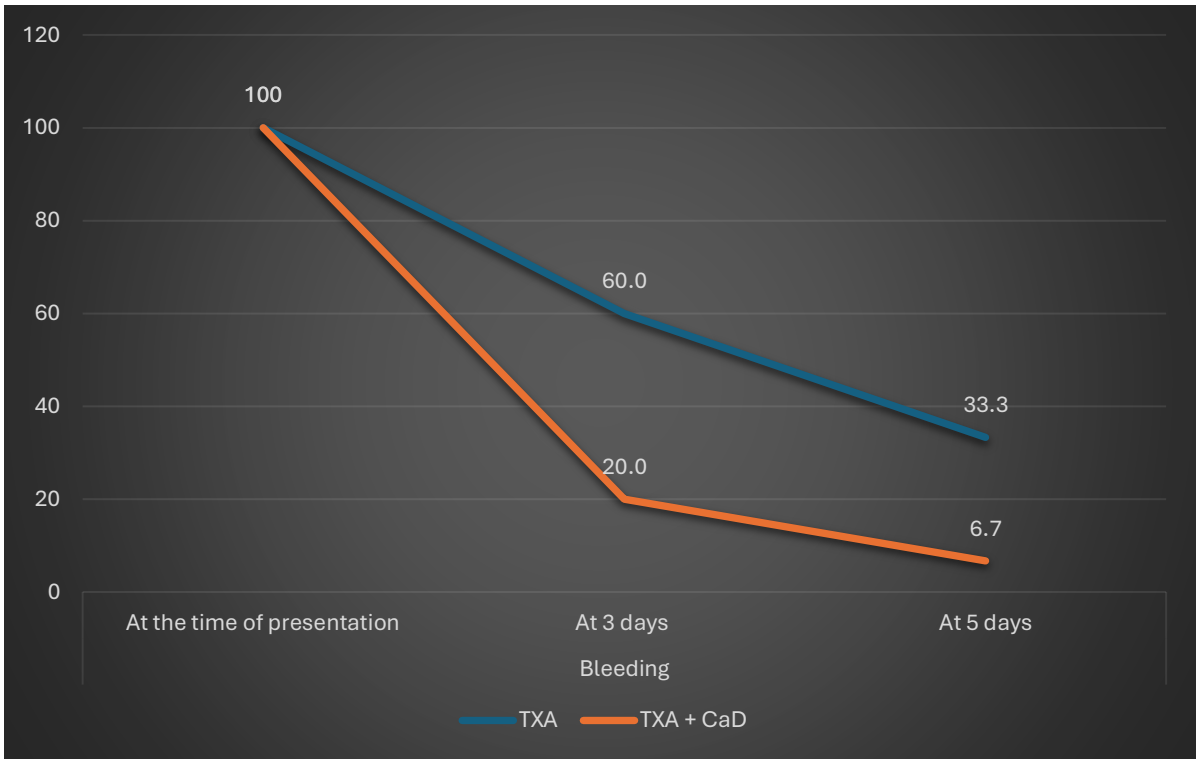

Figure 2: Comparison of study groups, by bleeding