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# COMPARISON BETWEEN INTRAVENOUS BOLUS DOSE VERSUS INFUSION OF TRANEXAMIC ACID TO REDUCE BLOOD LOSS IN PATIENTS UNDERGOING GYNECOLOGICAL SURGERIES: A RANDOMIZED CONTROLLED STUDY

KABERI BEHERA A[1], RUBA VIKNESH C[2], DR. E. THULASIRAM[3]
[1]POSTGRADUATE
DEPARTMENT OF ANAESTHESIA,SAVEETHA MEDICAL COLLEGE AND HOSPITAL
SAVEETHA NAGAR,THANDALAM, CHENNAI BANGALORE, NH 48, CHENNAI
TAMILNADU: 602105
CORRESPONDING AUTHOR NAME
[2]DESIGNATION- SENIOR RESIDENT, DEPARTMENT OF ANAESTHESIA ,
SAVEETHA MEDICAL COLLEGE AND HOSPITAL ,SAVEETHA NAGAR,THANDALAM, CHENNAI BANGALORE, NH 48, CHENNAI
TAMILNADU: 602105
[3]SENIOR LECTURER, DEPARTMENT OF ORTHODONTICS & DENTOFACIAL ORTHOPEDICS, SREE BALAJI DENTAL COLLEGE & HOSPITAL, CHENNAI, INDIA

**ABSTRACT**

**Background:** Excessive perioperative blood loss in gynaecological surgeries remains an important concern, which often requires blood transfusions that entail risks of infection, immune reactions and higher medical care costs. It has been shown that tranexamic acid (Txa), an antifibrinolytic agent, significantly reduces blood loss and transfusion requirements in various surgical environments. However, the most effective dosing strategy, whether an intravenous bolus dose (IV) or a continuous infusion, is not well established in gynaecological surgeries.

**Methods:** A unique blind controlled trial was performed in 60 female Patients (ASA I-II), from 18 to 60 years, are subject to optional gynecological surgery in neural anaesthesia. Patients were randomly assigned to get a unique dose of Bolus IV TXA (10 mg/kg) 10 minutes before incision (TXB group) or continuous TXA infusion (1 mg/kg/h) started 10 minutes before incision and stayed and stayed for up to 4 hours after surgery (Grupo TXI). The primary result was the loss of intraoperative blood assessed by standardized blood measurement of soaked mushrooms. Secondary results included the need for blood transfusion, postoperative haemoglobin (HB) and haematocrit and the occurrence of thromboembolic events.

**Results:** Patients In the TXI group, showed significantly less estimated blood loss compared to the TXB group ($p < 0.05$). Fewer patients in the TXI group required blood transfusions during and after surgery. The HB postoperative levels were higher in the TXI group and no significant differences were observed in thromboembolic complications between groups.

**Conclusion:** The continuous infusion of Txa seems to be more effective than a single bolus dose to reduce the requirements of perioperative blood loss and transfusion in gynaecological surgeries. These findings support the use of a prolonged antifibrinolytic effect for optimal bleeding control without additional risk of thromboembolic events.

**Keywords:** tranexamic acid, blood loss, continuous infusion, intravenous bolus, gynaecological, antifibrinolytic surgeries

## INTRODUCTION

Haemorrhage during the duration of extensive gynaecological procedures poses significant clinical and economic issues, thus raising the risk of perioperative complications and possible death. Excessive bleeding is likely to necessitate blood transfusions, whose complications vary from immunological reactions to infection and transmission of disease via blood. Thus, there is a strong need to determine effective ways of minimizing intraoperative and postoperative bleeding. Among these is the application of antifibrinolytic drugs, one of which is tranexamic acid (TXA).

TXA is a synthetic analogue of lysine that competes with plasminogen to functionally impair fibrinolysis and thereby augment clot stabilization. Its efficacy to reduce blood loss has been well studied in trauma settings and orthopaedic surgeries like joint replacement procedures. Additionally, large trials and the CRASH-2 trial have demonstrated that TXA can reduce mortality from haemorrhage when administered early and maintained for an adequate duration. However, the optimal administration timing for gynaecological surgery remains debated with variation in surgery techniques, patients, and perioperative care.

In the context of gynaecologic procedures, the extent of hemodynamic variation and tissue manipulation is most important, particularly when the operation is uterine and pelvic organ-related. Many studies suggest the use of tranexamic acid (TXA) to minimize haemorrhage in myomectomies and cesarean sections, but few studies have directly compared the relative efficiency of a single intravenous (IV) bolus dose versus continuous infusion in a well-defined elective gynaecologic surgical cohort. A single bolus dose is convenient to administer and will achieve a rapid increase in plasma TXA concentration, potentially allowing for an immediate haemostatic effect. Alternatively, a continuous infusion could provide a more sustained antifibrinolytic effect, potentially useful in the context of a long operation or in those at high risk of postoperative bleeding.

Against this background, we conducted a randomized single-blinded controlled trial in patients who were undergoing below-umbilical gynaecological surgeries under neuraxial anesthesia. Our main objective was to quantify the efficacy of a single bolus dose of tranexamic acid (TXA) 10 mg/kg intravenously compared to continuous intravenous infusion of TXA 1 mg/kg/h in preventing intraoperative and early postoperative blood loss. Secondary objectives included the quantification of transfusion requirement, haemoglobin and haematocrit postoperatively, and the development of thromboembolic events. By measuring these outcomes, we aspired to establish evidence-based recommendations for the optimization of TXA administration regimens in gynaecological surgery and consequently enhance patient safety and the conservation of healthcare resources.

## MATERIALS AND METHODS

### DESIGN AND STUDY ENVIRONMENT

This randomized, without blind and controlled study. It was performed in the anaesthesia department at Saveetha Medical College and Hospital. The approval of the Institutional Ethical Committee was obtained before the start of the study, and the written consent of all participants was acquired. The trial adhered to the principles of Helsinki's statement and relevant consort guidelines.

**Inclusion and exclusion criteria**

Inclusion criteria

- Physical state I and II
- Female patients from 18 to 60 years
- Elective underground gynaecological surgery (for example, hysterectomy, ovarian cystectomy))
- Neuraxial anaesthesia

**Exclusion criteria**

- Physical state III and IV
- Known tranexamic acid hypersensitivity

• History of thromboembolic events (for example, CVA, CAD)

• Obesity (suggestive body mass index of morbid obesity)

**Sample and randomization**

A total of 60 participants were registered, with 30 patients in each group, determined by an a priori power calculation based on the expected differences in the loss of perioperative blood. Patients were randomly assigned through a random list generated by computer in two groups:

1. Group TXB : patient received a single dose of bolus IV of Txa (10 mg/kg).

2. Group TXI: patient received a continuous infusion of Txa (1 mg/kg/h) for up to 4 hours after the operation.

The concealment of the allocation remained using sealed opaque envelopes.

**Anesthetic protocol**

Pre -Anaesthetic evaluations were performed the day before surgery. Standard monitoring (ECG, pulse oximetry, non -invasive blood pressure) was applied when reaching the operating room. Under aseptic precautions, neuraxial anesthesia (combined spinal or epidural spinal) was administered, which guarantees that the average blood pressure remained within 20% of the baseline. Intravenous access was established with Ringer's lactate solution (100 ml/h).

**Intervention**

• Group TXB : A single IV bolus of tranexamic acid (10 mg/kg), diluted at 100 ml of normal saline solution, administered 10 minutes before the skin incision.

• Group TXI: A TXA IV load dose (1 mg/kg/h infusion), started 10 minutes before the incision and continued up to 4 hours after the operation.

**Result measures**

• Primary result: Intraoperative blood loss, measured by standardized gauze weighing. A completely soaked sponge was considered equivalent to 50 ml of blood loss.

• Secondary results:

- incidence of intra blood transfusion and after the operation.

- Haemoglobin and haematocrit levels at 6 am after surgery.

- Postoperative complications, including clinical evidence of thromboembolism (deep venous thrombosis, pulmonary embolism).

The loss of blood greater than 10% of the total blood volume was handled with crystalloid or colloid solutions. Hemodynamic instability or blood loss> 20% of the total blood volume caused transfusion of red blood cells packaged at the discretion of anaesthesiologist.

**Statistical analysis**

The data were analysed using the SPSS software (version 23.0, IBM, USA). Descriptive statistics (mean ± frequencies) were used to characterize the demography of the patient and operational variables. Independent T test was applied to compare blood loss between TXB and TXI groups. A value $p < 0.05$ was considered statistically significant.

## RESULTS

### Patient Flow and Baseline Characteristics

A total of 70 patients were screened, of whom 10 were excluded due to not meeting inclusion criteria or declining participation. The remaining 60 were randomized equally into TXB and TXI groups (Figure 1). Baseline demographic and clinical characteristics were comparable between the two groups, with no significant differences in age, BMI, ASA status, or duration of surgery.

**Table 1. Baseline Characteristics of Study Participants**

| Characteristic | TXB Group (n=30) | TXI Group (n=30) | p-value |
|---|---|---|---|
| Age (years), Mean ± SD | 45.3 ± 8.2 | 44.6 ± 7.9 | 0.72 |
| BMI (kg/m²), Mean ± SD | 26.1 ± 3.4 | 25.9 ± 3.7 | 0.84 |
| ASA I/II (n) | 22 / 8 | 20 / 10 | 0.57 |
| Duration of Surgery (min) | 100.2 ± 20.4 | 102.5 ± 19.8 | 0.69 |

### Intraoperative Blood Loss

On average, patients receiving the continuous infusion of TXA (TXI group) demonstrated lower intraoperative blood loss compared to those in the bolus-only group (TXB). Mean blood loss was 300.5 ± 62.3 mL in TXB versus 220.1 ± 50.2 mL in TXI ($p < 0.05$). This difference was consistent across various types of gynecological procedures, as shown in Table 2.

**Table 2. Intraoperative Blood Loss (mL) by Surgical Procedure**

| Procedure Type | TXB Group | TXI Group | p-value |
|---|---|---|---|
| Total Abdominal Hysterectomy | 325.0 ± 48.5 | 245.2 ± 42.7 | <0.05 |
| Ovarian Cystectomy | 270.4 ± 55.6 | 190.6 ± 48.3 | <0.05 |
| Myomectomy | 310.8 ± 58.7 | 230.9 ± 49.1 | <0.05 |
| **Overall** | **300.5 ± 62.3** | **220.1 ± 50.2** | **<0.05** |

### Blood Transfusion Requirements

Fewer patients in the TXI group required blood transfusions (4 patients) compared to the TXB group (8 patients), although this difference did not reach statistical significance ($p = 0.08$). When transfusions were administered, the total volume of packed red blood cells was lower in the TXI group (mean of 1.4 units per transfused patient) compared to the TXB group (mean of 2.1 units per transfused patient).

### Hemoglobin and Hematocrit Values

At 6 hours post-surgery, mean hemoglobin levels in the TXI group were significantly higher (11.8 ± 1.3 g/dL) compared to the TXB group (10.9 ± 1.4 g/dL, $p < 0.05$). Correspondingly, hematocrit levels were also higher in the TXI group (35.6% ± 3.1) than in the TXB group (33.2% ± 3.5, $p < 0.05$) (Figure 2).

**Figure 1**: **CONSORT Flow Diagram of the study**

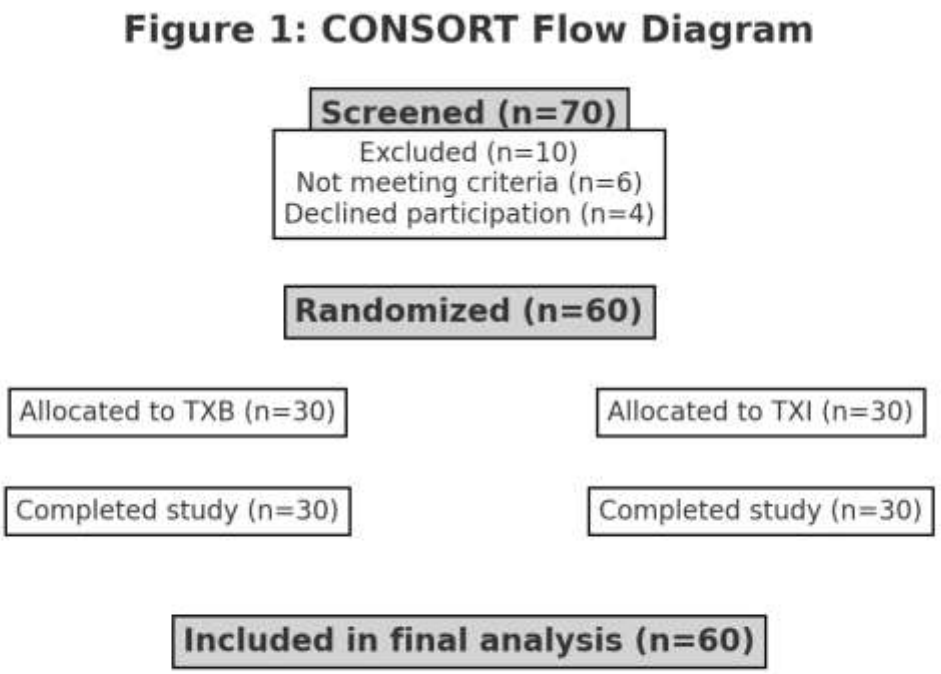


Figure 1 presents the CONSORT flow diagram, detailing patient enrollment, allocation, and follow-up. Seventy patients were initially assessed for eligibility, with ten excluded due to not meeting inclusion criteria or declining to participate. Of the remaining sixty, thirty were randomized into the bolus-only TXB group, and thirty into the continuous-infusion TXI group. All participants completed the study and were analyzed, with none lost to follow-up or withdrawn during the trial.

**Figure 2**: **Postoperative Hemoglobin and Hematocrit Comparison between Groups**

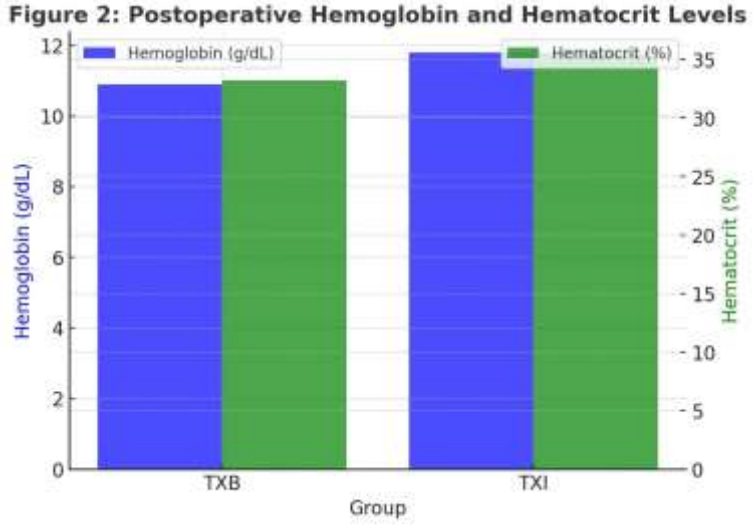

Figure 2 highlights comparative postoperative hemoglobin and hematocrit values for both groups at six hours post-surgery. The TXI group showed statistically higher mean hemoglobin (11.8 ± 1.3 g/dL) than the TXB group (10.9 ± 1.4 g/dL). Hematocrit levels followed a similar pattern, averaging 35.6% for TXI versus 33.2% for TXB. These findings suggest that continuous tranexamic acid infusion better preserves red blood cell indices and may reduce perioperative blood loss.

### Thromboembolic and Other Complications

No clinically detectable cases of deep vein thrombosis, pulmonary embolism, or other serious adverse events were observed in either group during the hospital stay or at the 2-week follow-up. Mild postoperative nausea and headache were reported in both groups, with no intergroup differences.

## DISCUSSION

Minimization of intraoperative blood loss is essential to the minimization of risks of transfusion and optimization of outcomes in gynecologic surgery. Results of this study indicate that continuous tranexamic acid infusion produces significant intraoperative blood loss reduction relative to that following a single bolus dose, which is in keeping with previous experiences in orthopedic and trauma settings. Reduced estimated blood loss in the tranexamic acid group can be attributed to the sustained antifibrinolytic plasma concentrations, which have the effect of neutralizing the progressive enhancement in fibrinolytic activity that can persist through surgical operations and extend into the initial postoperative period.

By comparison, the bolus-only method, while initially achieving high plasma concentrations of TXA, may be less successful in suppressing fibrinolysis throughout the length of the operation, particularly with longer than two-hour cases. This pharmacokinetic profile disparity is most applicable in gynecologic procedures, where extensive tissue planes can be incised and pelvic vasculature can be extensive, thereby increasing the potential for persistent blood loss long after the immediate intraoperative interval.

The results of our study show a trend towards fewer transfusion needs in the TXI group, although this difference was not statistically significant. This impact may be attributed in part to the relatively small sample size or heterogeneity in the nature and degree of surgical procedures performed. The TXI group's fewer units of blood products used do, however, suggest the potential clinical and resource benefits of ongoing TXA use.

Of special mention, no undue increase in thromboembolic events was noted, adding to the credibility of the safety profile of TXA at recommended doses. As with earlier large-scale trials, low thrombosis rates have been reported with TXA, and thus fears for hypercoagulability may be exaggerated, considering that patients can be adequately selected. In fact, all participants in the study underwent screening for thromboembolic risk factors, and exclusion criteria were strict to ensure patient safety.

Some limitations exist. First, the limited number of patients within our analysis may limit generalizability of our findings to large populations. Second, we did not assess other dosing regimens (e.g., increased infusion rate or longer duration) that may augment the efficacy of TXA. Third, measurement bias may exist by utilizing sponge weight and visual estimates for reporting blood loss. Fourth, heterogeneity of surgical technique, in spite of standardized technique, may have influenced the results.

In general, the current study contributes to the increasing evidence that continuous infusion of TXA is superior to single bolus in reducing perioperative blood loss in gynecologic surgery without escalating the risk of thromboembolic events. In the future, it would be necessary to have multicenter trials with increased sample sizes to establish these findings and individualize dosing regimens.

## CONCLUSION

In the current randomized single-blinded controlled trial, continuous infusion of tranexamic acid (1 mg/kg/h) was more effective in decreasing intraoperative blood loss and sustaining higher postoperative hemoglobin levels than a single intravenous bolus dose (10 mg/kg). No rise in thromboembolic or other serious complications was noted, highlighting the safety of both regimens. These findings emphasize the usefulness of extended antifibrinolytic therapy for gynecologic procedures and validate the introduction of a continuous infusion regimen to clinical practice. More extensive studies are advised in order to confirm these results and further clarify optimum dosing intervals for various groups of surgical patients.

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