Faculty of Medicine, Cairo University Postgraduate Research Protocol Template

(Please read carefully provided guidance documents for a comprehensive understanding and proper formulation of your thesis protocol and required forms)

1. Study

a- Proposed Study Title: The use of Tranexamic acid in preventing intraoperative and postoperative hemorrhage in bariatric surgery
b- Degree:M.Sc
c- Date of Registration of MSc or MD: January 2024

2.Candidate

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4. Scientific committee approval

(Was it scientifically approved by the department?) Yes

Date of approval:

5. Background and Rationale: (Describe the research question and justification for undertaking the study explaining the aspects of novelty in the study)

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. A body mass index (BMI) over 25 is considered overweight, and over 30 is obese.[1]
The definition of overweight and obesity is abnormal or excessive fat buildup that poses a health risk. Over 25 is classified as overweight, and over 30 as obese based on body mass index (BMI). The worldwide burden of illness report from 2017 shows that the problem has reached epidemic proportions, with over 4 million deaths annually attributable to being overweight or obese.[2]
Bariatric surgery is the most effective treatment of morbidly obese patients to allow substantial, sustained weight loss and to improve or resolve obesity-associated comorbidities, thereby reducing mortality. According to US practice guidelines, patients qualify for bariatric surgery with a body mass index of 35 kg/m(2) and associated comorbidities, or a body mass index of 40 kg/m(2), after failure of conservative weight loss measures. Currently, the established procedures in the United States are the laparoscopic Roux-en-Y gastric bypass, adjustable gastric banding, sleeve gastrectomy, and biliopancreatic diversion with duodenal switch[2.]. Although bariatric surgeries are generally safe and effective, they can have deadly side effects that need to be promptly handled.Leaks, stenosis, bleeding, and venous thromboembolic events (VTE) are examples of early complications.Postoperative bleeding that requires intervention occurs in up to 11% of cases in both the RYGB and SG[3]. Fortunately, 85% of patients are likely to stop without surgical intervention[4].
Individuals with metabolic syndrome X are more likely to experience bleeding. Establishing an appropriate venous access, performing crystalloid resuscitation, blood product transfusions, serial hematocrits, hemodynamic monitoring, correcting any coagulopathies, and ceasing to administer VTE chemoprophylaxis are all examples of usual supportive care that should be started right away.
In the early postoperative phase, a skilled endoscopist can safely assess an anastomosis and administer therapeutic endoluminal treatments, such as clips or epinephrine injections, as first-line therapy[5]. Emergency surgical management is required if non-operative management fails due to hemodynamic instability. After an SG, bleeding typically occurs at the staple line, however splenic damage is also a possibility. The anastomoses are likely the sites of bleeding after RYGB, however intra-abdominal hemorrhage from the spleen, mesentery, and omentum may also occur. The surgeon must check for bleeding sites inside the gastric remnant, the biliopancreatic limb, and the Roux limb if there isn't an obvious site detected.[6]. Bleeding in bariatric surgery can also occur as a late complication.Bleeding Mild to moderate bleeding from marginal ulcers occurs in 5% of patients; massive hemorrhage is substantially less common[7].Like any patient with upper gastrointestinal bleeding, the patient may present with hematemesis, melena or hematochezia, and syncope or near-syncope. The primary goals of initial care should be intravenous proton pump inhibitors, reversal of antiplatelet or anticoagulant medication, and resuscitation with crystalloid or blood products, if necessary. Upper endoscopy is typically used for therapy and diagnosis. The GJA site is frequently the site of bleeding, most of which may be managed with routine endoscopic procedures. In one trial, just 4% of individuals with bleeding marginal ulcers needed surgery.[8]Tranexamic acid (TXA) stops fibrin's enzymatic breakdown, which lowers blood loss. In order to reduce bleeding and the need for blood transfusions, it is frequently used during surgery. A multicenter, randomised, placebo-controlled experiment (CRASH-2 trial) published its findings in 2011 and demonstrated that TXA (1 g loading dosage over 10 min, followed by an 8-hour infusion of 1 g) safely lowers mortality in patients with bleeding trauma. Regardless of baseline risk, starting TXA treatment within three hours of damage reduces the risk of bleeding fatality by approximately one-third.Restricting its application to individuals with serious injuries or a diagnosis of "hyperfibrinolysis" would lead to thousands of preventable deaths. Tranexamic acid (TXA) stops fibrin's enzymatic breakdown, which lowers blood loss. In order to reduce bleeding and the need for blood transfusions, it is frequently used during

surgery. A multicenter, randomised, placebo-controlled experiment (CRASH-2 trial) published its findings in 2011 and demonstrated that TXA (1 g loading dosage over 10 min, followed by an 8-hour infusion of 1 g) safely lowers mortality in patients with bleeding trauma. Regardless of baseline risk, starting TXA therapy within three hours of damage lowers the chance of bleeding fatality by almost one-third.[9] Extensive randomized studies in postpartum hemorrhage (20 060 patients) and trauma (20 211 patients) demonstrate that tranexamic acid dramatically lowers bleeding fatalities without raising the risk of thrombosis.[10] . It was first introduced to clinical practice for the management of patients with bleeding disorders, especially adapted to reduce bleeding in hemophiliacs undergoing oral surgical intervention[11]. Over the past ten years, tranexamic acid (TXA) has garnered increasing attention due to its potential to optimize post-operative bleeding; yet, its exact role in bariatric surgery remains unclear[12]. .Our study aims at evaluating the role of tranexamic acid in bariatric surgery since, The effect of conservative therapy using tranexamic acid for postoperative hemorrhage after bariatric surgery is still very much a novel technique[13]. However,Intravenous tranexamic acid at the time of laparoscopic sleeve gastrectomy is associated with a significant reduction of post-operative bleeding with no observed differences in thromboembolic events or mortality[14].

6. Objectives:(describe specific objectives or hypotheses behind the study)

Evaluate the role of tranexamic acid in preventing and decreasing intra-operative and post-operative in bariatric surgery.

7. Study Design:

A- Nature of the study

- Prospective study ■
- Retrospective study □

B- Design of the study: (Please insert √ in front of the suitable design)

1-	Case series	

2-	Qualitative	
3-	Survey	
4-	Cross sectional analytic	
5-	Case-control	
6-	Cohort (Longitudinal)	
7-	Randomized Clinical Trial	
8-	Non-randomized clinical trial	
9-	Animal study	
10-	Cellular study	

- **Other study design:** ☐

  Please describe:

8. Study Methods

- **Population of study:** (Please provide all details regarding participants including gender, age range and disease conditions. Indicate if this protocol involves children, prisoners, pregnant women or cognitively impaired or mentally disabled subjects. Also indicate if participants will be dived into groups and mention the characteristics of and number of participants in each group adequately)

  - Patients undergoing bariatric surgery at kasralainy school of medicine between January 2024 and August 2024

- **Study location:** (Please provide where the study will be conducted and from where study participants will be recruited)

  - Kasralainy hospital, Cairo university

- **Inclusion criteria:**
  - Age 18-60 years at time of surgery.
  - Body mass index (BMI) of more than 35 kg/m2 or more than 30 kg/m2 with a major co-morbidity associated with obesity.

- **Exclusion criteria:**
  - Previous history of DVT
  - Have experienced a tranexamic acid adverse reaction
  - Bleeding tendency
  - Administration of anti-coagulants or anti-platelets
  - Coagulopathy disease
  - Uncontrolled hypertensive

- **Methodology in details:**(the description should be chronological starting with randomization method in detail if RCT, group allocation and characteristics of each group. Also indicate what would be done to participants initially and at follow-up visits including the follow-up duration, if applicable)

Patients will randomly allocated (1:1) in two groups, group A and group B, oneweek before surgery by the coordinating researcher viacomputer-generated variable block randomization softwareby Ciwit BV (Castor EDC©). The patient, surgical team, andanesthesia team were blinded for treatment allocation. Thecoordinating researcher and hospital pharmacologist wereunblinded to properly prepare the infusion bags for eachindividual patient. Both were not involved in the surgicalprocedure nor in the follow-up. Patients in each group will have proper history taking, routine pre-operative assessment. The intervention group (B) will receive a single dose of 1500-mgTXA (Cyklokapron©) during the induction of the procedure.TXA will be administered intravenously, dissolved in 100-ml sodium chloride (NaCl) 0.9% in a time frame of 15–30 min,with a maximum of 100 mg/min. The control group (A) will receive a placebo during the induction of the procedure. The placebo Infusion contains 100-ml NaCl 0.9%, which will be administeredsimilarly. Both groups will be operated on within the same range of blood pressure. Assessment of intra-operative bleeding will be through the number of clips used on the stapleline. To determine postoperative hemoglobin levels, a bloodsample (one EDTA tube) will be obtained at day one postoperatively by venipuncture and analyzed in the hospital's clinical chemistry laboratoryaccording to standard procedures. Patients will be discharged at day3 post-op, on anti-coagulant 40mg/24H for two weeks. Follow up will be done after 30 days. Duple will be done to assess the incidence of DVT.

- **Intervention:**

☐ Diagnostic intervention (please describe):

☐ Therapeutic intervention (please describe):

☐ No intervention

- **Does the research involve?**

☐ Human participants

☐ Biological samples/Tissues

☐ Identifiable private data/Information

- **Type of consent of study participants:**

  ☐ Written consen

  ☐ No consent needed (Please justify)

- **Potential risks:**
  (Please mention all risks involved even mild ones as pain, discomfort, chance of infection or psychological effects)

  1-
  2-
  3-

- **Confidentiality of data:** (Please explain how privacy and confidentiality of data and records will be maintained)

9- Study outcomes:

- **Primary outcomes** (Most important measurable outcomes)

  1- Number of cases of bleeding in each group either intra-operative or post-operative

  2- definition of bleeding: hemoglobin drop >1

- **Secondary outcome parameters** (other outcomes to be assessed)

  1- Incidence of venous thrombosis

  2- Duration of surgery

  3- Length of hospital stay

  4- Need of reoperation

10- Sample sizeand technique(number of study subjects included and justification including the clinical and statistical assumptions supporting sample size calculation)

11- Statistical analysis (Please describe your data analysis plan)

12- Source of funding:(Please include source of funding even if self funding)

- Faculty of Medicine, Cairo Univer ☐
- Other sources ☐

Please specify:

13- Time plan:

When to start (**the start date should be after getting REC approval**)?

- When expected to finish?
- When to publish?

14- References:

1- WHO
2- Kissler HJ, Settmacher U. Bariatric surgery to treat obesity. Semin Nephrol. 2013 Jan;33(1):75-89. doi: 10.1016/j.semnephrol.2012.12.004. PMID: 23374896.
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11- Dunn CJ, Goa KL. Tranexamic acid. Drugs 57 (6):1005–1032, 1999.View Full Text | PubMed | CrossRef | Google Schola
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14- Klaassen RA, Selles CA, van den Berg JW, Poelman MM, van der Harst E. Tranexamic acid therapy for postoperative bleeding after bariatric surgery. BMC Obes. 2018 Dec 3;5:36. doi: 10.1186/s40608-018-0213-5. PMID: 30524741; PMCID: PMC627626

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