

Prophylactic Use Of Tranexamic Acid To Reduce Blood Loss In Hysterectomy For Benign Causes (Randomised Controlled Trial)

Thesis

Submitted for partial fulfillment of master degree

In Obstetrics and Gynecology

BY

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LIST OF ABBREVIATIONS

ABL	Actual blood loss
BV	Blood volume
DBP	Diastolic blood pressure
DVT	Deep venous thrombosis
EACA	E-aminocaproic acid
EBL	Estimated blood loss
ETS	Ethicon Endopath
GnRH	Gonadotrophin releasing hormone
HB	Hemoglobin
HCT	Hematocrit
HMWK	High-molecular-weight kininogen
NICE	National Institute for Health and Clinical Excellence
PIVKAs	proteins formed in vitamin K absence
SBP	Systolic blood pressure
SNOSE	Sequentially numbered, opaque, sealed envelopes
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
UAE	Uterine artery embolization
VKORC	Vitamin K epoxide reductase

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Protocol of thesis

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Introduction

Hysterectomy is one of the most frequently performed major gynecological surgical procedures. It is usually performed for the management of a number of benign disorders of the female pelvis when less radical interventions are unsuccessful, not tolerated, or unacceptable to the patient or felt by the physician to be inappropriate for the treatment of the patient's clinical condition. These benign disorders include ; leiomyomas, abnormal uterine bleeding, endometriosis ,pelvic relaxation and chronic pelvic pain (*Nieboer et al., 2009*).

Even when the indication for the procedure is benign, relatively high complication rates have been reported. Perioperative bleeding seems to represent the most common cause of complications (*Märta et al., 2016*).

One of the most common treatments of massive bleeding is blood transfusion, but there are many complications and risks associated with this practice (*Morrison et al.,2012*). With advancements in surgical techniques, autologous blood donations, cell salvage, and antifibrinolytic drugs, healthcare providers have been able

to decrease the number of blood transfusions and thus the associated complications . Decreasing perioperative bleeding through the prophylactic use of antifibrinolytic agents, such as aprotinin, tranexamic acid (TXA), and E-aminocaproic acid (EACA), has become increasingly popular (**Henry et al., 2011**).

Tranexamic acid is an antifibrinolytic agent that has shown to effectively reduce bleeding complications within other surgical and medical areas. It inhibits fibrin degradation, thereby promoting the blood's ability to form stable blood clots. In several countries, the drug is used as prophylactic treatment prior to major surgery (**Moake , 2014**).

In the haemostatic process, coagulation occurs rapidly at the site of a damaged vessel building a tight net of fibrin, while at the same time, the fibrinolytic system removes the fibrin deposits that could cause permanent vascular occlusion once vascular repair has taken place. The coagulation and fibrinolytic system are believed to be in a state of dynamic balance which maintains an intact vascular system (**Guyton and Hall , 2011**).

Tranexamic acid is a potent antifibrinolytic agent that exerts its effect by blocking lysine binding sites on plasminogen molecules and has the potential to enhance the effectiveness of the patient's own haemostatic mechanisms. Consequently, clot breakdown (fibrinolysis) is inhibited and excessive or recurrent bleeding is reduced **(Roberts et al.,2016)**.

Side effects and adverse reactions of TXA are rare and appear limited; mild side effects include nausea, vomiting and diarrhea. Absolute contraindications include active intravascular clotting disorders and use of TXA in conjunction with other procoagulant drugs could also increase the likelihood of thrombotic complications **(Hunt ,2015)**.

TXA is being used in wide range of surgical procedures including cardiac, orthopedic, neurosurgery and trauma surgery which are significant in decreasing blood loss and transfusion requirements. While in obstetric and gynaecology the use of TXA has been studied for populations undergoing elective cesarean delivery or vaginal delivery. The studies demonstrated decreased mean estimated blood loss in the TXA group compared with the placebo group **(Carless , 2014)**.

Currently, TXA is being used in a wide range of surgical procedures without increased risk of thrombosis or other adverse effects. The results of several large clinical trials and many small trials support its use to decrease bleeding and reduce mortality and have a proven safe pharmaceutical profile. It is yet to be determined if the increased use of antifibrinolytic agents actually reduces the rate of blood transfusions, but TXA has been shown to reduce the degree of blood loss perioperatively (**Ducloy et al.,2011**). This inexpensive and safe drug is increasingly being used since aprotinin went off the market and because it is more potent than EACA (**Jessica et al., 2016**).

Overall, These findings lead to the conclusion that TA should be considered as prophylactic treatment prior to elective benign hysterectomy in order to reduce the risk of substantial bleeding and reoperations (**Shakur et al., 2010**).

Research hypothesis

Aim of study

This study aims to assess the efficacy of tranexamic acid as antihemorrhagic agent in decreasing intraoperative bleeding in women undergoing hysterectomy for benign causes.

Research hypothesis

In women undergoing hysterectomy for benign causes, tranexamic acid may decrease blood loss intraoperative.

Research question

In women undergoing hysterectomy for benign causes., does the prophylactic tranexamic acid decrease intraoperative bleeding?

Operationalizing the research question

1-Participants

- Women admitted at Ain Shams University Maternity Hospital for hysterectomy for benign causes.
- Recruitment starts after approval of the research.

Inclusion criteria :

- All women undergoing hysterectomy for benign causes including; leiomyomas, abnormal uterine bleeding, endometriosis, pelvic relaxation and chronic pelvic pain will be potentially eligible to participate in the study.
- Women's age between 40:55 years (premenopause).

Exclusion criteria:

- Malignant condition for hysterectomy.
- Contraindication to tranexamic acid.
 - Thrombophilia.
 - Previous or active thromboembolic disease.
 - Family history thromboembolism.
 - Allergy to Tranexamic acid.
 - Renal impairment.
 - Ongoing hematuria.
 - History of Subarachnoid hemorrhage.
 - Antithrombotic treatment.

2-Intervention

1-The approval of the local ethics committee of our hospitals and oral consents of the women will be required.

2-Complete detailed history will be taken from all women who will participate in the study.

3-Examination :

a-General examination including vital data (eg. Blood pressure, pulse and temperature).

b-Abdominal examination including assessment of uterine size and mobility.

4-Investigations :

a- preoperative lab including complete blood count , random blood sugar and coagulation profile.

b-Ultrasound will be done to assess uterine size and pathology.

5-Preanesthetic medications will be prepared including prophylactic antibiotic and study solutions (Tranexamic acid, placebo).

6-A prepared 10 ml syringe containing either 10 ml tranexamic acid (100mg/ml) or 10ml ringer lactate will be handed according to the randomization list.

7-The patients will be randomly assigned to either one of two groups (80 per each group).

(1)Group T:drug group.