بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

Potential Benefit of Combined Topical and Intravenous Administration of Tranexamic Acid in Congenital Heart Surgery

Thesis

Submitted for partial fulfillment of the Master Degree
in Anesthesiology, Intensive Care and Pain Management

By

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Abdelrahman Mohamed Tharwat Abdelaziz Ismail

Potential Benefit of Combined Topical and Intravenous Administration of Tranexamic Acid in Congenital Heart Surgery

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ABSTRACT

Objective: Pediatric patients who undergo repair of congenital heart diseases on cardiopulmonary bypass are at great risk of postoperative bleeding. The major causes of bleeding are thrombocytopenia, platelets dysfunction, hemodilution and increased fibrinolysis during cardiopulmonary bypass (CPB). Non-surgical postoperative bleeding occurs due to micro-vascular bleeding from pericardial and mediastinal tissues when blood comes in contact with non-endothelial surfaces of the Cardio-Pulmonary Bypass (CPB) machine, compounded by liberal use of heparin and a complex interaction of humoral and cellular pathways. **Aim of the Work:** The aim of the study is to asses if there is potential benefit of intrapericardial topical application of tranexamic acid when it is combined with the intravenous administration in reduction of postoperative bleeding after pediatric cardiac surgery on cardiopulmonary bypass (CPB). **Patients and Methods: Type of the study**: Interventional, randomized and double blinded clinical trial. **Study Setting**: The operating theaters of Ain Shams University Hospitals. **Study period**: Over one year (from March 2020 to March 2021). **Standard management**: Intravenous Tranexamic acid (TxA) injection. **Results:** The estimated blood loss postoperatively in first 24hrs. Were less in the combined group than the IV group. Requirements of blood transfusion also were statically significant in combined group than IV group from aspects of volume of PRBCs transfusion, Total number of patients exposed to transfusion and transfusion rate. There is no difference regarding ICU stay and need of surgical re exploration. **Conclusion**: The combined use of low dose IV and topical intrapericardial tranexamic acid in children with congenital heart disease undergoing on pump cardiac surgery reduced the risk of post-operative bleeding and need for blood products transfusion when compared to the administration of IV tranexamic acid only suggesting a potential benefit of topical tranexamic acid in hemostasis.

Keywords: Adenosine Diphosphate, Tranexamic acid

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List of Abbreviations

ACT	:	Activated clotting time
ADP	:	Adenosine Diphosphate
aPTT	:	Activated partial thromboplastin time
CPB	:	Cardiopulmonary by pass
DIC	:	Disseminated Intravascular Coagulopathy
E-ACA	:	E-Aminocaproic acid
PARs	:	Protease activated receptors
PT	:	Prothrombin time
RCT	:	Randomized controlled trials
TF	:	Tissue factor
TXA	:	Tranexamic acid

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Protocol of a Thesis for Partial Fulfillment of Master Degree in Anesthesiology, Intensive Care and Pain Management

Title of the Protocol: **Potential Benefit of Combined Topical and Intravenous Administration of Tranexamic Acid in Congenital Heart Surgery**

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What is already known on this subject? AND What does this study add?

Pediatric patients after cardiac surgery with cardiopulmonary bypass are at high risk of excessive postoperative bleeding .One possible cause of this bleeding is increased fibrinolysis during cardiopulmonary bypass. The efficacy of administration of the antifibrinolytic tranexamic acid (TxA) in reducing postoperative cardiac surgery bleeding had been previously demonstrated.

This study is designed to evaluate the effect of topical addition of TxA to the intravenous route in reducing postoperative bleeding after cardiac surgery for pediatrics with congenital heart diseases.

1. INTRODUCTION

Pediatric patients who undergo repair of congenital heart diseases on cardiopulmonary bypass are at great risk of postoperative bleeding. The major causes of bleeding are thrombocytopenia, platelets dysfunction, hemodilution and increased fibrionlysis during cardiopulmonary bypass (CPB) **(Eisses and Chandler, 2008, Williams et al., 1998).**

Non-surgical postoperative bleeding occurs due to micro-vascular bleeding from pericardial and mediastinal tissues when blood comes in contact with non-endothelial surfaces of the Cardio-Pulmonary Bypass (CPB) machine, compounded by liberal use of heparin and a complex interaction of humoral and cellular pathways.

Fibrinolysis within the pericardium is very high. The injured pericardium during surgery releases large amount of tissue plasminogen activator which hinders fibrin formation in the pericardial cavity and results in increased blood loss **(Khalil et al., 2004).**

There are reports that demonstrated higher levels of thrombine-antithrombin III complexes and fibrin degradation products in the pericardium compared to blood stream **(Taksaudom et al., 2017).**

Tranexamic acid (a lysine analogue) is antifibrinolytic agent which reversibly inhibits lysine binding sites on plsmiongen molecules preventing fibrin binding. It also prevents plasmin platelets activation thereby it improves hemostasis by a dual mechanism **(Eaton, 2008).**

There are several randomized controlled trials that assessed the effect of intravenous TxA in reduction of postoperative bleeding in pediatrics after cardiac surgery **(Farino et al., 2019).** This study is designed to evaluate if there is additional benefit of topical application of TxA combined with intravenous route in reduction of postoperative bleeding in pediatrics undergoing congenital heart diseases repair.

2. **AIM/ OBJECTIVES**

The aim of the study is to asses if there is potential benefit of intrapericardial topical application of tranexamic acid when it is combined with the intravenous administration in reduction of postoperative bleeding after pediatric cardiac surgery on cardiopulmonary bypass (CPB).

3. METHODOLOGY:

Patients and Methods

- **Type of the study:** Interventional, randomized and double blinded controlled trial.
- **Study Setting:** The operating theaters of Ain Shams University Hospitals.
    - **Study period:** Over one year (from March 2020 to March 2021).
    - **Standard management :** IV Tranexamic acid injection
- **Study population:**

Inclusion criteria:

1. Age group: more than one year with weight less than 20 Kg.
2. Elective repair of congenital heart diseases using cardiopulmonary bypass.

Exclusion criteria:

1. History of bleeding disorders or preoperative anticoagulation therapy.
2. Impaired liver or renal functions.
3. History of seizers.

Sampling method:

Patients will be randomly allocated by computer generated randomization and using opaque sealed envelopes to two groups A and B.

- **Group A:** patients will receive intravenous TxA acid as a bolus followed by intravenous infusion till the end of surgery.

- **Group B:** patients will receive the previous intravenous regimen in addition to topical intrapericardial TxA acid.

Sample size justification:

Using PASS 11 program for sample size calculation and according to previous literature ***(Couturier et al., 2014)***, the expected mean blood loss in patients with IV tranexamic acid = 18±16.9ml/kg; assuming that topical tranexamic acid will decrease blood loss by 50%, sample size of 45 patients per group can detect the difference between the two groups with Power 80% setting an error at 0.05.

Ethical considerations:

The study protocol will receive ethical approval from the Research Ethical Committee, Faculty of Medicine Ain Shams University. Informed consent will be obtained from parents/legal guardian of each patient.

Study Procedures:

Patients will be randomly allocated into two groups

- **Group A: (the intravenous group)**

After induction of anesthesia the patients will receive a loading bolus dose of TxA (10 mg/kg) over a period of five minutes followed by an infusion of 1 mg/kg/h till the end of surgery. Another 10 mg/kg will be administered into the prime of the cardiopulmonary bypass. The patients will have 20 ml of normal saline poured intrapericardially by the surgeon after protamine administration.

Group B: (the intravenous plus intrapericardial topical application)

In this group 50 mg of TxA will be diluted in 20 ml of normal saline and administered topically on the pericardial and mediastinal cavities after protamine administration and hemostasis