Dated: 13/3/2023

SYNOPSIS FOR FCPS-II

(GENERAL SURGERY)

"COMPARISON BETWEEN THE EFFICACY OF RIVAROXABAN VS ENOXAPARIN IN POST-OPERATIVE DEEP VENOUS THROMBOSIS PROPHYLAXIS AFTER EXPLORATORY LAPAROTOMY"

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COMPARISON BETWEEN EFFICACY OF RIVROXABAN VS ENOXAPARIN IN POST-OPERATIVE DVT PROPHYLAXIS AFTER EXPLORATORY LAPAROTOMY

Unique identifier. _____

Reg. No. _____ Group: R / E Dosage:_____

Patient Name:_____ Age: _____

Gender: M/F Date of Admission: _____ Date of Discharge_____

Diagnosis:_____

Operation_____

Previous DVT Yes / No

POST OPERATIVE VARIABLES

VARIABLE	VALUES AT DAY 5	VALUES AT DAY 10
DEEP VENOUS THROMBOSIS ON CDUS (YES/NO)		
WELL'S SCORE (-2 TO 9)		

CONSENT FORM

Title of Research: Comparison Between the Efficacy of Rivaroxaban and Enoxaparin in Post-Operative Deep Venous Thrombosis (DVT) Prophylaxis After Exploratory Laparotomy

You are invited to participate in a research study aimed at comparing the effectiveness of two medications, rivaroxaban and enoxaparin, in preventing blood clots (DVT) following surgery. This study involves patients who have undergone exploratory laparotomy. If you choose to participate, you will be randomly assigned to receive either rivaroxaban or enoxaparin post-surgery. Your health will be monitored closely through regular follow-ups, including Doppler ultrasound studies on the 5th and 10th days after surgery to check for any blood clots.

Both medications are approved for the prevention of blood clots, but may have side effects such as bleeding. We will take all necessary precautions to minimize these risks. Participation in this study may help enhance our understanding of DVT prevention and benefit future patients undergoing similar surgeries. Your personal information will be kept strictly confidential and used only for research purposes. Data will be anonymized to protect your privacy.

Participation in this study is entirely voluntary. You are free to withdraw at any time without any negative consequences. If you have any questions about the study, please contact Dr. Muhammad Mashhood Ahmad Shad at 03390420285. By signing below, you agree to take part in this study.

Patient Name and Signatures _____

Patient's CNIC No. _____

Date and Time _____

Witness 1 _____

CNIC No. _____

Witness 2 _____

CNIC No. _____

INTRODUCTION

Deep vein thrombosis (DVT) is the formation of blood clots in deep veins more likely to occur in lower limbs than in upper limbs. It is one of the major but preventable causes of morbidity and mortality and leads to 60,000 to 100.000 deaths every year in the United States.[1] Although DVT is a major complication in many orthopedic surgeries,[2] it also occurs in up to 4.9 % of abdominal surgeries lasting more than 2 hours.[3]

Medications as well as mechanical techniques are used as primary prophylaxis of DVT[1]. Rivaroxaban is one of the oral medications used for DVT prophylaxis after surgeries. [4]Rivaroxaban is a factor Xa inhibitor commonly used in once daily dosage.[5] In a trial on Orthopedic setting, Rivaroxaban is considered superior to enoxaparin in preventing DVT.[6] Rivaroxaban has improved efficacy as compared to LMWH but has an increased risk of bleeding in Orthopedic patients. Moreover, Rivaroxaban is more cost-effective as compared to Enoxaparin.[7] In another study, incidence of DVT in enoxaparin group was 26.61% vs 9.5% in Rivaroxaban group. [8]Exploratory laparotomy is a cost-effective procedure as compared to other emergency interventions and is common in low- and mid-income countries.[9] In emergency general surgery incidence of DVT is highest in GI surgeries (1.705%) and DVT is a significant burden on resources in emergency general surgery.[10] The ASH 2019 guidelines for DVT prophylaxis after surgery recommend mechanical prophylaxis over no prophylaxis, pneumatic compression over graduated compression stockings, and pharmacological prophylaxis with low-molecular-weight heparin or unfractionated heparin for major general surgery[11]. Current practice at Mayo hospital Lahore is according to ASH 2019 guidelines for DVT prophylaxis.

This research is crucial to compare the relative efficacy of Rivaroxaban versus enoxaparin in postoperative DVT prophylaxis in general surgical settings. As there is no study conducted on

Pakistani population regarding efficacy of these drugs, locally relevant data can optimize patient care in Pakistan, guiding more efficient and effective treatment strategies.

RESEARCH QUESTION: To assess the comparative efficacy of Rivaroxaban vs Enoxaparin in preventing deep vein thrombosis (DVT) in patients undergoing emergency exploratory laparotomy in general surgical settings in local population of Pakistan.

OBJECTIVE: To compare the outcome of Rivaroxaban vs Enoxaparin as post-operative DVT prophylaxis in patients undergoing emergency exploratory laparotomy in terms of DVT findings detected by color Doppler ultrasound after

HYPOTHESIS: There is a difference in the efficacy of Rivaroxaban vs Enoxaparin as post-operative DVT prophylaxis in patients undergoing emergency exploratory laparotomy.

OPERATIONAL DEFINITIONS:

Exploratory Laparotomy: A surgical intervention performed to examine the abdominal cavity, often indicated for patients presenting with acute abdominal conditions that cannot be diagnosed through less invasive methods. This procedure is crucial for diagnosing and sometimes treating injuries or diseases within the abdominal space.[12]

Deep Venous Thrombosis (DVT): The formation of blood clots in deep veins, mostly in legs as detected by color Doppler ultrasound as obliterated and non-compressible vein at 5^{th} and 10^{th} post operative days.[13]

Post-Operative Period: The duration immediately following surgery during which the patient is monitored for recovery and potential complications. This period typically encompasses the first 30 days post-surgery, aligning with the common timeframe used in clinical research to assess short-term postoperative outcomes

MATERIALS AND METHODS:

Study Settings: Male and Female West Surgical Wards, Mayo Hospital, Lahore

Study Design: Randomized Control Trial

Duration of Study: Six (06) months after approval of synopsis

Sampling Technique The study will utilize the Clinical Trial Randomization Tool provided by the National Cancer Institute for random allocation of participants. The asymptotic maximal method will be used with a maximal tolerance imbalance of 3.

Sample Size: A sample size of 106 in each group is estimated with 5% level of significance amd 90% power of the test with anticipated p1 = 9.5% and p2 = 26.61%.

INCLUSION CRITERIA:

- Patients aged 18 to 80 years
- Both male or female patients
- Patients who have undergone emergent exploratory laparotomy for any reason whether traumatic or non-traumatic
- Patients with expected immobility for more than 24 hours

EXCLUSION CRITERIA:

- Patients with diagnosed pre-operative DVT
- BMI more than 40
- Patient who are on mechanical ventilation post operatively
- Patient with postoperative Myocardial infarction, ischemic heart disease or cerebrovascular accident
- Patients who have undergone limb surgery in addition to exploratory laparotomy

- Patients who are allergic or intolerant to either Rivaroxaban or Enoxaparin
- Patients with a known history of bleeding disorder or bleeding complications
- Patients who are currently taking anticoagulant medications or have taken them in the last 48 hours
- Patients with a history of thrombocytopenia or HIT (Heparin-induced thrombocytopenia)
- Any patient developing postoperative bleeding

DATA COLLECTION:

After formal approval of the synopsis, patients eligible for the study will be identified upon admission to the surgical ER using convenience sampling. Once consented and enrolled, each patient will be assigned a unique identifier. The Clinical Trial Randomization Tool will use these identifiers to randomly allocate patients to either the Rivaroxaban or Enoxaparin group while maintaining a balance between the groups within the maximally tolerated imbalance value of 3. Rivaroxaban (Tab. Xcept) will be given 10mg orally once daily and Enoxaparin (Inj. Clexane) will be given 4000IU (40mg or 0.4ml) subcutaneously once daily for 7 days.

All the patients will be scheduled for complete duplex ultrasonography by the radiologist who is blind to the treatment group within 48 hours after surgery to rule out any previous DVT. Patients having already established DVT will be excluded.The complete duplex ultrasonography of bilateral lower limb veins from common femoral, popliteal to tibial veins will be performed by the radiologist after 5^{th} and 10^{th} postoperative day to detect evidence of deep venous thrombosis on CDUS to assess presence or absent of deep venous thrombosis and simultaneously assessed using Well's score to assess the risk of DVT. In case any patient develops DVT postoperatively in either group will be marked as treatment failure and will be

subjected to anticoagulation with LMWH at therapeutic dosage as per international guidelines and later shifted to oral warfarin 5-10mg once a day with INR monitoring.

DATA ANALYSIS:

The IBM SPSS statistics V25.0 for Windows program will be used to conduct the statistical analysis of the data (IBM, Armonk, New York, USA). The % for descriptive data will be displayed for variables including gender, BMI classes, surgical indication, blood transfusion, and DVT diagnosis. Age is one of the variables for which the mean and standard deviation will be determined. The chi-square test will be used to compare the outcome data of the two groups to identify any statistically significant differences; a p-value of 0.05 or less will be regarded as statistically significant. Age, gender, surgical indication, blood transfusion, and BMI classes will be used to stratify outcome data, and a post-stratification chi-square test will be used.

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