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A COMPARATIVE STUDY ON SAFETY PROFILE AND EFFICACY OF FONDAPARINUX AND ENOXAPARIN IN PATIENTS WITH ST- SEGMENT ELEVATION MYOCARDIAL INFARCTION AT TERTIARY CARE HOSPITAL IN KURNOOL

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ABSTRACT

Objective :A study was conducted to evaluate the safety profile and relative efficacy of fondaparinux and enoxaparin in STEMI patients ,to analyze the outcomes of fondaparinux and enoxaparin in the STEMI patients.

Materials and Methods: This is a prospective observational study on efficacy and safety of fondaparinux and enoxaparin in ST segment elevation myocardial infarction using either of the medicines. An aggregate of 100 cases were recently detected ST segment elevation myocardial

infarction and compared of which 50 were specified fondaparinux, and the other 50 were specified enoxaparin. Data was analysed using chi-square test in MS EXCEL software.

Results: The outcomes of the study Reinfarction, bleeding, death, stroke in subjects receiving fondaparinux (30) and enoxaparin (38) were identified. The subjects receiving fondaparinux were found to be more effective when compared to enoxaparin.

Conclusion: This study shows that the ST segment elevated myocardial infarction patients receiving both fondaparinux and enoxaparin. Fondaparinux was found to be more effective reducing the composite of death or myocardial reinfarction without increasing the severe bleedings and strokes when compared to the Enoxaparin in the hospital.

Keywords: ST segment elevated myocardial infarction, Fondaparinux, enoxaparin.

INTRODUCTION

- STEMI is due to the occlusion of coronary arteries by a thrombus at the site of atherosclerotic plaque rupture. The aim of the treatment is to restore the actual blood flow through the blocked coronary arteries or vessels either pharmacologically with the thrombolytic agents or mechanically by percutaneous coronary intervention (PCI). 1
- This reperfusion therapy is associated with the administration of adjuvant treatments designed to prevent the reocclusion of coronary arteries. This treatment includes anti platelet therapy (aspirin, clopidogrel) and anticoagulants (low molecular weight heparin, unfractionated heparin UFH)
- Despite the availability of these treatments in the STEMI,1/3rd of the STEMI patients die, suffer from reinfarction during their hospitalization and occurrence of strokes.2
- These results are due to the limited antithrombotic efficacy and their effects on bleeding .so, consequently the challenge for more effective anti-thrombotic strategies without increasing the bleeding risk has to be administered as the primary treatment for STEMI patients.3
- Notably fondaparinux was found to be more effective and showed substantial benefits in a large phase III trials in STEMI patients.4

FONDAPARINUX:

- Fondaparinux is a synthetic selective factor Xa inhibitor with a high efficacy and good safety in terms of bleeding risk, prevention of re-infarction and in the treatment of venous thromboembolism.
- Fondaparinux is a synthetic Penta saccharide and it is also known as “BLOOD THINNER”.
- It is used to treat serious blood clots that can travel to the lungs, heart and brain causing serious breathing problems, heart attack or stroke.
- It may also be used to prevent blood clots after certain surgeries such as hip fractures, abdominal, knee or hip replacement with an increased risk of blood clots.5

Route of elimination:

- In individuals with normal kidney function, fondaparinux is eliminated in urine mainly as unchanged drug.6

MECHANISM OF ACTION:

- The anti-thrombotic activity of fondaparinux is the result of AT III mediated selective inhibition of factor Xa.

By selectively binding to AT III fondaparinux potentiates (about 300 times) the neutralization of factor Xa by AT III.

- Neutralization of factor Xa interrupts the blood coagulation cascade and thus inhibits thrombin formation and thrombus development. It is thought that fondaparinux is unlikely to induce thrombocytopenia via a heparin induced thrombocytopenia (HIT) like mechanism given its chemical structure. As a result, fondaparinux has been used as an alternative anti-coagulant in heparin induced thrombocytopenia (HIT) patients.
- However, it is important to note that rare cases of HIT have been reported in patients treated with fondaparinux. 7

Enoxaparin (Low molecular weight heparin)

- Enoxaparin is used to prevent and treat harmful blood clots. This helps to reduce the risk of a stroke or heart attack. This medication helps keep your blood flowing smoothly by lowering the activity of clotting proteins in the blood.
- Enoxaparin is an anticoagulant, also known as a "blood thinner." It is a type of heparin. Conditions which increase your risk of developing blood clots include certain types of surgeries (such as knee/hip replacement, abdominal), long periods of being immobile, certain types of heart attack, and a specific type of chest pain called unstable angina.
- For some medical conditions, enoxaparin may be used in combination with other "blood thinners.8

Half life:

- The half-life of enoxaparin is about 4 hours after a single dose administered subcutaneously and about 7 hours after several doses. One source mentions a half-life ranging from 1 hour to 4.5 hours. 9

MECHANISM OF ACTION:

- Enoxaparin binds to antithrombin III, a serine protease inhibitor, forming a complex that irreversibly inactivates factor Xa, which is frequently used to monitor anticoagulation in the clinical setting.
- Following factor Xa inactivation, enoxaparin is released and binds to other anti-thrombin molecules.
- Factor IIa (thrombin) is directly inhibited by enoxaparin, however with less potency than unfractionated heparin (UFH).

Due to the cascade of effects resulting from enoxaparin binding, thrombin Iis unable to convert fibrinogen to fibrin and form a clot, preventing thromboembolic events. 10

METHODOLOGY

STUDY SITE: The study was conducted in the Gowri Gopal hospital ,an In-patient hospital ,budhawarpeta, Kurnool.

DURATION OF STUDY: The study was conducted for a period of 6 months.

STUDY DESIGN: This is a prospective observational study

SAMPLE SIZE: 100 patients.

SOURCE OF DATA: Patient data collection form. Interview with patient and their attender or relatives. Patient investigation reports.

STUDY CRITERIA: The patients were selected based on the following inclusion and exclusion criteria.

INCLUSION CRITERIA:

- The patients who are diagnosed with STEMI as per ECG.
- Patients with age of 18 years and above.

- Patients prescribed with either fondaparinux or enoxaparin.
- Patients who are willing to give voluntary consent in order to participate in the study.

EXCLUSION CRITERIA:

- Specialized population like pediatrics, pregnant women and breastfeeding women.
- Patients who are prescribed with other anticoagulants.

STATISTICAL METHOD:

- **Chi-square test,** the collected data was analyzed by using MS-Excel software statistics to produce results from the data.

RESULT AND DISCUSSION

A prospective observational study was conducted in Gowri gopal hospital, Kurnool for a period of six months. A total of 100 patients were recruited under inclusion criteria upon receive of ICF(inform consent form). In that 100 patients 50 patients were included in group receiving Fondaparinux and 50 patients were included in group receiving Enoxaparin.

Age wise distribution:

The study found that (30 – 40) years of age – 6 patients (12%), 41-50 years of age – 16 patients (32 %), 51-60 years of age- 10 patients (20 %), 61-70 years of age – 11 patients(22%), 71-80 years of age – 7 patients (14%) had the highest number of fondaparinux and enoxaparin patients were (31-40) years of age – 4 patients (8%), 41-50 years of age -10 patients (20%), 51-60 years of age- 12 patients (24%), 61-70 years of age – 16 patients (32%), 71 -80 years of age -8 patients (16%) P value (0.564)were observed in Gowri gopal hospital as shown in Table.1 and Figure.

Table1:Enrollement of patients in both treatment group

Age	Fondaparinux	Enoxaparin
31-40	6	4
41-50	16	10
51-60	10	12
61-70	11	16
71-80	7	8

Table. 1 Age wise distribution

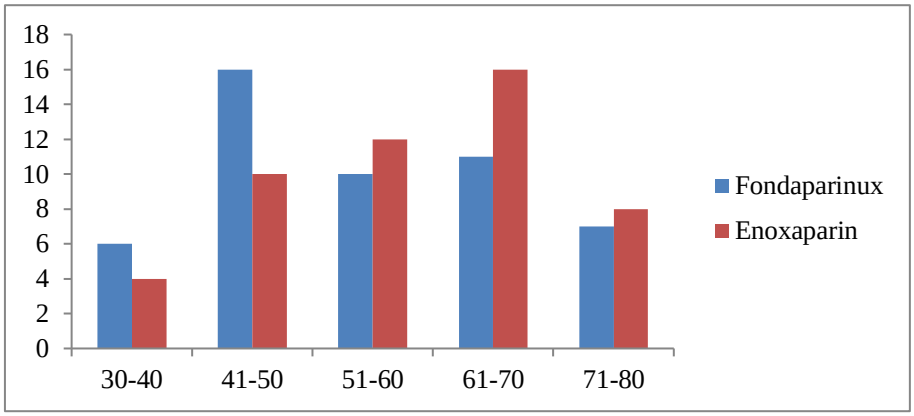

Figure 1Age wise distribution

6.2 Gender wise distribution:

The maximum number of fondaparinux in the study was found to be 31-40 years of age – 4 male patients and 2 female patients, 41-50 years of age 11 male patients and 5 female patients, 51-60 years of age 7 male patients and 3 female patients, 61-70 years of age 6 male patients and 5 female patients, 71-80 years of age 3 male patients and 4 female patients P value (0.738) as shown in Table. 2 and Figure. 2

	Fondaparinux	
Age	Male	Female
31-40	4	2
41-50	11	5
51-60	7	3
61-70	6	5
71-80	3	4

Table 2 Gender wise distribution

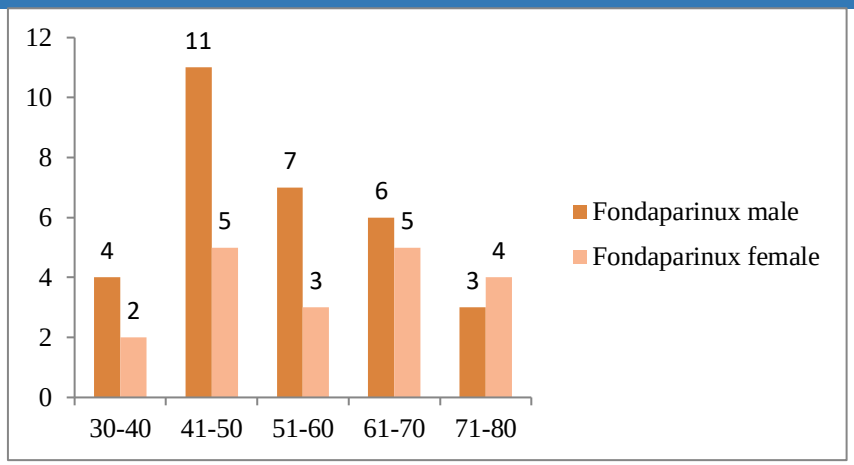

Figure 2 Gender wise distribution

- Patients taking enoxaparin ranged in age from 31-40 years old with 3 male patients and 1 female patient, 41-50 years old with 4 male patients and 6 female patients, 51-60 years old with 8 male patients and 4 female patients, 61-70 years old with 4 male patients and 7 female patients, 71-80 years old with 5 male patients and 3 female patients P value (0.687) were observed in gowri gopal hospital as shown in Table. 3 and Figure.3

	Enoxaparin	
Age	**Male**	**Female**
31-40	**3**	**1**
41-50	**4**	**6**
51-60	**8**	**4**
61-70	**9**	**7**
71-80	**5**	**3**

Table 3 Gender wise distribution

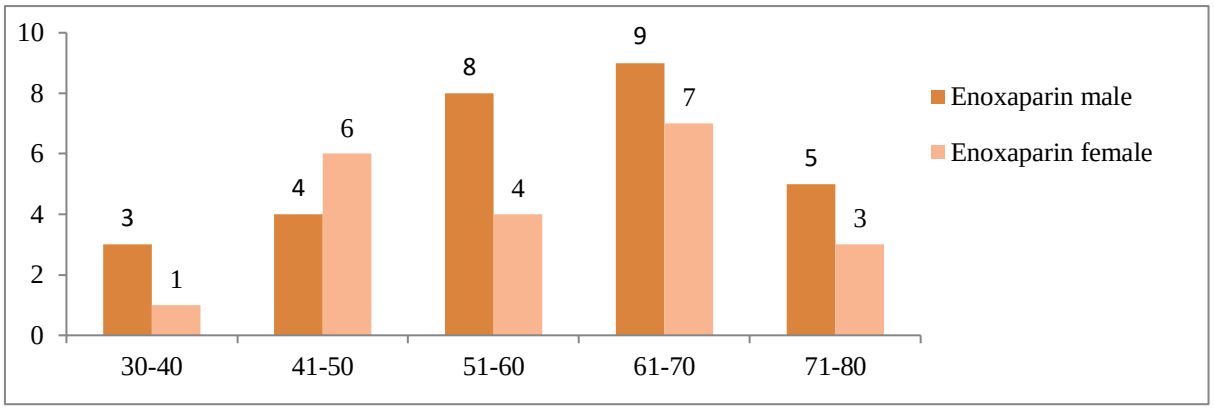

Figure 3 Gender wise distribution

Clinical outcomes wise distribution

- Out of 50 patients who were using fondaparinux 30 patients were found to be having a stroke, reinfarction and bleeding. Among these 30 patients 15 patients were found to be bleeding(50%), 10 patients were found to be stroke(33%), 5 patients were found to be reinfarction(16%).
- Out of 50 patients who were using enoxaparin 38 patients were found to be having a stroke, reinfarction, and bleeding. Among these 38 patients 18 patients were found to be bleeding(86%), 13 patients were found to be stroke(34%), 7 patients were found to be reinfarction(18%) P value (0.954) as shown in Table. 4 and Figure. 4

Table 4 clinical outcomes distribution

Clinical outcomes	Fondaparinux	Enoxaparin
Bleeding	15	18
Stroke	10	13
Reinfarction	5	7

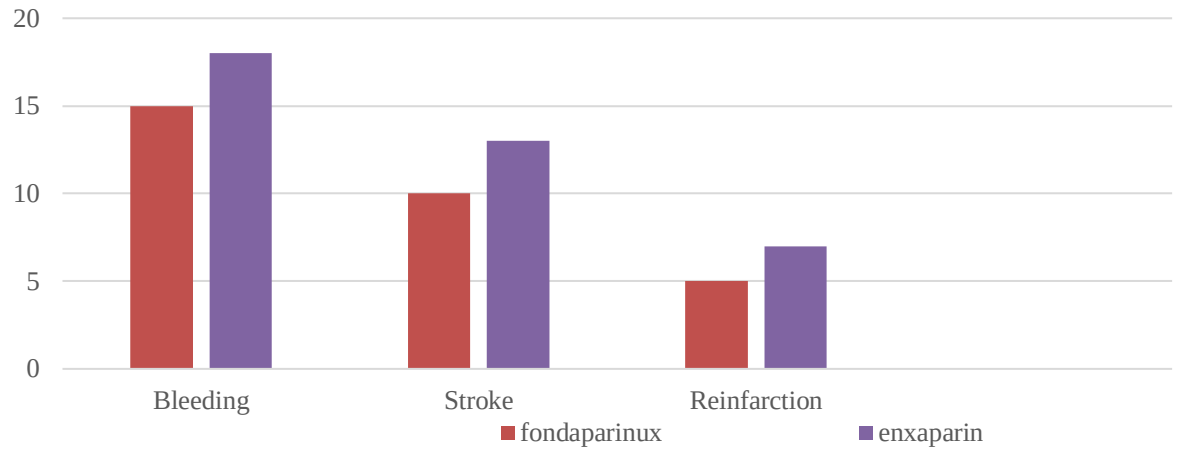

Figure 4 clinical outcomes distribution

Ejection fraction wise distribution: (DAY 1)

- Out of 50 patients who were receiving fondaparinux 6 patients were having mild ejection fraction (12%) and 26 patients were having moderate ejection fraction (52%) and 18 patients were having severe ejection fraction (36%).

Severity	Ejection fraction	Fondaparinux	Enoxaparin	P Value
Mild	46-55%	6	4	0.467
Moderate	36-45%	26	32	
Severe	<35%	18	14	

- Out of 50 patients who were receiving enoxaparin 4 patients were having mild ejection fraction (8%) and 32 patients were having moderate ejection fraction (64%) and 14 patients were having severe ejection fraction (28%), (p=0.467).

Table 5 Ejection fraction wise distribution (Day1)

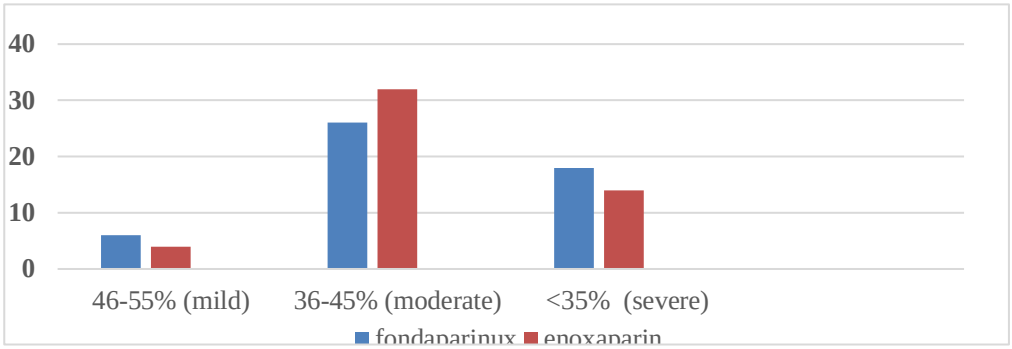

Figure 5 Ejection fraction wise distribution (Day 1)

Ejection fraction wise distribution: (DAY 4)

- Out of 50 patients who were receiving fondaparinux 19 patients were having mild ejection fraction (38%) and 16 patients were having moderate ejection fraction (32%) and 9 patients were having severe ejection fraction (18%).
- Out of 50 patients who were receiving enoxaparin 26 patients were having mild ejection fraction (52%) and 11 patients were having moderate ejection fraction (22%) and 09 patients were having severe ejection fraction (18%), (p=0.373).
-

Severity	Ejection fraction	Fondaparinux	Enoxaparin	P Value
Mild	46-55%	19	26	0.373
Moderate	36-45%	16	11	
Severe	<35%	09	09	

Table 6 Ejection fraction wise distribution (Day 4)

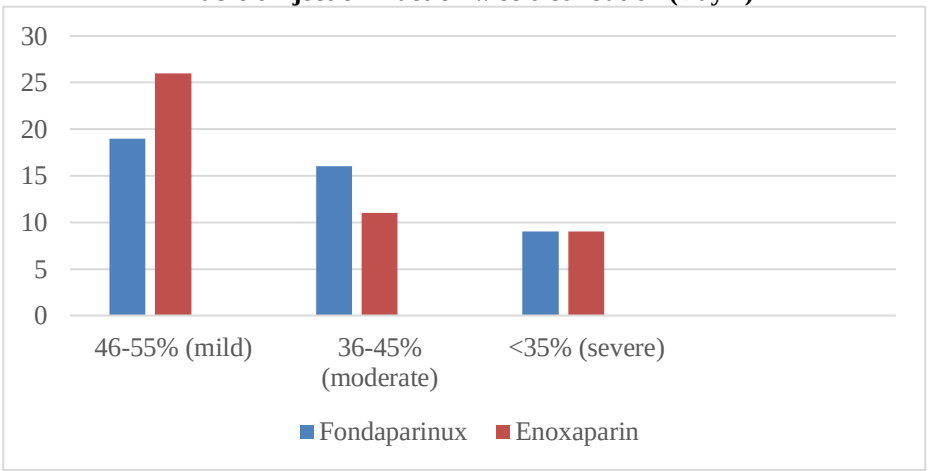

Figure 6 Ejection fraction wise distribution (Day 4)

Ejection fraction wise distribution: (DAY 7)

- Out of 50 patients who were receiving fondaparinux 6 patients were having mild ejection fraction (12%) and 4 patients were having moderate ejection fraction (8%) and 2 patients were having severe ejection fraction (2.5%).
- Out of 50 patients who were receiving enoxaparin 7 patients were having mild ejection fraction (14%) and 1 patient is having moderate ejection fraction (2%) and 5 patients were having severe ejection fraction (10%), (p=0.209).

Severity	Ejection fraction	Fondaparinux	Enoxaparin	P Value
Mild	46-55%	6	7	0.209
Moderate	36-45%	4	1	
Severe	<35%	2	5	

Table 7 Ejection fraction wise distribution (Day 7)

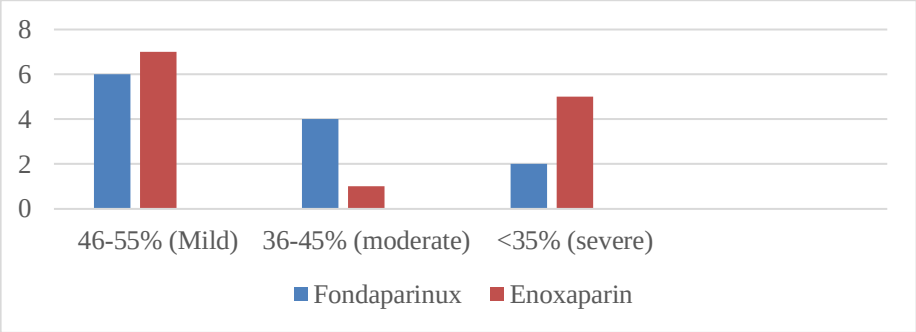

Figure 7 Ejection fraction wise distribution (Day7)

IV. DISCUSSION

Myocardial infarction is the occlusion of the coronary arteries by a thrombus that leads to the interruption in the blood supply to the myocardium of heart leads to the elevations in ST segmentleading to STEMI. The treatment given for the restoration of the actual blood flow in the coronary arteries and the treatment includes either pharmacological therapy or by the mechanicalsurgeries. It is the most common condition occurring in most of the people of age group (30-60). Despite the availability of various treatments 1/3rd of patients with STEMI patients die , suffer from reinfarction during their hospitalization and occurrence of strokes.11

In the study **Jonas oldgren et al.,** was studied that effects of fondaparinux in patients with ST- segment elevation acute myocardial infarction not receiving reperfusion treatment showed clearly that fondaparinux was notably found effective than enoxaparin with decreasing the risk ofbleeding outcome and also reduced the occurrence of stroke and deaths they have done age wise, gender wise, clinical outcomes wise distribution which includes (death,bleeding,stroke,reinfarction). Concluded that fondaparinux was found to be effective with lower odds than

enoxaparin (p=0.541).12

In our study 100 patients were included who were diagnosed with ST segment myocardial infarction and divided into two groups 50 patients in the fondaparinux group and 50 patients in the enoxaparin group. The results of the current analysis provide a clear Evidence that fondaparinux in the STEMI patients was found superior to the enoxaparin in reducing the major outcomes (bleeding, stroke, reinfarction) by one half while maintaining similar efficacy, which resulted in superior net clinical benefit. We have done clinical outcomes wise distribution (bleeding) that shows no of patients having bleeding in fondaparinux group are lesser when compared to enoxaparin group. In order to assess the efficacy Ejection fraction of both groups were compared based on the severity and clearly found that Ejection fraction is improved more in fondaparinux group when compared to enoxaparin. On the day 1 Ejection fraction moderate and severe patients were more and on day 4 Ejection fraction is improved in 65% of patients andon day 7 Ejection fraction is improved in almost 92% of patients in fondaparinux group and 90%of patients in enoxaparin group.

V.CONCLUSION

In the ST segment elevated myocardial infarction patients receiving both fondaparinux and enoxaparin . Fondaparinux was found to be more effective reducing the composite of death or myocardial reinfarction without increasing to the enoxaparin in the hospital.

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