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ORIGINAL ARTICLE

Thrombolytic Efficacy Of Enoxaparin Compared With Unfractionated Heparins In Cardiac Emergency

MUHAMMAD IMRAN ASHRAF[1], SHAZANA RANA[2], MUHAMMAD SALEEM AKHTAR[3], ADNAN AFZAL[4], JAVARIA FATIMA[5], SAFDAR ALI[6], ASIF SHAHZAD[7], AMAL SHAUKAT[8]
[1]Associate Professor of Pharmacology, Rai Medical College Sargodha, Pakistan.
[2]Associate Professor of Pharmacology, HITEC-IMS Taxilla Cantt. Pakistan.
[3]Senior Registrar. Department of Medicine, Rai Medical College Sargodha, Pakistan.
[4]Assistant Professor of Medicine, Rai Medical College Sargodha. Pakistan
[5]PGR 5 M.D cardiology, Faisalabad institute of cardiology Faisalabad
[6]Assistant Professor of Biochemistry, Sargodha Medical College Sargodha
[7]Ph.D(scholar) physiology Physiology department, Government college university Faisalabad
[8]Lecturer, Department of Food Science and Technology, University of central Punjab
Correspondence to Dr. Muhammad Imran Ashraf

ABSTRACT

Background: Antithrombotic treatment with heparin together with antiplatelet agents reduces the incidence of ischemia in patients with coronary artery disease. associated with fewer adverse reactions.
Aim: To evaluate and compare the clinical and obtained results of the use of enoxaparin and standard unfractionated heparin in patients with coronary heart disease.
Methods: This is a non-invasive planned surveillance demonstration conducted at a tertiary hospital in Pakistan. Adult male and female patients with coronary artery infection (CAD) between the ages of 30 and 70 were recently analyzed or included patients with a history of heart cancer. The intermediate layer is injected with enoxaparin for 5 days. Resting the ECG position, prothrombin time, and ADRs were measured individually in all patients from 1 to 21 days.
Result: Compared to the patient's unfractionated heparin, normal prothrombin times were generally higher (P and <0.002), while total hypokalemia was lower. (P and <0.04) in the patient's enoxaparin stratification. Angina pectoris and side effects such as death, morbidity, encephalopathy and sudden onset were less common in the patient's enoxaparin fraction than in the unfractionated heparin fraction, and the contrast was negligible
Conclusions: Antithrombotic therapy with enoxaparin and aspirin is safer and more convincing than unfractionated heparin and headache drugs because it reduces the incidence of ischemic events in patients with unstable or tissue angina. The myocardium dies in the early stages.
Keywords: Anticoagulant, coronary heart disease, enoxaparin, safety, and efficacy, unfractionated heparin

INTRODUCTION

The burden of non-communicable diseases (NCDs) has increased considerably over the past few decades compared to communicable diseases. Moreover, the majority of people suffering from NCDs reside in developing countries including Pakistan. The already inadequate and stretched healthcare systems in these countries are an indication that the mortality due to NCDs is also higher; Nearly 60% people die prematurely in countries that are low income and middle-income.[1,2]Coronary heart disease (CHD), a NCD and also called coronary artery disease (CAD) is the leading cause of death in Pakistan and worldwide. CHD is a condition where the vascular supply to the heart is impeded by atheroma, thrombosis or spasm of coronary arteries. This may impair sufficient supply of oxygenated blood to cardiac tissue to cause myocardial ischemia that, if severe or prolonged, may cause the death of cardiac muscle cells (myocardial infraction).[8]

Previously CHD was thought to affect people only in developed countries, but now CHD is responsible for higher mortality and morbidity rates even in developing countries such as Pakistan, especially in younger people, with increasingly disproportionate rates.[7] Data on CHD incidence rates is not available in prospective national cohort registries of CHD in Pakistan. In a study by Gupta et al. 2008, it was found that unadjusted CHD rates ranged from 1.6% to 7.4% among people residing in rural areas and 1–13.2% among urban residents respectively.[5] Gaziano et al., 2006, concluded that the age-standardized CVD mortality rates per 100,000 in people aged 30–69 years were180 in Britain, 280 in China, and 405 in Pakistan respectively. Also, 45% of CHD-related deaths in Pakistan occur in people <70 years of age compared to only 24% in western countries in a similar age Strata.[6] In developed countries, ischemic heart disease is predicted to rise by 30–60% between 2018 and 2019. In developing countries, rates are predicted to increase by 120% in women and 137% in men from 1995 to 2019.[4]

The most common risk factor for CHD is smoking, diabetes, and hypertension.[3] Aspirin or clopidogrel (if patients are allergic to aspirin), are antiplatelet agents that effectively reduce short term and long term risks of myocardial infarction after an episode of unstable CAD. Various agents like cholesterol modifiers, antiplatelets, beta blockers, nitroglycerin, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and calcium channel blockers (CCB) are prescribed as

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monotherapy or combination therapy to treat CAD.[9] According to standard treatment guidelines (STGs), antithrombotic therapy, consisting of intravenous infusion of unfractionated heparin (UFH) plus oral antiplatelet therapy (aspirin) represent the current therapy for hospitalized patients with coronary heart disease.[4,9,12] This treatment has a high likelihood of being unsuccessful due to unpredictable anticoagulation caused be using standard unfractionated heparin. Also, the standard unfractionated heparin may be neutralized by protein binding and activated platelet. The low molecular weight heparins (LMWH) have several advantages over UFH. They have a more predictable anticoagulant effect with a high ratio of anti-factor Xa to anti-factor IIa, do not require monitoring for anticoagulation, are less likely to cause heparin induced thrombocytopenia and exhibit resistance to activated platelet inhibition.[7,8]The purpose of the present study was to evaluate and compare the clinical and cost outcomes of CAD patients treated with Enoxaparin versus CAD patients treated with a standard UFH.

MATERIALS AND METHODS

This was a noninvasive prospective observational descriptive study. It was carried out in a multi-specialty tertiary care teaching hospital situated in Sargodha, Pakistan. It was carried out over a 12 months period; from January 2019 to December 2019.

Inclusion Criteria: Patients with CHD either who were newly diagnosed or those with a history of CHD who have received unfractionated heparin or enoxaparin in the past

- Patients able to give informed consent
- Male and female patients aged 30–70 years.

Exclusion Criteria

- Patients receiving anticoagulants other than Enoxaparin and UFH
- Patients with increased risk of bleeding, ulcer disease or known gastro intestinal bleeding during the last 5 years

METHODS

The patients who fulfilled the study criteria were selected for the study. They were divided into two parallel Strata. Strata 1 received treatment with enoxaparin and Strata 2 received treatment with unfractionated heparins initially as an IV bolus of 5000 IU followed by a continuous infusion at a rate of 1000 IU/h adjusted according to activated partial thromboplastin time, administered within 2 h. American Heart Association recommends treatment with 70–162 mg of aspirin daily is recommended for type I patients with stable CHD or high-risk type IIb patients with stable CHD[10]. Aspirin and other medications were administered to both the Strata immediately, in accordance with the standard practice after admission to hospital and were continued throughout the study. The patients were followed for two visits on the 1st and 21st day respectively. Resting electrocardiogram was administered in all patients during each visit. The choice of the medication (enoxaparin versus unfractionated heparin) received by the patients was made by their physician based on the patient's affordability. An approval for conducting the study was obtained from the Institutional Human Ethics Committee of the hospital. All the patients registered in the Inpatient Department and Coronary Cardiac Intensive Care Unit (CCICU) were screened. An informed consent form was given to the patients.

Clinical parameters such as the average prothrombin time, occurrence of myocardial infarction, recurrence of angina and occurrence of death were analyzed. Occurrence of major or minor bleeding, stroke (hemorrhagic, nonhemorrhagic) thrombocytopenia, hypokalemia and allergic reactions were monitored. Cost comparison analysis was performed by equating individual costs of initial treatment with Enoxaparin and Unfractionated heparin comprising of the costs of hospital services, physician services and 5 days of medication costs (unfractionated heparin/enoxaparin). T-test and the Chi-square test were applied to compare the clinical and costs outcomes of both the drug Strata.

RESULTS

A total of 148 patients was selected for the study. Patients were divided into two Strata: one receiving enoxaparin comprising of 81 patients and other receiving unfractionated heparin comprising of 67 patients. Initially, 214 patients were admitted in CCICU Out of which 148 (69.15%) patients were treated with heparins. Remaining participants were excluded from the study due to various reasons such as lack of interest in participating in the study and having received heparins for <5 days. Totally,94 (63%) participants were males and 54 (37%) participants were females. Majority of the patients (both males and females) had coronary heart disease and were aged below 60 years.Out of 148 patients enrolled in the study, CHD was mostly observed in patients with myocardial infraction (39%) followed by patients with ischemia (36%), patients with unstable angina (18%) and patients with stable angina (13%) respectively. The average weight of the patients was 60 kg in unfractionated heparin Strata and was 59.66 kg in the enoxaparin Strata. The average number of medications consumed by patients in the unfractionated heparin and enoxaparin Strata was 9.89 and 8.96, respectively. The most commonly prescribed medications in both the Strata were antilipidemics, ACE inhibitors, antiplatelets, nitrates, digitoxin, diuretics and beta blockers. The common comorbidities found in our study were diabetes mellitus, hypertension, bronchial asthma, hypothyroidism and pulmonary edema [Table 1]. Table 2 represents average prothrombin time, ADRs, and cost comparison analysis in both the unfractionated heparin and enoxaparin Strata. Compared to unfractionated heparin Strata of patients, the average prothrombin time in the enoxaparin Strata of patients was significantly higher ($P < 0.002$). Bleeding (14%), hypokalemia (12%) and other minor ADRs (nausea, headache and sudden cough) (16%) were found more in the unfractionated Strata of patients compared to bleeding (7%), hypokalemia (0%) and other minor ADRs (nausea, headache and sudden cough) (9.99%) in patients consuming enoxaparin. Compared to unfractionated heparin Strata of patients, hypokalemia was significantly lower in the enoxaparin Strata of patients ($P < 0.04$).

Characteristics of the study population	Study Strata (%) Unfractionated heparin	Enoxaparin	P
Gender			
Male	51	54.	0.61
Female	44	61	
Age in years			
>60	26	33	0.70
<60	22	28	
Average weight of the patients (kg)	65	58	
Average number of drugs per prescription Diagnosis	10	8.9	
Unstable angina	8	7	0.400
Stable angina	6.32	5	0.80
Myocardial infarction	20	26	0.77
Ischemic heart disease	16	23	0.84
Most commonly prescribed medication at first day of admission			
Antilipedimics	37	33	0.01
ACE inhibitors	30	29	0.24
Antiplatelet	52	56	0.01
Nitrates	28	24	0.14
Digitoxin	6	5	0.88
Diuretics	14	18	0.90
Beta blocker	9	12	0.51
Diabetes mellitus	30	28	0.1
Hypertension	20	19	0.68
Bronchial asthma	8	6	0.04
Hypothyroidism	2	1	0.90
Pulmonary edema	1	1	0.48

Table 1: Baseline patient characteristics in the treatment group

Table 2:
Baseline clinical outcomes in the two treatment groups

Characteristics of the study population	Study strata on 21st day(%) Unfractionated heparin	Enoxaparin	P
cases with T-wave Inversion (%)	34	37	0.30
Cases with ST-segment depression (%)	9	11	0.78
Number of cases with T-wave inversion + ST-segment Depression (%)	11	13	0.67
Average prothrombin time (s)	27	322	0.002
Recurrence of angina	8	9	0.71
ADRs			
Bleeding	15	9	0.29
Hypokalemia	13	1	0.04
Other ADRs includes nausea, headache, sudden cough etc.,	18	11	0.37

DISCUSSION

The studyconsiders was attempted to assess and compare the clinical and taken a toll results of enoxaparin and UFH in patients with CAD. CAD patients have several comorbidities such as diabetes, hypertension, and bronchial asthma. As a result, the phenomenon of poly pharmacy is seen in these patients. Previous studies have shown that poly pharmacy leads to more ADRs, drug-drug interactions and increases the disease burden of the patient. The most common medications prescribed in our study were lipid lowering medication, ACE inhibitors, and antiplatelets. Previous studies have shown similar results[14].

Coronary heart disease can normally be managed by primary care doctors in outpatient clinics and standard treatment should involve usage of drugs like antiplatelets, antianginals, beta blockers and antilipidemics but during emergency, anticoagulants are used for prophylactic treatment[6]. Past randomized clinical trials have appeared that LMWH is at slightest as great as, in case not superior than, UFH in avoiding preoperative profound venous thrombosis and thromboembolism after major stomach surgery and add up to hip or knee arthroplasty[16]. The advantage of LMWHs isn't canceled by an increment in hemorrhagic complications. At slightest two studies[17] have moreover archived the prevalent adequacy and security of LMWH managed at domestic as compared to in-hospital intravenous UFH, in treating patients with set up profound vein thrombosis. As of late, clinical trials have moreover been distributed showing that LMWH may be useful in treating blood vessel maladies[8]. Our results suggest enoxaparin is as effective as unfractionated heparin for the treatment of CHD and in addition is a safer choice. We conducted a follow up on 1stand 21st day since previous studies had shown that complications may occur when UFHs are used. During the first 3–5 days after treatment, there were no complications. Thrombocytopenia occurs after about 6 days of treatment and often results in much more profound decrease in platelet count and an increased risk of thromboembolism. In patients taking LMWH, the platelet count should be performed at a 2–4 day interval from day 4 to 14.[9] In our study we performed platelet count for both Strata of patients taking LMWH and UFH on 1st and 21st day platelet count but did not find any adverse effects of heparin induced thrombocytopenia in both Strata of patients.

Conclusions

The recommended treatment of angina, myocardial infarction, and ischemic heart disease should comprise of enoxaparin with antiplatelets. The present report has shown that enoxaparin has more benefits than UFH. By observing clinical outcomes and cost comparison analysis we conclude that although UFH is less expensive than enoxaparin, enoxaparin has better overall clinical outcomes such as higher prothrombin time, less recurrence of angina and less occurrence of ADRs compared to UFH.

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