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AN OBSERVATION ON EFFICACY AND SAFETY OF LOW MOLECULAR WEIGHT HEPARIN WITH ASPIRIN AND UNFRACTIONATED HEPARIN WITH ASPIRIN IN TREATMENT OF MYOCARDIAL INFARCTION: A HOSPITAL BASED STUDY

Cardiology

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ABSTRACT

BACKGROUND INFORMATION: Myocardial Infarction is the common condition that affects most of the people in world. In the management of Myocardial Infarction. this study focuses on the comparison of efficacy, safety and outcomes of low molecular weight heparins with aspirins and unfractionated heparins in treatment of Myocardial Infarction.

AIM: To observe the Efficacy, Safety and Outcomes of Low Molecular Weight Heparin With Aspirin versus Unfractionated Heparin With Aspirin in treatment of Myocardial Infarction.

METHODOLOGY: The study will be conducted in Government General Hospital, Guntur.This study method involves all the patients who are included in the inclusion and exclusion criteria. Patients are observed for outcomes with the use of medications. An informed consent will be taken from the patient. The patient's data will be analyzed and tabulated by using suitable statistical tools.

RESULTS: Out of 77 subjects 38 members in unfractionated heparin group and 39 members in low molecular weight heparin group completed follow- up of study. The mean cure rate of unfractionated heparin and low molecular weight heparin groups are 2.94±1.05 days, 2.51±0.92 days respectively. Cure rate and relapse rate of unfractionated heparin group was found to be 68.42% and 32.4% whereas for low molecular weight heparin group it was found to be and 79.48%and 21.05%. Incidence of side effects is more for unfractionated heparin when compared to low molecular weight heparin.

CONCLUSION: Low molecular weight heparin with aspirin is effective in terms of efficacy and safety when compared with unfractionated heparin.

KEYWORDS

Low Molecular Weight Heparin, Unfractionated Heparin, Myocardial Infarction & Aspirin

INTRODUCTION:

The term acute myocardial infarction should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of cTn values with at least 1 value above the 99th percentile URL and at least 1 of the following:

- Symptoms of myocardial ischemia;
- New ischemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology.

Identification of a coronary thrombus by angiography or autopsy (not for types 2 or 3 MIs)[1]

ETIOLOGY:

Nonmodifiable risk factors for atherosclerosis include the following:

- Age
- Sex
- Family history of premature coronary heart disease
- Male-pattern baldness

Modifiable risk factors for atherosclerosis include the following :

- Smoking or other tobacco use
- Hypercholesterolemia and hypertriglyceridemia,including inherited lipoprotein disorders
- Dyslipidemia
- Diabetes mellitus
- Hypertension
- Obesity (abdominal obesity)
- Psychosocial stress
- Sedentary lifestyle and/or lack of exercise
- Reduced consumption of fruits and vegetables
- Poor oral hygiene
- Type A personality
- Elevated homocysteine levels
- Presence of peripheral vascular disease

MI can also occur for causes other than atherosclerosis. Nonatherosclerotic causes of MI include the following:

- Coronary occlusion secondary to vasculitis
- Ventricular hypertrophy (eg, left ventricular hypertrophy, hypertrophic cardiomyopathy)
- Coronary artery emboli, secondary to cholesterol, air, or the products of sepsis
- Coronary trauma
- Primary coronary vasospasm (variant angina)
- Drug use (eg, cocaine, amphetamines, ephedrine)
- Arteritis
- Coronary anomalies, including aneurysms of coronary arteries
- Factors that increase oxygen requirement, such as heavy exertion, fever, or hyperthyroidism
- Factors that decrease oxygen delivery, such as hypoxemia of severe anemia
- Aortic dissection, with retrograde involvement of the coronary arteries
- Respiratory infections, particularly influenza[2,3,4]

PATHOPHSYIOLOGY:

The atheromatous plaque responsible for acute MI develops in a dynamic process in multiple stages. Starting with arterial intimal thickening, which consists of vascular smooth muscles with very minimal or no inflammatory cells, this process can be observed soon after birth. Subsequently, the formation of fibrous cap atheroma occurs, which has a lipid-rich necrotic core that is surrounded by fibrous tissue. Eventually, a thin-cap fibroatheroma develops, this is also known as a vulnerable plaque which is composed mainly of a large necrotic core separated from the vascular lumen by a thin fibrous cap

that is infiltrated by inflammatory cells and is deficient of smooth muscle cells, making it vulnerable to rupture.

The process of acute coronary thrombosis leading to ACS involves the pathogenic mechanism of plaque rupture, and less frequently plaque erosion.

The Brasilia Heart Study Group indicates that changes in high-density lipoprotein (HDL) during an MI may alter the antiatherogenic function of HDL to transport lipids from arterial walls.The investigators noted a simultaneous decrease in lipid transfer to HDL and in the capacity of HDL to efflux cholesterol from cells occurs in the acute period after an MI.**[5]**

SIGNS AND SYMPTOMS:
Patients with typical MI may have the following symptoms in the days or even weeks preceding the event (although typical STEMI may occur suddenly, without warning):
- Fatigue
- Chest discomfort
- Malaise

Typical chest pain in acute MI has the following characteristics:
- Intense and unremitting for 30-60 minutes
- Substernal, and often radiates up to the neck, shoulder, and jaw, and down the left arm
- Usually described as a substernal pressure sensation that also may be characterized as squeezing, aching, burning, or even sharp
- In some patients, the symptom is epigastric, with a feeling of indigestion or of fullness and gas[6]

DIAGNOSIS:
Laboratory tests used in the diagnosis of MI include the following:
- Cardiac biomarkers/enzymes: The American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology (ESC) guidelines recommend that cardiac biomarkers should be measured at presentation in patients with suspected MI, and that the only biomarker that is recommended to be used for the diagnosis of acute MI at this time is cardiac troponin due to its superior sensitivity and accuracy.
- Troponin levels: Troponin is a contractile protein that normally is not found in serum; it is released only when myocardial necrosis occurs
- Complete blood cell count
- Comprehensive metabolic panel
- Lipid profile

Electrocardiography
The ECG is the most important tool in the initial evaluation and triage of patients in whom an acute coronary syndrome (ACS), such as MI, is suspected. It is confirmatory of the diagnosis in approximately 80% of cases.

Cardiac imaging
For individuals with highly probable or confirmed acute MI, coronary angiography can be used to definitively diagnose or rule out coronary artery disease,[8]

TREATMENT:
A number of different medications can also be used to treat a heart attack:
- Blood thinners, such as aspirin, are often used to break up blood clots and improve blood flow through narrowed arteries.
- Thrombolytics are often used to dissolve clots.
- Antiplatelet drugs, such as clopidogrel, can be used to prevent new clots from forming and existing clots from growing.
- Nitroglycerin can be used to widen your blood vessels.
- Beta-blockers lower your blood pressure and relax your heart muscle. This can help limit the severity of damage to your heart.
- ACE inhibitors can also be used to lower blood pressure and decrease stress on the heart.
- Pain relievers may be used to reduce any discomfort youmay feel.[9],[10]

REVIEW OF LITERATURE:
Pengcheng He et al..,(2018)., there is no difference between both groups with respect to cure time but our study proved that low molecular weight heparin is rapid in cure rate compared to unfractionated heparin.[11]

The study conducted by **Tajeldin M Abdallah** et al., in which low molecular weight heparin has better cure rate.[12]

According to study conducted by **Ahmed M** et al., there is very less percentage of cure rate in low molecular weight heparin group but our study showed that the better cure rate is achieved with low molecular weight heparin group compared to unfractionated heparin group. With usage of drugs along with advantages there are some disadvantages also in terms of occurrence of side effects.[13]

AIM:
To observe the Efficacy, Safety and Outcomes of Low Molecular Weight Heparin With Aspirin versus Unfractionated Heparin With Aspirin in treatment of Myocardial Infarction: A Hospital Based Study.

OBJECTIVES:
- To compare the efficacy of low molecular weight heparin with aspirin and unfractionated heparin with aspirin in treatment of cardiovascular disease.
- To compare the safety of low molecular weight heparin with aspirin and unfractionated heparin with aspirin in terms of adverse drug profiles.

METHODS AND METHODOLOGY
STUDY DESIGN: Prospective Observational Study.

STUDY PERIOD: The study is proposed to be conducted in the following 6 months period i.e., from September 2018 to April 2019.

STUDY METHOD: The study will be conducted in Government General Hospital, Guntur, a 1187 bedded tertiary care teaching hospital. This study method involves all the patients who matched the inclusion and exclusion criteria. Patients are observed for the efficacy, safety and outcomes with the use of medications. An informed consent will be taken from the patient. We will compare the data between two drugs and assess the patient's outcome. The patient's data will be analyzed and tabulated by using suitable statistical tools

STUDY MATERIALS:
- Inform consent form**.**
- Data collection form**.**

INCLUSION CRITERIA:
- Age >18years.
- Subjects with myocardial infarction.
- Subjects who are willing to provide written consent form.

EXCLUSION CRITERIA:
1. Have contraindications for the use of either of the study medications.
2. Subjects who are not willing to participate in study.

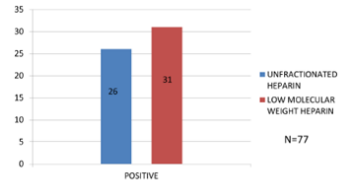
EFFICACY EVALUATION PARAMETERS:
- **Cure Rate:** Defined as the proportion of the patients who responded to treatment and symptomatically relieved (i.e. no complaints and other symptoms of MI) till the 28th day of follow up.
- **Relapse Rate**: Defined as the proportion of the patients affected with myocardial infarction with in 28th day of follow up.

STATISTICAL ANALYSIS: SPSS version 11.0.3 And Microsoft excel (2013)

RESULTS:
Table 1 represents cure rate varies from one patient to another and the difference between both groups is analysed using Chi-square test. Cure rates of low molecular weight heparin with aspirin was found to be 79.48% (31/39) and unfractionated heparin was found to be 64.82% (26/38). The p value was found to be 0.047 which is statistically significant.

S.NO	Cure Rate	No. of cases	
		LMWH	UFH
1.	Positive	31	26
2.	Negative	8	12

Figure-1describes cure rate in treatment groups



Below table-2 gives information about relapse rate of mi after using both medications. in that after using unfractionated heparin n=14, low molecular weight heparin n=8 are observed and p value was observed to be 0.03856

Relapse rate of the subjects	Unfractionated heparin	Low molecular weight heparin	None
	14	8	55

Figure-2 describes relapse rate in treatment groups

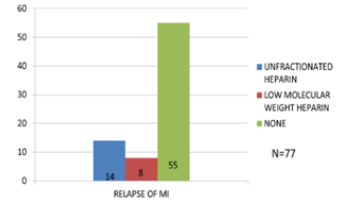
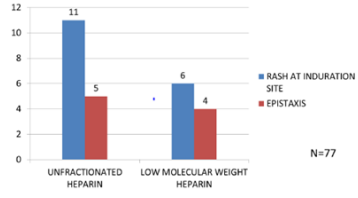


Table-3 describes in total 77 subjects only 26 are appeared with ADR'S in that induration at injection site n=17 and epistaxis n=9 are observed.

S.NO	ADR'S	UFH	LFH	TOTAL
1	INDURATION AT INJECTION SITE	11	6	17
2	EPISTAXIS	5	4	9

Figure-3 describes the total incidence of ADRS in treatment groups



DISCUSSION:

According to study conducted by **Pengcheng He** et al..,(2018)., there is no difference between both groups with respect to cure time but our study proved that low molecular weight heparin is rapid in cure rate compared to unfractionated heparin. These results were similar with the study conducted by **Tajeldin M Abdallah** et al., in which low molecular weight heparin has better cure rate.

In our study Relapse rate and cure rate of unfractionated heparin group was found to be 36.84% (Fig.15),64.82% (Fig:17) respectively low molecular weight heparin whereas 20.51% (Fig.15),79.48%(Fig:17) for group. According to study conducted by **Ahmed M** et al., there is very less percentage of cure rate in low molecular weight heparin group but our study showed that the better cure rate is achieved with low molecular weight heparin group compared to unfractionated heparin group. With usage of drugs along with advantages there are some disadvantages also in terms of occurrence of side effects. To the maximum extent physician tries to select the drug with maximum efficacy and low incidence of side effects i.e., maximum tolerability. In our study unfractionated heparin group has more no. of side effects compared to low molecular weight heparin group. In the unfractionated heparin group, rash and epistaxis are the major side effect experienced by subjects with incidence of 14.28% (n= **11**, In fig.18) and epistaxis with the incidence of 13.15% (n=5, Fig.18) whereas in the low molecular weight heparin group, rash and epistaxis is not a major side effect compared with unfractionated heparin with incidence of rash 7.89% (n= **6**, In Fig.18) and epistaxis with 5.19% (n=4, fig.18). Perhaps if we compare overall incidence of all side effects in both groups it shows rash with incidence of 22.07%(n=17, fig.18) and epistaxis with incidence of 11.68% (n=9, fig.18) for unfractionated heparin and low molecular weight heparin groups respectively. It clearly states that low molecular weight heparin group is better tolerable in terms of side effect profiles. Unfractionated heparin group has major incidence of rash and epistaxis than side effects compared to low molecular weight heparin group.

CONCLUSION:

Based on our current prospective observational study we concluded that males were predominant than females. Myocardial infarction is mostly caused by smoking and alcohol with comorbidities of hypertension and diabetes mellitus in this region. It showed that low molecular weight heparin with aspirin was effective than unfractionated heparin with aspirin in terms of cure rate and relapse rate, and had fewer incidences of adverse effects in the treatment of myocardial infarction. So, low molecular weight heparin with aspirin can be used effectively over unfractionated heparin with aspirin in the management of myocardial infarction as it had low Relapse rate and better Cure rate with less incidence of Adverse drug reactions.

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