ORIGINAL ARTICLE

Incidence of Heparin-Induced Thrombocytopenia in Patients Treated with Unfractionated Versus Low Molecular Weight Heparin after Acute Coronary Syndrome

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ABSTRACT

Objective: To compare the incidence of heparin-induced thrombocytopenia with the use of unfractionated versus low molecular weight heparin.
Study Design: Case-control type of study.
Place and duration of study: Department of Cardiology, Bahawal Victoria Hospital Bahawalpur from 1st October 2011 to 31st March 2012.
Methodology: All the patients presenting with the diagnosis of acute coronary syndrome and getting either low molecular heparin (LMWH) or unfractionated heparin (UFH) were enrolled. We recorded the data regarding age, gender, diagnosis, previous history of exposure to UFH, the type of heparin being administered and the timing of onset of thrombocytopenia. Platelet counts of all these patients were monitored after every 24 hours. Clinical scoring for probability of heparin-induced thrombocytopenia was done. The data was analyzed using SPSS software version 10.
Results: Overall frequency of heparin induced thrombocytopenia was 2.7 %. There was a significant difference in the frequency of HIT in the two patient groups exposed to LMWH and UFH respectively
Conclusion: Risk of heparin-induced thrombocytopenia is less with the use of unfractionated heparin.
Keywords: Low molecular weight heparin, Unfractionated heparin, Heparin-induced thrombocytopenia.

INTRODUCTION

Heparin is a drug widely used for thromboprophylaxis or treatment in many clinical situations, including cardiovascular surgery and invasive procedures, acute coronary syndromes, venous thrombo-embolism, atrial fibrillation, peripheral occlusive disease, dialysis and during extracorporeal circulation[1-3]. After seven decades of clinical use, heparin still remains the most commonly used anticoagulant in clinical practice. Heparin use in medical practice is increasing due to the increase in the number of vascular interventions and aging population. It is estimated that up to 30% of in-hospital patients need some form of heparin during their hospital stay and 600,000 new cases of heparin-induced thrombocytopenia (HIT) are reported every year[4,5].

Heparin induced thrombocytopenia (HIT) is a relatively common immune mediated disorder with the potential for serious thromboembolic complications. It is associated with the use of unfractionated heparin and may be defined as a decrease in platelet count during or shortly after exposure to this anticoagulant.[6-8] HIT is divided into 2 types.[,14] Type 1 HIT or nonimmunologically mediated thrombocytopenia or heparin-associated thrombocytopenia, is associated with a larger dose of heparin[4,9] Type 2 HIT or immunologically mediated thrombocytopenia is caused by heparin-dependent antibodies[4,10]. Patients classically present with a low platelet count (<150,000 per cubic millimeter) or a relative decrease of 50 percent or more from baseline[11-13], although the fall may be less (e.g., 30-40%) in some patients. Thrombotic complications develop in approximately 20-50% of patients[12,13]. A delay of 5 to 10 days is typical in patients who have had no exposure, whereas precipitous declines in platelet counts (within hours) occur in patients with a history of recent exposure to heparin[7,13].

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METHODOLOGY

The study was conducted in the department of Cardiology, Bahawal Victoria Hospital Bahawalpur from 1st October 2011 to 31st March 2012. All the patients presenting with the diagnosis of acute coronary syndrome (unstable angina as well as acute myocardial infarction) and getting either low molecular heparin (LMWH) or unfractionated heparin (UFH) were enrolled. Patients with any autoimmune

or connective tissue disease (like SLE), chronic liver disease and renal failure were excluded from the study because thrombocytopenia accompanying these comorbid conditions could lead to mis-interpretation of results. We recorded the data regarding age, gender, diagnosis, previous history of exposure to UFH, the type of heparin being administered and the timing of onset of thrombocytopenia (if occurred) in a pre-designed proforma. Platelet counts of all those patients who were included in the study were monitored after every 24 hours. The patients were divided into two groups based upon whether they were getting UFH or LMWH. The data was analyzed using Statistical Package for Social Sciences (SPSS) software version 10.

RESULTS

During the study period 517 patients were enrolled. Of these, 393 got UFH during hospital stay and 124 got LMWH. Any patient who developed thrombocytopenia (platelet count < 100,000/cmm) during or shortly after exposure to heparin was suspected of having heparin induced thrombocytopenia and the probability of HIT was determined using the so called '4Ts' clinical scoring system[4,15,16] as shown in Table 1. Majority of patients (65%) were males. Characteristics of the patients are given in Table 2. Overall frequency of heparin induced thrombocytopenia according to the clinical score was 2.7%. There was a significant (p <0.001) difference in the frequency of HIT in the two patient groups exposed to LMWH and UFH respectively (Table 3).

Table 1: Clinical scoring system for heparin-induced Thrombocytopenia

Parameters	Clinical score		
	2	1	0
Thrombocytopenia	>50% platelet fall	30%-50%	< 30%
Timing of thrombo-cytopenia	Day 5-10	> Day 10	< Day 4
Thrombosis	Proven new thrombus	Recurrent progressive thrombosis	None
Other possibilities of thrombocyto-penia	None	Possible	Definite

Total score 0-3 Low probability; 4-5 Moderate probability; 6-8 High probability of HIT

Table 2: Characteristics of the patients

Variable	Value
Mean age (years)	
Male	49 ± 9
Female	56 ± 7
Gender	
Male	n = 338
Female	n = 179
Diagnosis	
Unstable angina	n = 269
Myocardial infarction	n = 248
Mean baseline platelet count ($\times 10^9$/L)	208 ± 51
Frequency of HIT	n = 14
HIT in LMWH	n = 1
Hit in UFH	n = 13
Mean time of onset (days) after exposure	7 ± 2
Previous exposure to UFH	n = 1
Decrease in platelet count	
<30%	n = 0
30 -50%	n = 3
>50%	n = 11
Clinical Score	
0 – 3	n = 0
4 – 5	n = 2
6 – 8	n = 12

Table 3: Frequency of HIT in patients exposed to LMWH versus UFH

	=n
LMWH	
Hit	1
No hit	123
UFH	
Hit	13
No hit	380

P value <0.001

DISCUSSION

Heparin-induced thrombocytopenia is caused by antibodies against complexes of platelet factor 4 (PF4) and heparin. These antibodies are present in nearly all patients who receive a clinical diagnosis of the disorder.[13,17] In patients with heparin-induced thrombocytopenia, the thrombotic risk is more than 30 times that in control populations.[13,18] Previously published data report an incidence of heparin-induced thrombocytopenia of 0.5-5 % in patients treated with heparin after acute ischemic stroke or acute coronary syndrome.[1,6,19,20] The results of our study are also consistent with those reported earlier. The shortcoming of our study is that we couldn't carry out the antibody assay because of lack of the facility at local level. So we had to rely upon clinical scoring

only. Moreover the study showed that the risk of developing heparin-induced thrombocytopenia is significantly lessened by using low molecular weight heparin instead of unfractionated heparin. Constantly increasing incidence of risk factors for stroke as well as coronary artery disease and subsequently the acute ischemic strokes and acute coronary syndrome is, at the same time, increasing the number of patients needing anticoagulation. Heparin is a commonly used anticoagulant in the hospital settings. In order to decrease the incidence of heparin induced thrombocytopenia, the use of LMWH should be encouraged instead of UFH.

CONCLUSION

Low molecular weight heparin is a relatively safer alternative to unfractionated heparin as an anticoagulant because it poses a lesser risk of heparin-induced thrombocytopenia.

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