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Clinical presentation and evaluation of the utility of the 4t scoring system in the diagnosis of heparin induced thrombocytopenia among patients at sultan qaboos university hospital

Abstract

Objectives: Heparin induced thrombocytopenia (HIT), albeit uncommon, is a potentially fatal complication heparin therapy. Early diagnosis and prompt intervention has been shown to prevent catastrophic thrombotic complications seen in patients with this condition. The aim of this study is to evaluate the frequency of HIT among Sultan Qaboos University Hospital (SQUH) patients and assess the utility of the 4T scoring system (which is validated clinical tool that predicts the likelihood of HIT).

Methods: This is a retrospective cohort study. All patients who were suspected to have HIT and had a HIT assay (by ELISA) between June 2006 and December 2014 were identified from the LabTrack system. Data were collected on their clinical presentation, outcome and the variables included in the 4T scores (i.e. degree of thrombocytopenia, timing of thrombocytopenia, evidence of thrombosis and absence of other causes of thrombocytopenia) were collected using the electronic patient records. The total 4T scores were calculated. Sensitivity, specificity and negative and positive predictive values were calculated.

Results: Out of 129 consecutive patients, 64 were males and 65 were females. Mean age was 57years. 9% had thrombosis (% venous, % arterial and % both). 0(and 0%) had a low 4T score (score 0-3), 3(2%) had intermediate (score 4-5) and 6(4.6%) had high scores (score 6-8). 9(7%) of all patients were positive (HIT ELISA optic Density >1.0 unit) and 120(92%) were negative. A positive result was seen in 0 (0%) of the low risk group, 3(2%) of the intermediate risk group and 9(7%) of the high risk group.

Conclusion: The study illustrates the validity of the 4Ts scoring system in our patient population with high negative predictive value, in agreement with the published literature. In addition, it illustrates the over use of resources and highlights the need to improve the awareness among clinician about this validated predictive tool to avoid over investigation or over treatment

Keywords: heparin induced thrombocytopenia, 4T scorning system, catastrophic thrombosis, ELISA, SQUH

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Introduction

The use of heparin have increased in the last years in hospitalized both as prophylaxis and therapeutic. One of the encounter complications of heparin especially with unfractionated heparin though it can be seen with Low molecular weight heparin is thrombocytopenia which could be transient non immune or more badly the immune mediated type heparin induced thrombocytopenia (HIT). Heparin-induced thrombocytopenia is a profoundly dangerous, potentially lethal, immunologically mediated adverse drug reaction to unfractionated heparin or, less commonly to low molecular weight heparin.[1] Despite thrombocytopenia, bleeding is rare; rather, HIT is strongly associated with thromboembolic complications involving both the arterial and venous systems.[2] Recent data show that up to 8% of heparinized patients will develop the antibody associated with HIT and that approximately 1-5% of patients on heparin will progress to develop HIT with thrombocytopenia.[3]

The diagnosis can be made utilizing a clinical scoring system based on the pretest probability of HIT known as the 4Ts: Thrombocytopenia, Thrombosis, Timing, and other causes[4] showed in Table 1. For the laboratory tests two general types of assays can be used to detect antibodies.[3,4] Most widely commercial enzyme immunoassays test for antibodies reactive against PF4/heparin: ELISA test are very sensitive (91% to >97%), whereas a negative test strongly suggests the absence of HIT.[4] In contrast, platelet activation assays detect HIT antibodies.

Upon their platelet-activating properties.[4] However the functional assays are usually not available in all centers and difficult to perform. Diagnosis of HIT requires both the clinical criteria of the 4Ts score supported by the laboratory investigations. It usually challenging in hospitalized patients as majority of the patients will have other causes of thrombocytopenia and also not all physicians are applying the 4Ts score for the pretest probability as recent studies have shown.[5–7] The primary objective of this study is to evaluate the frequency of HIT among Sultan Qaboos University Hospital (SQUH) patients and the secondary objective is to assess the utility of the 4T scoring system (which is validated clinical tool that predicts the likelihood of HIT).

Table 1 A clinical scoring system based on the pretest probability of HIT

Parameters/ point	0	1	2	Total Score
Thrombocytopenia	Drop in platelets <30% and platelets nadir <10 x109	Drop in platelets 30-50%	Drop in platelets>50%	0-3 is low risk
Timing	>15days or <4days	uncertain	5-10days, less than 4 if patient exposed to heparin in the last 3month	4-5 is moderate risk
Thrombosis	none	Progression of previous thrombosis	New thrombosis	6-8 is high risk
Other causes	Definite	probable	none	

Method

All records from patients admitted between June 2006 and December 2014 different wards including internal medicine, general surgery, intensive care unit, cardiothoracic and orthopedic and who had antiPF4/heparin test done were identified from the Lab Track system and screened. There were no specific inclusion criteria, all patients who received heparin (either LMWH or UF heparin) and suspected to have HIT were included. Data collection including demographic data, diagnosis, the 4T scores (i.e. degree of thrombocytopenia, timing of thrombocytopenia, evidence of thrombosis and absence of other causes of thrombocytopenia), outcome and the type of alternative treatment positive patients have received. Due to retrospective design of the study some data were not documented by the physicians in charge that may led to potentially biasing in overall score either by over or under estimation of the score. The data and the result were extracted from the electronic medical records from the lab track and track care system. The screening cut-off for different groups were according to the current 4T scoring system and was as followed: low score was ≤3, intermediate 4-5 and high risk groups >5. The laboratory testing for antiF4/hearing was done by ELIZA test. The diagnosis was established by hemostasis consultant by fulfilling the current recommendation of positive testing along with intermediate and high pretest 4T score.

The primary outcome: the frequency of HIT positive patients among all included patients in the study. The secondary outcome measures: I) Sensitivity, specificity, positive predictive value and negative predictive value of 4T scoring system in correlation with the result of ELIZA testing. II) The frequency of patients who have their 4T scoring documented in their files before ordering the test. Statistical analysis of the continuous data was reported as mean± slandered deviation or by median. Categorical variables were expressed as percentage. Further analysis was done using IBM SPSS window version 20.0. This study was approved by our local ethical committee on 25/8/2013.

Results

Between June 2006 and December 2014, about 129 patients who had anti PF4/heparin testing. Hence there were no exclusion criteria in our study all 129 patients were included. Patients' characteristics are summarized in Table 2. The 4Ts score was actually not documented in the file of the majority of the patients (only 3% had the 4Ts score documented in their medical records. Therefore the 4Ts score was computed from the data available in the medical records of the hospital (Track care system) and the test result from the Lab track.

81patients were in the low risk group (with 4Ts score 1-3) and about 42patients are in the intermediate group (with 4Ts score 4-5) and 6patients were in the high risk group. 9(7%) of all patients were positive (HIT ELISA optic Density >1.0unit) and 120(92%) were negative. A positive result was seen in 0 (0%) of the low risk group, 3(2%) of the intermediate risk group and 6(7%) of the high risk group. The characteristic of patients with positive HIT assay were summarized in Table 3. For the 4Ts score, the sensitivity was 100% and the negative predictive value was .The specificity was 98.7 % and the positive predictive value of 87% (Tables 4–6).

Table 2 Patients' characteristics

Characteristics	N (%)
Gender	
Male	64(49.6)
Female	65(50.4)
Median age	60(14-80)
Type of Heparin	
LMWH	94(72.1)
UFH	35(27.9)
Patient Location	
Medical	86(66.7)
ICU	37(28.7)
Surgical	6(4.6)

Table 3 Characteristic of patients with HIT

Age	Sex	Type of heparin	4Ts Score	Anti-PF4/ heparin result	Alternative therapy	Outcome
33years	Female	LMWH	4	Positive	NA	NA
50years	Males	LMWH	6	Positive	Fondaparinux	Recovered
52years	Female	LMWH	5	Positive	Fondaparinux	Recovered
70years	Male	UF	6	Positive	NA	NA
65years	Male	LMWH	6	Positive	Fondaparinux	Recovered

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Table Continued....

Age	Sex	Type of heparin	4Ts Score	Anti-PF4/ heparin result	Alternative therapy	Outcome
66years	Male	LMWH	4	Positive	NA	NA
75years	Female	UF	4	Positive	NA	NA
51years	Female	LMWH	2	positive	NA	NA
14years	Female	UF	4	positive	NA	NA

Table 4 Score category of negative & positive cross tabulation

Test Result	Score category of negative & positive			
		Negative	Positive	Total
Negative	Count	81	1	82
	% within test-result	98.80 %	1.20 %	100.00 %
	% within Score category of Negative & Positive	100.00 %	14.30 %	93.20 %
Positive	Count	0	6	6
	% within test-result	0.00 %	100.00 %	100.00 %
	% within Score category of Negative & Positive	0.00 %	85.70 %	6.80 %

Table 5 Chi-square tests

	Value	df	A Symp. Sig. (2-sided)	Exact Sig. (2-Sided)	Exact Sig. (1-Sided)
Pearson Chi-Square	74.509[a]	1	0		
Continuity Correction[b]	61.628	1	0		
Likelihood Ratio	38.067	1	0		
Fisher's Exact Test				0	0

Table 6 Symmetric measures

		Value	Asymp. Std. Error	Approx.Tb	Approx. Sig.
Measure of Agreement	Kappa	0.917	0.082	8.632	0
N of Valid Cases		88			

Discussion

This study showed that majority of anti-PF4 /heparin was performed on internal medicine patients who are thrombocytopenic with low 4Ts score probability. Using pretest probability decision of low score to avoid testing for HIT could avoid testing in all patients with low score (81patients with low 4Ts score 62% of all patients). Overall, there were rare cases with documented 4Ts score in their medical records which indicate infrequent use of this validated score.

From our study there were no clear causes could be attributed to the infrequent use of 4Ts score as it was retrospective observation. However, we can speculate that the reason for this could be attributed to first: lack of awareness and knowledge about the 4Ts score and it is usefulness as a negative predictive score as previous similar studies have showed. Second ,there was no restriction for ordering antiPF4/heparin from the homeostasis laboratory and consultant .In our institute there was no policy to fill the 4Ts score prior of ordering the test and any patient with low 4Ts score should not have the test ordered. As previously published the high sensitivity of 4Ts score was also observed in our cohort study to rule out HIT. As well the specificity of 4Ts score was reasonably high in keeping with recent published retrospective studies, though this should be interpreted with caution due to small size of patients and not all cases with positive antiPF4/ heparin were confirmed with functional tests. It was interesting that in the majority of the cases whenever heparin was replaced, it was with fondaparinux though it was not firmly recommended at that time but there was no progression of thrombosis or new thrombosis in majority of the cases.

Conclusion

Our study has some limitations. First the retrospective design of the study may affect the accurate calculation of the 4Ts score as compare to prospective study. However, some variables in 4Ts most likely will not be affected such as thrombocytopenia and the time of platelets drop as it was recorded in the laboratory system as objective measures. There were maybe some bias in the thrombosis events and other causes of thrombocytopenia that may be not documented well in the medical records of the patients. Second, the small size may be a concern for the accuracy of the result however with 62% of the patients tested with antiPF4/heparin and were negative and there are in the low risk group is reasonably precise estimate.

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Conflict of interest

The author declares no conflict of interest.

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