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Original Research Article.

Prevalence and Clinical Predictors of Heparin Induced Thrombocytopenia

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ABSTRACT

Back Ground: Heparin induced thrombocytopenia (HIT) is thrombocytopenia or thrombosis with one or more positive tests for HIT antibodies. To diagnose HIT, platelet count monitoring; at least every other day until hospital discharge for day 14 (whichever occurs sooner). A platelet count fall of 50% or greater from baseline or any thrombosis occurs 5 to 10 days after heparin starting with exclusion or other causes of thrombocytopenia are highly suggestive of HIT. Laboratory confirming assays are helpful as platelet activations assay. Management of HIT includes discontinuing of any type of heparin and using an alternative anticoagulant as DTIs (liperudin, argatropan, bivalerudin). Warfarin should be delayed pending substantial recovery of the platelet account.

Methods: This study was conducted to 100 patients receiving heparin in a variety of clinical settings to assess the prevalence of HIT trying to identify clinical predictors of such complication. To all these patients platelet count every other day from base line to day 14 was done then the 4T score system was applied to all patients.

Results: Only 6 patients developed HIT; 4 of them developed thrombosis and 3 patients died in hospital due to these thromboembolic events. UFH, surgical treatment and first heparin exposure were the clinical predictors of HIT.

Conclusion: HIT is a serious and life threatening complication of heparin therapy that should be early diagnosed and properly managed to prevent its thromboembolic complications.

Keywords: Heparin, Unfractionated Heparin (UFH), Thrombocytopenia.

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INTRODUCTION

Although the prevalence of HIT has decreased with the use of low molecular weight heparin in the past ten years, HIT remains a life threatening prothrombotic state.

HIT can be complicated by thrombosis even after withdrawal of heparin, explaining why substituting heparin with an alternative anticoagulant (danaproid, leprudin, argatroban) is always necessary. However, management by these alternative treatments is difficult.[1]

AIM OF THE STUDY

- To assess the prevalence of heparin induced thrombocytopenia in patients receiving heparin
- To identify clinical predictors of such complication.

PATIENTS AND METHODS

100 Consecutive patients of either sex in Nile and Ain-Shams hospitals were included in an observational single arm study. Heparin and its derivatives were indicated in a variety of clinical setting (medical treatment, surgical treatment, cardiac surgery, pregnancy and children) in variable durations of therapy and variable doses. According to presence or absence of HIT; patients were divided into two groups: Group 1: Patients who didn't develop thrombocytopenia and Group II: Patients who developed thrombocytopenia. All patients assigned written informed consent at baseline. Thrombosis or other sequelae (maximum points for new thrombosis, skin lesions or acute systemic reaction), ant other causes for thrombocytopenia excluded.

Table 1: Demographic and baseline characteristics

Variable		No.	%
Age	M	47	-
	SD	22	-
sex	Male	50	50%
	Female	50	50%
Type of treatment	Medical	50	50%
	Non cardiac surgery	30	30%
	Cardiac surgery	20	20%
Type of heparin	LMWH	50	50%
	UFH	50	50%
Previous exposure to heparin	Yes	39	39%
	No	61	61%
Different co-morbidities	Diabetes mellitus	16	16%
	Hypertension	11	11%
	Chronic renal failure	14	14%
	Respiratory disease	5	5%
	Smoking	5	5%
	Pregnant patients	10	10%
	Pediatrics.	10	10%

Table 2: HIT According to platelet count

Platelet count by day	Final result	N	M	SD	t	p
Day 0	Group1	94	260.33	93.299	1.6	>0.05
	Group II	6	224.67	49.103		
Day2	Group1	94	246.70	88.654	2.2	<0.05
	Group II	6	165.69	59.547		
Day4	Group1	94	243.12	88.250	2.3	<0.05
	Group II	6	161.17	40.543		
Day6	Group1	94	241.32	89.045	2.7	<0.05
	Group II	6	141.14	56.001		
Day8	Group1	94	241.89	89.264	3.1	<0.05
	Group II	6	129.00	65.263		
Day10	Group1	94	244.77	88.538	2.8	<0.05
	Group II	6	143.00	57.515		
Day12	Group1	94	246.27	88.264	2.7	<0.05
	Group II	6	149.17	56.757		
Day14	Group1	94	245.88	88.848	2.3	<0.05
	Group II	6	161.17	52.632		

Group1=(-VE); Group II=(+VE); N: Number, M: Mean, SD: Standard deviation; P>0.05= No statistical significance; P<0.05= Statistical significance; P<0.05= High statistical significance; Group I (-VE): Patient who didn't develop HIT; Group I (-VE): Patient who develops HIT.

Table 3: Platelet count at baseline and follow up

Platelet count by day	Group I (n)	Group II (n)
Day 0	260 ± 93	225 ± 49
Day 2	247 ± 89	165 ± 60 (1)
Day 4	243 ± 88	161 ± 40 (1)
Day 6	241 ± 89	141 ± 56 (1)
Day 8	242 ± 89	129 ± 65 (1)
Day 10	245 ± 89	143 ± 58 (1)
Day 12	246± 88	149 ± 57(1)
Day 14	246 ± 89	161 ± 53 (1)

P value < 0.05 between groups; P value <0.05 within grops

Table 4: HIT according to age

Age	N	M	SD	t	P
Group I(-VE)	94	45.66	22.091	1.9	>0.05
Group II (+VE)	6	62.83	5.707		

N: number, M mean, SD: standard deviation.

Table 5: HIT according to sex

Sex	Male	Female	Total
Group I(-VE)	47	47	94
Group II (+VE)	3	3	6
Total	50	50	100

Table 6: HIT according to type of treatment

Type of treatment	Medical	Surgical	Total	X2	P
Group I(-VE)	49	45	94	1.6	>0.05
Group II (+VE)	1	5	6		
Total	50	50	100		

Table 7: HIT according to type of heparin

Total of heparin	LMWH	UFH	Total	X2	P
Group I(-VE)	48	46	94	0.8	>0.05
Group II (+VE)	2	4	6		
Total	50	50	100		

Table 8: HIT according to previous exposure to heparin

Previous exposure	No	Yes	Total	X2	P
Group I(-VE)	56	38	94	1.3	>0.05
Group II (+VE)	5	1	6		
Total	61	39	100		

Table 9: HIT in pregnant and non-pregnant females

Pregnancy	Non pergnant	pregnant	Total	X2	P
Group I(-VE)	37	10	47	0.02	>0.05
Group II (+VE)	3	0	3		
Total	40	10	50		

Table 10: HIT according to site of thrombosis

Site of thrombosis	No	Venous	Arterial	Total	X2	P
Group I (-VE)	94	0	0	94	65.2	>0.05
Group II (+VE)	2	3	1	6		
Total	96	3	1	100		

Table 11: Clinical probability of HIT

Clinical probability	No.	%
NAD	94	94%
Low	1	1%
Intermediate	4	4%
High	1	1%
Total	100	100%

Table 12: Predictors of HIT

Variable		No.	%	P value	OR
Sex	Male	3	50%	_	1
	Female	3	50%		
Type of heparin	UFH	4	66.5%	>0.05	2.1
	LMWH	2	33.5%		
Type of treatment	Medical	5	82%	>0.05	5.1
	Surgical	1	18%		
Previous exposure	Yes	1	18%	>0.05	3.4
	No	5	82%		

RESULTS AND DISCUSSION

Heparin induced thrombocytopenia (HIT) as an immune reaction in response to platelet factor 4-heparin complexes, with results in increased platelet activation and thrombocytopenia beginning on the 4th-5th day after heparin exposure induced by 1gG antibody production.

Platelet microparticle formation contributes to venus thrombosis.[2] Accurate diagnosis of HIT is based on the presence of clinical features, including a 50% fall in platelet count, appropriate timing of thrombocytopenia development of new thrombosis and the absence of a more likely cause of thrombocytopenia.

Documentation of an anti-PF4 heparin antibody is necessary, but is not sufficient to make the diagnosis since antibody formation occurs in a variety of clinical setting without the development of thrombocytopenia or thrombosis.[2]

Once HIT is suspected or confirmed, all forms of heparin should be discontinued and an aleternative from the anticoagulation should be administered until the platelet count recovers. Treatment options include intravenous administration of argatroban, lepirudin and bivlirudin, subcutaneous administration of fondaparinux has also been described. Wafarin therapy, if indicated, should be avoided until platelet recovery. Re-exposure to heparin can be avoided by use of alternative antricoagulants for most circumstance.[2]

In this observational, single arm study we tested the prevalence, predictors and outcome of HIT depending in diagnosis on application of the 4T score system on all patients after platelet count monitoring for two weeks and clinical follow u of all patients for the development of thromboembolic events.

The main finding of out study were that the total prevalence of HIT was 6% according to clinical diagnosis based on the 4T score system and most of these patients (66%) were intermediate clinical probability. Also we found that UFH therapy (OR: 2.1), surgical treatment (OR: 5.4) and first exposure to heparin (OR 3.4) were predictors for the development of HIT.

Other findings were that HIT was common in older rather than younger patients (mean age: 63 years) and very rare in children and had adverse outcome as 4 patients (66%) had thromboembolic events, mostly venous (3 patients) and 3 patients (50%) died in hospital due to such complication.

We also found that, no different between males and females in the development to HIT and although it is common in females it is very rare during pregnancy. Furthermore patients undergoing cardiac surgery have the highest risk of developing HIT.

Consistent with previous studies on HIT and its outcome, HIT occurred in only a small number of our patients, but it remains a serious and life threatening problem.

In a study by Warkentine et al, 2003 2.4% of the patients who underwent cardiac surgery developed HIT.[3] Five to 10 days after cardiac surgery.

In another population Warkentine et al, reported that 3% of patients who underwent orthopedic surgery developed HIT. Among non-surgical medical patients 1% developed HIT after heparin administration.

In 2005 Warkentine et al reported in a prospective study on 665 patients participating in clinical trial of UFH versus LMWH after orthropedic surgery, that HIT is more common in patients received UFH rather than patients received LMWH as 9 of 665 patients developed HIT, all of them received UFH.[4]

CONCLUSION

The previously of HIT is 6% in this study population as only 6 of 100 patients developed HIT.

Unfractionated heparin surgical treatment and first heparin exposure were the clinical predictors of HIT. HIT have an adverse outcome and high mortality rates as most patients developed life threatening thromboembolic complications.

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