INTERNATIONAL JOURNAL OF CLINICAL
AND BIOMEDICAL RESEARCH

Research article

HEPARIN INDUCED THROMBOCYTOPENIA AND HEMODIALYSIS

AMAL S. ELHASSADE[1*], AHLAM MOHAMED BEN NASER[2]

AUTHOR DETAILS

[1]Faculty of medical technology, Derna, Libya.
[2]Faculty of medical technology, Department of laboratory medicine, Derna, Libya.

Corresponding author email:
email: elhassade.amal@gmail.com

ABSTRACT

Unfractionated heparin is the most commonly used anticoagulant for hemodialysis (HD). It is well-known that heparin can cause immune-mediated thrombocytopenia due to immunoglobulin antibody formation against the complex of platelet factor 4 (PF4) and heparin. Heparin may also contribute to HD-associated platelet activation, thrombocytopenia, and increased PF4 release from platelets during a heparin dialytic session. The present study was conducted to study the effect of unfraction heparin as anticoagulant in newly treatment hemodialysis patients. **Material and method**: A sample of 72 people were selected, 32 patients on dialysis for first time from unite of kidney dialysis. At the same time a group of 40 randomly selected healthy adults to participate in the study as control. By Automated cell counter (sysmex X 21) platelets from all patients on dialysis before starting heparin and after one month later were estimated. **Result**: The mean value of platelets in patients after treated with heparin was significant lower $(192.3 \pm 20.7) \times 10^9/l$ as compare before treated with heparin $203 \pm 20.7 \times 10^9/l$ (P = 0.001). **Conclusion:** From this study, heparin as anti-coagulant has effect on decrease platelets count but still patients have no thrombocytopenia platelets level $\geq 150 \times 10^9/l$.

Keywords: unfractionated heparin, anticoagulant, dialysis, thrombocytopenia.

INTRODUCTION

Unfractionated heparin (heparin) is the most commonly used anticoagulant for hemodialysis (HD)[1]. Heparin can cause serious adverse effects including heparin induced thrombocytopenia (HIT) which is a common serious and potentially life threat condition.

Heparin may also contribute to HD-associated platelet activation, thrombocytopenia, and increased PF4 release from platelets during a heparin dialytic session [2]. Typically, IgG isotype HIT antibodies develop after 5-14 days of heparin exposure. The incidence of heparin-induced thrombocytopenia (HIT) was estimated at 3.9% in newly treated hemodialysis patients[3]. Also, dialysis is often complicated by clotting of the dialysis lines and/or dialyzer due to hypercoagulation regardless of

the etiology. When a diagnosis of HIT based on clinical symptoms of thrombocytopenia and immunoassay for PF4/heparin complex antibodies is employed, it remains unclear whether a few patients have HIT. An antigen-based immunoassay to detect the presence of antibodies in a patient's circulation that binds to the PF4/heparin complex is highly sensitive but less specific. Two different types of HIT are recognized. The first, HIT type I also called heparin induced thrombocytopenia in the past, this form affect up to 10% of patients under treatment with heparin and is characterized by mild and transient asymptomatic thrombocytopenia (rarely less than 100×10^9 /l) that develops early usually within the first two days of starting heparin and disappears quickly once heparin is withdraw.

The second form of HIT, HIT type II, is immune mediated and associated with a risk of thrombosis. It has been proposed that the term HIT type I be changed to non- immune heparin associated thrombocytopenia and that the term HIT type II be changed to HIT to avoid confusion between the two syndrome. [4]

MATERIAL AND METHODOLOGY

Study design : A case control study was designed evaluate platelets count in patients on dialysis before starting heparin and after stopping heparin and compared platelets count with healthy individual not using heparin.

Ethical approval: Approval was granted from the Research and Ethics Committee of the faculty. Consent was gotten from all participated patients.

Sample size and sampling method: A sample of 72, 32 were on hemodialysis and 40 were healthy individual were included in the study and measure platelets count by automated cell counter for all.

Inclusion criteria: patients on hemodialysis aged 15 year and more were selected from unite of dialysis, most of them were the first time for dialysis, control aged 20 and all had no history of any medical problem may affect platelets count .

Exclusion criteria: the study include healthy individual who use any drugs affect platelets count and haveing any previous disease affect platelet

Methodology: Five ml of blood samples from all patients and controlled were collected by vein puncture in EDTA container. A whole blood specimen containing formed cellular elements, 20 µl of blood is diluted with a premeasured 1.9 ml volume of ammonium oxalate, sorensens phosphoate buffer, thimerosal, and purified water. Fresh capillary or anticoagulant whole blood is added to the diluents, which lyses erythrocytes but preserves platelets for 1:10 dilution of the blood [4]. The diluted specimen is added to a hemocytometer for manual enumeration of platelets in special circumstances. By Automated cell counter (sysmex X 21) platelets from all patients on dialysis before starting heparin and one month later were estimated.

Statistical analysis: Result are expressed as mean values ± SD. Data were analyzed by t test using. Significant difference was considered to exist at P value less than 0.05.

RESULTS

Total of 72 sample were included in this study, 40 normal healthy persons were included in the study as control subject mean age (25.06 ±3.73) with a range 20-50 year and they were clinically healthy and free of any serious illness.

Thirty-two patients were selected from the unit of kidney dialysis from Al-wahda, Teaching Hospital, Derna, mean age (42.3±16.8) with a range (15-90) year. The mean value of platelet count in patients before starting heparin 203×10^9/l with standard deviation ± 20.7 while mean value with standard deviation after one month $192.3 \pm 20.7 \times 10^9$/l. The mean platelets count in healthy individual 267.09 with standard deviation 69.0×10^9/l. By applying unpaired t test, we found that, there were significantly decreased value of platelets count between patients before starting heparin and healthy individual $P \leq 0.01$ as in table 1, and there was significant decrease in platelet before starting heparin and after one month of stopping it $P \leq 0.001$ as in table 2.

Table 1. Platelet in pregnant, non pregnant

Parameters	Healthy individual (10^9/l)	Patients before starting heparin (10^9/l)
Mean ± SD	267.09 ± 69	209.29 ± 57.4
P –value	≤ 0.01	

Table 2. Comparing Platelets count level $\times 10^9$ /l in patients requiring hemodialysis before starting heparin and after stopping heparin

Parameters	Before treatment	After treatment
Number of patients	32	32
Mean ± SD	203.0 ± 20.7	192.3 ± 20.7
P- value	$P \leq 0.001$	

DISCUSSION

Heparin induced thrombocytopenia is the development of thrombocytopenia due to administration of the forms of anticoagulant (anti-blood clotting inhibitor) heparin.

Unfractionated heparin is the most commonly used anticoagulant for hemodialysis[5] (HD). It is well-known that heparin can cause immune-mediated thrombocytopenia due to immunoglobulin antibody formation against the complex of platelet factor 4 (PF4) and heparin. Heparin may also contribute to HD-associated platelet activation, thrombocytopenia, and

increased PF4 release from platelets during a heparin dialytic session[6]. Typically, IgG isotype HIT antibodies develop after 5- 14 days of heparin exposure. The incidence of heparin-induced thrombocytopenia (HIT) was estimated at 3.9% in newly treated hemodialysis patients[7]. Also, dialysis is often complicated by clotting of the dialysis lines and/or dialyzer due to hypercoagulation regardless of the etiology. When a diagnosis of HIT based on clinical symptoms of thrombocytopenia and immunoassay for PF4/heparin complex antibodies is employed, it remains unclear whether a few patients have HIT.

Few reports on the frequency of HIT in dialysis patients are known, although heparin is employed as the most useful anticoagulant during dialysis. It was believed that the frequency of HIT would be low in a survey targeting to all dialytic patients including both acute and chronic stages[8]. Two surveys involving different subjects show quite different figures on the frequency of HIT. A relatively high frequency of 3.2% was reported for newly treated subjects receiving dialysis in three months[9], and a low rate frequency of 0.6% is described in chronic dialysis patients treated for over 3 months[10,11]. Thus, the frequency of HIT in a dialysis population is different between newly treated and chronic maintained dialytic groups. HIT in the former shows a similar incidence to the heparin-sensitive group, and HIT in the later group is rarely identified as HIT or recurrence of HIT when a patient experiences changes in the immunological tolerance brought about by cardiovascular surgery, orthopedic surgery, and high-dose administration of erythropoietin with an adverse platelet-stimulating reaction.

This study include all patients who were first time on dialysis (newly treated) and come to the unite monthly platelets count before starting heparin, in comparing with healthy individual was significantly lower, Mean ± SD (209 ± 57.4) as compare to healthy controls (267.09 ± 69) × 109/l $P \leq 0.001$.

At the same time platelets count level was significant decrease in patients after taking heparin (192.0 ± 20.75) as compare before start to take heparin (203.0 ± 20.7) × 109 /l.

heparin as anti-coagulant has effect on decrease platelets count but still patients have not thrombocytopenia platelets level ≥ 150 × 109/l.

CONCLUSION

Heparin induced non immune thrombocytopenia since with decreasing in platelets count there were no symptoms of thrombosis, it's a benign form not associated with an increase risk of thrombosis, the mechanism of HIT type I is still unknown but it is likely to be non-immune, probably related to its platelet pro-aggregating effect.

REFERENCES

1. Sonawane S, Kasbekar N, Berns JS. The safety of heparins in end-stage renal disease. Semin Dial. 2006;19:305-10.
2. Matsuo T, Chikahira Y, Yamada Y, Nakao K, Uesima S, Matsuo O. Effect of synthetic thrombin inhibitor (MD805) as an alternative drug on heparin induced thrombocytopenia during hemodialysis. Thromb Res. 1988;52; 165-71.
3. Nakao K, Yamada T, Matsuo O. Effect of a new anticoagulant (MD 805) on platelet activation in the hemodialysis circuit. Thromb Res. 1986; 41: 33-41.
4. Yamamoto S, Koide M, Matsuo M, Suzuki S, Ohtaka M, et al. Heparin-induced thrombocytopenia in hemodialysis patients. Am J Kidney Dis. 1996;28:82-5.
5. Koepke JA. Platelet count'. practical Laboratory Hematology 1991; 24:293-6.
6. Sonawane S, Kasbekar N, Berns JS. The safety of heparins in end-stage   renal disease. Semin Dial. 2006;19:305-10.
7. Matsuo T, Chikahira Y, Yamada Y, Nakao K, Uesima S, Matsuo O. Effect   of synthetic thrombin inhibitor (MD805) as an alternative drug on heparin induced thrombocytopenia during hemodialysis. Thromb Res. 1988;52; 165-71.
8. Yamamoto S, Koide M, Matsuo M, Suzuki S, Ohtaka M, Saika S, Matsuo T. Heparininduced thrombocytopenia in hemodialysis patients. Am J Kidney Dis. 1996;28:82-5.
9. Hutchison CA, Dasgupta I. National survey of heparin-induced thrombocytopenia in the haemodialysis population of the UK population. Nephrol Dial Transplant.2005;20:444-6.
10. Yamamoto S, Koide M, Matsuo M, Suzuki S, Ohtaka M, Saika S, Matsuo T. Heparin induce thrombocytopenia in hemodialysis patients. Am J Kidney Dis. 1996;28:82-5 .
11. Matsuo T, Kobayashi H, Matsuo M, Wanaka K, Nakamoto H, Matsusima H, Sakai R. Frequency of anti-heparin-PF4 complex antibodies (HIT antibodies) in uremic patients on chronic intermittent hemodialysis. Pathphysiol Haemost Thromb. 2006;35:445-50.