WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 8, 194-199. Research Article ISSN 2277– 7105

HEPARIN INDUCED THROMBOCYTOPENIA AND HEMODIALYSIS

Amal S. Elhassade*[1], Mukul Tailang[3] and Ahlam Mohamed Ben Naser[2]

[1]Faculty of Medical Technology, Derna, Libya.

[2]Faculty of Medical Technology, Department of Laboratory Medicine, Derna Libya.

[3]S.O.S. in Pharmaceutical Sciences, Jiwaji University, Gwalior (M.P.) India.

Article Received on
13 June 2016,

Revised on 03 July 2016,
Accepted on 23 July 2016

DOI: 10.20959/wjpr20168-6783

***Corresponding Author**
Dr. Amal S. Elhassade
Faculty of Medical
Technology, Derna, Libya.

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 unfractionated heparin as anticoagulant agent in newly treatment of hemodialysis patients. **Material and method**: Samples from 72 persons were selected. Out of which 32 patients were on dialysis for first time in Alwahda teaching hospital, Derna-Libya and at the same time a group of 40 healthy adults were randomly selected to participate in the study as control. Platelets from all the patients on dialysis before starting heparin treatment and one month after heparin treatment were estimated by Automated cell counter (Sysmex X 21). **Result**: The mean platelet value in patients after the treatment with heparin was significantly lower (192.3 ± 20.7) × 10^9/l than the non-treated group (203 ± 20.7 × 10^9/l) (P = 0.001). **Conclusion:** Present studies reveal that heparin, as anti-coagulant agent, significantly decreases platelet count without producing thrombocytopenia.

KEYWORDS: Thrombocytopenia, PF4, immunoglobulin.

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 threatening condition.

Heparin may also contribute to HD-associated platelet activation, thrombocytopenia, and increases the release of PF4 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 hyper coagulation 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, affects 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 withdrawn. The second form, HIT type II, is immune mediated and is 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]

MATERIALS AND METHODS

Study design

A case control study was designed to evaluate platelets count in patients on dialysis before starting heparin and after stopping heparin treatment and the results were compared with the platelets count of healthy individual not using heparin.

Ethical approval

Approval was granted from the Research and Ethics Committee of the faculty. Consent from all the participated patients was also taken.

Sample size and sampling method

A sample of 72 individuals, 32 on hemodialysis and 40 healthy individuals were included in the study. Platelets count was measured by automated cell counter for all the subjects.

Inclusion criteria

Patients on hemodialysis aged 15 year and more were selected; most of them were on dialysis for the first time. Control group, aged 20 and above had no history of any medical problem.

Exclusion criteria

The study includes healthy individuals who did not use any drug which may affect platelets count and did not have any previous history of any disease which affects platelet count.

METHODOLOGY

Platelets count from all the patients on dialysis before starting heparin and one month later were estimated by Automated cell counter (sysmex X 21).

Five ml of blood sample from all individuals were collected by vein puncture in EDTA container. A whole blood specimen contained formed cellular elements. A 20µl of blood was diluted with a premeasured 1.9 ml volume of ammonium oxalate, Sorensens phosphoate buffer, thimerosal and purified water. Fresh capillary or anticoagulant whole blood was added to the diluents, which lyses erythrocytes but preserves platelets for 1:10 dilution of the blood.[4] The diluted specimen was added to a hemocytometer for manual enumeration of platelets in special circumstances.

Statistical Analysis

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

RESULTS

A total of 72 samples were included in this study. Out of which, 40 normal persons, clinically healthy and free of any serious illness with a mean age of 25.06 ±3.73 years ranging from 20-50 years of age were included as control. Thirty two patients with a mean age of 42.3±16.8 years ranging from 15 - 90 year of age were selected from the unit of kidney dialysis from Al-wahda Teaching Hospital, Derna, The mean value of platelet count in patients before starting heparin treatment was found to be 203±20.7 × 10^9/l while the same after one month

of heparin treatment was 192.3 ± 20.7 × 10^9/l. However, the mean platelets count in healthy individual was found to be 267.0 ±69.0 × 10^9/l.

By applying unpaired t-test, it was found that there was a significant decrease in platelets count in patients before starting heparin and healthy individual ($P \leq 0.01$) (Table 1) and before starting heparin and after one month of stopping the treatment ($P \leq 0.001$) (Table 2).

TABLE 1: COMPARISON OF PLATELET COUNT IN HEALTHY INDIVIDUAL AND PATIENTS BEFORE STARTING HEPARIN TREATMENT

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: COMPARISON OF PLATELET COUNT IN PATIENTS REQUIRING HEMODIALYSIS BEFORE AND AFTER HEPARIN TREATMENT

Parameters	Before treatment (× 10^9 / l)	After treatment (× 10^9 / l)
Number of patients	32	32
Mean ± SD	203.0 ± 20.7	192.3 ± 20.7
P- value	P ≤ 0.001	

DISCUSSION

Heparin induced thrombocytopenia is the development of thrombocytopenia due to administration 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.[7] 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[8] and a low rate frequency of 0.6% is described in chronic dialysis patients treated for over 3 months.[10] 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.

The present study includes all patients who were on dialysis for the first time. Monthly platelet count before starting heparin treatment ($209 \pm 57.4 \times 10^9$/l, $P \leq 0.001$), as compared to healthy individual ($267.09 \pm 69 \times 10^9$/l, $P \leq 0.001$) was found to be significantly lower.
At the same time platelet count level was significantly decreased in patients after heparin treatment ($192.0 \pm 20.75 \times 10^9$/l, $P \leq 0.001$) as compared to the same before starting heparin treatment ($203.0 \pm 20.7 \times 10^9$/l, $P \leq 0.001$).

Heparin as anti-coagulant has an effect on decreasing platelet count without producing thrombocytopenia.

CONCLOSION

With decrease in platelets count there were no symptoms of thrombosis which shows that it's a benign form not associated with an increased 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. (2006) 'The safety of heparins in end-stage renal disease' *Semin Dial,* 19: 305-310.
2. Matsuo T, Chikahira Y, Yamada Y, Nakao K, Uesima S, Matsuo O. (1988) 'Effect of synthetic thrombin inhibitor (MD805) as an alternative drug on heparin induced thrombocytopenia during hemodialysis' *Thromb Res,* 52: 165-171.
3. T, Nakao K, Yamada T, Matsuo O (1986) 'Effect of a new anticoagulant (MD 805) on platelet activation in the hemodialysis circuit' *Thromb Res,* 41: 33-41.

4. Yamamoto S, Koide M, Matsuo M, Suzuki S, Ohtaka M, et al. (1996) 'Heparin-induced thrombocytopenia in hemodialysis patients' *Am J Kidney Dis*, 28: 82-85.
5. Koepke JA. 'Platelet count'. Practical Laboratory Hematology, 1991; 24: 293-296.
6. Sonawane S, Kasbekar N, Berns JS. (2006) 'The safety of heparins in end-stage renal disease' *Semin Dial*, 19: 305-310.
7. Matsuo T, Chikahira Y, Yamada Y, Nakao K, Uesima S, Matsuo O. (1988) 'Effect of synthetic thrombin inhibitor (MD805) as an alternative drug on heparin induced thrombocytopenia during hemodialysis' *Thromb Res*, 52: 165-171.
8. Yamamoto S, Koide M, Matsuo M, Suzuki S, Ohtaka M, Saika S, Matsuo T. (1996), 'Heparininduced thrombocytopenia in hemodialysis patients' *Am J Kidney Dis*, 28: 82-85.
9. Hutchison CA, Dasgupta I. (2005), 'National survey of heparin-induced thrombocytopenia in the haemodialysis population of the UK population' *Nephrol Dial Transplant*, 20: 444-446.
10. Yamamoto S, Koide M, Matsuo M, Suzuki S, Ohtaka M, Saika S, Matsuo T. (1996), 'Heparin induce thrombocytopenia in hemodialysis patients' *Am J Kidney Dis*, 28: 82-85.
11. Matsuo T, Kobayashi H, Matsuo M, Wanaka K, Nakamoto H, Matsusima H, Sakai R. (2006), 'Frequency of anti-heparin-PF4 complex antibodies (HIT antibodies) in uremic patients on chronic intermittent hemodialysis' *Pathphysiol Haemost Thromb*, 35: 445-450.