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Heparin-Induced Thrombocytopenia in Pediatrics Mini Review

Andrea Carolina Zarate Vergara[1], María Alexandra Pérez Sotelo[2] and Irina Suley Tirado Pérez[3*]

[1]Pediatric Intensive Care, University of Santander, Santander, Colombia

[2]Department of Pediatric Oncology Hematology, International Hospital of Colombia, Colombia

[3]Master Pediatric Palliative Care, University of Santander, Santander, Colombia

[*]**Corresponding author:** Irina Suley Tirado Pérez, Master Pediatric Palliative Care, Graduate Student o f Pediatric Intensive Care, University of Santander, Colombia, E-mail: irinasuley@gmail.com

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Abstract

The use of heparin has a potential risk of developing heparin-induced thrombocytopenia, which, although infrequent, is of great importance due to high morbidity and mortality that requires rapid diagnosis and timely treatment. A clinical case of a patient with dilated cardiomyopathy, with extracorporeal support is described, which is anticoagulated with heparin by protocol, presenting an adverse effect little reported in the literature such as heparin-induced thrombocytopenia requiring Fondaparinux with failure to start bivalirudin.

Keywords: Bivalirudin; Heparin-induced; Thrombocytopenia; ECMO; Pediatrics

Introduction

Heparin is a medicine widely used in pediatrics as well as in adults for prophylaxis and treatment of thromboembolism, maintenance of permanent arterial and venous cannulas, cardiac catheterization, cardiopulmonary bypass, extracorporeal membrane oxygenation, dialysis, anticoagulation in special cases such as deficiency of S protein and cases of antiphospholipid, this drug is an anticoagulant have a potential risk of developing heparin-induced thrombocytopenia [1,2]

Heparin-Induced Thrombocytopenia (HIT) is very infrequent in the pediatric population; reported cases are related to anticoagulation in cardiac pathology or post-surgical major surgery, this adverse reaction is presented as a prothrombotic disorder through antibody-mediated platelet activation [3,4]. Although this disorder is rare and its frequency has decreased with the use of low molecular weight heparin, in a patient exposed to cardiac surgeries it maintains a constant frequency. A relationship has also been found in the presentation peaks with the highest frequency of cases of thrombosis, which occurs mostly in neonates and adolescents [1,5].

This pathology has a high morbidity and mortality which is why timely diagnosis is essential, we must bear in mind that there are factors that can increase the risk of presenting this pathology when he is under anticoagulation with heparin, which can be hereditary by immobilization and by major surgery. Complications are serious and lead to thromboembolism [1]. Therefore, a clinical case of an adolescent patient submitted to oxygenation by extracorporeal membrane, with systemic anticoagulation with heparin that presents thrombocytopenia induced by this is described, leading to require initiation of management with bivalirudin.

Clinical Case

Adolescent of 12 years with diagnosis of dilated cardiomyopathy, with decompensated cardiac failure that required support with extracorporeal venoarterial oxygenation membrane during fifteen days, studying with pulmonary edema, requiring catheterization where end-diastolic pressure of the left ventricle of 41 mmhg is confirmed by what is performed atrioseptostomía, with end-diastolic pressure after the still high procedure of 31 mmhg, anticoagulated with heparin, during its evolution it is presented with thrombocytopenia and clots in the circuits, for which they request assessment by hematology service, it is suspected heparin-induced thrombocytopenia for which the patient required management with fondaparinux while bivalirudin was available and due to renal failure requires venovenous hemofiltration, fondaparinux was started by clots in the continuous circuits, posteriorly, peritoneal dialysis was started, which he tolerated adequately.

Discussion

Heparin thrombocytopenia is described in 5% of the general population, in children undergoing cardiac surgery are described with a prevalence of 1%-3% with an increase in the incidence in recent years that may correspond to the increase in knowledge of this adverse effect [2].

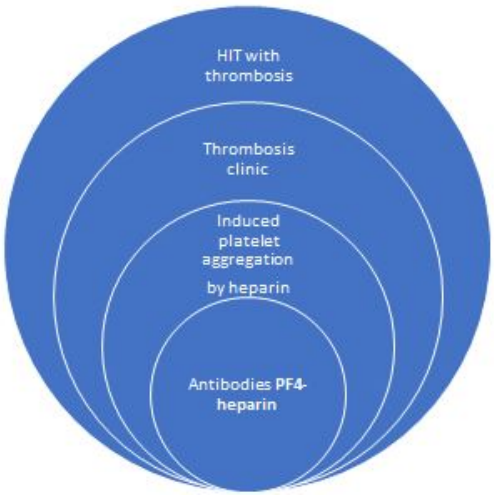

Figure 1: Relationship between ATC anti pf4-heparina and HIT clinic.

This adverse effect of heparin is produced by the formation of a complex against heparin, which leads to platelet activation and the production of thrombin. Platelet α-granules produce platelet factor 4 (PF4), which is a highly active protein. positive that after heparin exposure, it binds to it and neutralizes its action, producing a PF4-heparin complex that serves as a primary antigen for antibodies such as IgG that bind to the exposed complexes of PF4, generating IgG compound -PF4-heparin, which bind and thus activate the platelets, which will generate new propagation of the cycle leading to thrombosis [6,7] **(Figure 1)**. Thrombocytopenia is produced by elimination of platelets by the reticuloendothelial system or by the massive aggregation of these in the formation of thrombi, also the antibodies of patients with heparin-induced thrombocytopenia stimulate monocytic cells to express tissue factor and secrete interleukin 8, leading to the production of thrombin, the latter is very important in the treatment by direct thrombin inhibitors **(Figure 2)**.

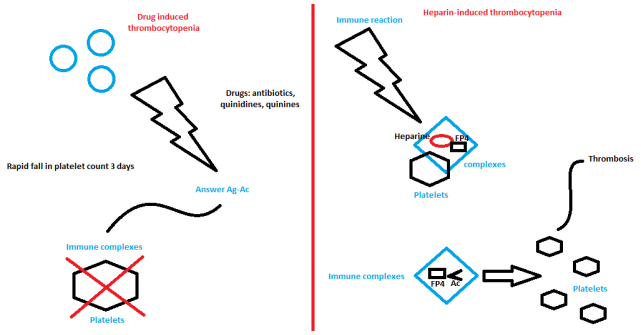

Figure 2: Representation of Drug induced thrombocytopenia and Heparin-induced thrombocytopenia.

Our patient required anticoagulation for being a carrier of cardiac heart disease with ECMO requirement and cardiac surgery having strong risk factors to potentially develop heparin-induced thrombocytopenia, as well as belonging to the most frequent age group with this adverse effect. This effect occurs approximately 4 days after the onset of heparin producing platelet depletion that may be accompanied by a thrombotic or hemorrhagic event or in the presence of heparin-dependent antibodies, the latter are not always present, in a study in pediatric patients undergoing cardiac surgery with Management with anticoagulation for extracorporeal circulation with heparin, obtaining only antibody isolation in 1.4% of patients [8], so in our patient, although these antibodies were not performed or if a negative result was obtained, they did not exhibit this adverse event, others study God also shows that in patients undergoing cardiac surgery they have a lower prevalence of anti FP4 antibodies [9,10]. The 4ts score is used to determine the risk of HIT that assigns scores based on the degree of thrombocytopenia, timing of thrombocytopenia, thrombosis or other sequelae, other causes of thrombocytopenia [11-13].

The mainstay of the treatment is the suspension of heparin and the use of the direct inhibitors of thrombin bind to 3 active sites and 2 exosites in thrombin and inhibits the formation of fibrin. Which are danaparoid, lepirudin and argatroban and bivalirubin. A molecule of these 20 amino acid polypeptides binds to thrombin, which transiently inhibits thrombin, which is increasingly used for anticoagulation in ECMO [12], was used in our patient, which is bivalirudin. Fondaparinux until obtaining bivalirudin which has been used as a good alternative in pediatric population when there is no greater option to anticoagulation [14-17]

Conclusion

Heparin-induced thrombocytopenia is a fatal affectation in the pediatric population due to its high morbidity and mortality, which is why it is necessary to understand its pathophysiology to identify its clinical presentation early, to know its risk factors, to timely suspend the anticoagulation with heparin and to initiate if requires alternative anticoagulants.

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