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Incidence of heparin-induced thrombocytopenia type II and postoperative recovery of platelet count in liver graft recipients: a retrospective cohort analysis

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ARTICLE INFO

Article history:
Received 28 May 2013
Received in revised form
4 August 2013
Accepted 30 August 2013
Available online 25 September 2013

Keywords:
Anticoagulation
Heparin-induced thrombocytopenia
High-risk recipient
Liver transplantation

ABSTRACT

Background: Thrombocytopenia in patients with end-stage liver disease is a common disorder caused mainly by portal hypertension, low levels of thrombopoetin, and endotoxemia. The impact of immune-mediated heparin-induced thrombocytopenia type II (HIT type II) as a cause of thrombocytopenia after liver transplantation is not yet understood, with few literature citations reporting contradictory results. The aim of our study was to demonstrate the perioperative course of thrombocytopenia after liver transplantation and determine the occurrence of clinical HIT type II.

Method: We retrospectively evaluated the medical records of 205 consecutive adult patients who underwent full-size liver transplantation between January 2006 and December 2010 due to end-stage or malignant liver disease. Preoperative platelet count, postoperative course of platelets, and clinical signs of HIT type II were analyzed.

Results: A total of 155 (75.6%) of 205 patients had thrombocytopenia before transplantation, significantly influenced by Model of End-Stage Liver Disease score and liver cirrhosis. The platelet count exceeded 100,000/μL in most of the patients ($n = 193$) at a medium of 7 d. Regarding HIT II, there were four (1.95%) patients with a background of HIT type II.

Conclusions: The incidence of HIT in patients with end-stage hepatic failure is, with about 1.95%, rare. For further reduction of HIT type II, the use of intravenous heparin should be avoided and the prophylactic anticoagulation should be performed with low-molecular-weight heparin after normalization of platelet count.

All authors read and approved the final version of the manuscript.
The author(s) declare that they have no competing interests. No funding.

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0022-4804/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2013.08.034

1. Introduction

Unfractionated heparin (UFH) sodium or low-molecular-weight heparin (LMWH) is used in anticoagulant protocols at several transplant institutions to prevent deep vein thrombosis after liver transplantation. A well-described side effect of heparin administration is the heparin-induced thrombocytopenia type II (HIT type II). The pathophysiology of HIT type II consists of an immune-mediated development of thrombocytopenia with the formation of IgG antibodies against heparin when it is bound to the platelet factor 4 [1]; thrombocytopenia is caused by the resulting platelet activation with the formation of blood clots leading to the clinical presentation of thromboses [2]. The clinical probability of HIT type II can be estimated using the 4Ts test scoring model [3]. The enzyme-linked immunoabsorbent assay (ELISA) test is commonly used as an HIT type II screening modality because it is widely available, simple, and rapid. The optical density (OD) of the ELISA results correlates with clinical probability of HIT [4].

In patients with end-stage liver dysfunction scheduled for liver transplantation thrombocytopenia is common due to various reasons. In the period before transplantation, thrombocytopenia originated in patients with liver cirrhosis or advanced hepatic fibrosis, on the one hand from portal hypertension or augmented splanchnic flow to the portal venous system leading to hypersplenism with sequestration of platelets in the spleen and consecutive thrombocytopenia [5,6] and on the other hand from reduced platelet production because of low levels of thrombopoetin and endotoxemia [7].

In the early period after transplantation, mild to moderate thrombocytopenia is a common disorder as well. Many factors can contribute to early postoperative thrombocytopenia. Apart from sequestration of platelets in the liver graft as a predominant mechanism, the other primary reasons for this include immunologic injury, hemodilution, platelet consumption, and graft dysfunction [8–11]. The role of HIT type II, especially in the postoperative setting, is not yet understood. In the current literature, there are contrary results and the prevalence of HIT type II after liver transplantation is still unclear. The aim of the present study was to analyze the occurrence of HIT type II. We, therefore, retrospectively analyzed the platelet course in patients disposed for liver transplantation from admission to the hospital until 3 wk after transplantation and evaluated the medical records for the occurrence of HIT type II. We assessed the variables predictive of thrombocytopenia and analyzed the impact of thrombocytopenia on outcome and the role of HIT type II in pre- and posttransplant thrombocytopenia.

2. Patients and methods

2.1. Patients and study design

In this single-center study, we retrospectively enrolled 205 consecutive patients with end-stage or malignant liver disease, who had undergone full-size, orthotopic liver transplantation between January 2006 and December 2010 in the transplantation surgery center of the University Hospital of Tübingen. We reviewed retrospectively the medical data of the patients beginning from admission to the hospital and analyzed the perioperative course of thrombocytes. Serial platelet counts were obtained from the medical records starting the day before liver transplantation and 0, 1, 3, 5, 7, 10, 13, 16, 21, and 25 d after liver transplantation to determine the postoperative course of thrombocytes to detect atypical pre- or postoperative courses of platelets. Pretransplant variables assessed included recipient age, underlying liver disease, Model of End-Stage Liver Disease (MELD) score, and Child-Pugh score.

2.2. Study objectives

The primary objective was to show the occurrence of HIT type II after liver transplantation. The secondary objective was to show the course of thrombocytopenia after transplantation.

2.3. Classification of thrombocytopenia

Pretransplant thrombocytopenia was classified according to the platelet count based on common toxicity criteria from the National Cancer Institute as follows: group 1: 150,000/μL (lower limit normal) to 75,000/μL; group 2: 75,000/μL to 50,000/μL; group 3: 50,000/μL to 25,000/μL; and group 4: <25,000/μL.

2.4. Immunosuppression

According to the standard of care, our standard immunosuppression protocol consisted in the administration of prednisone, basiliximab, tacrolimus, and mycophenolate mofetil. In case of viral hepatitis type C, the immunosuppression was performed with cyclosporine instead of tacrolimus.

2.5. Anticoagulation

Our standard postoperative anticoagulation was initiated 6 h after transplantation using intravenous UFH (5000 IU/d) for deep vein thrombosis prophylaxis. The dose was chosen according to a target partial thromboplastin time of 35–40 s during the intensive care treatment and changed into subcutaneous LMWH on the normal ward.

2.6. Definition of HIT type II

Clinical suspicion of HIT was based on newly developing pre- or postoperative thrombocytopenia, atypical course of existing thrombocytopenia, and/or the occurrence of thrombotic events. All patients suspected for HIT type II were assigned retrospectively to the 4T score. HIT was considered positive when all the following criteria were met: (1) platelet count <100,000/μL and a 30%–50% decrease in the platelet count, (2) no other cause of thrombocytopenia, (3) positive IgG-ELISA (>0.5 OD/mn) and/or heparin-induced platelet activation (HIPA) test, (4) time of heparin treatment over 5 d, and (5) recovery of the platelet count after discontinuation of the heparin treatment.

2.7. Statistical analysis

Statistical analysis, including multivariate analysis, was performed using SPSS software, version 20 (SPSS, Inc, Chicago,