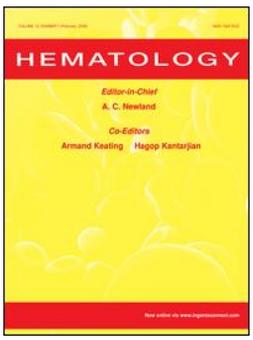

Taylor & Francis
Taylor & Francis Group

Hematology

ISSN: (Print) 1607-8454 (Online) Journal homepage: https://www.tandfonline.com/loi/yhem20

Concomitant use of argatroban and warfarin during hemodialysis in heparin-induced thrombocytopenia

Fabrizio Vianello, Lucrezia Furian, Maurizio Nordio, Martina Treleani & Fabrizio Fabris

To cite this article: Fabrizio Vianello, Lucrezia Furian, Maurizio Nordio, Martina Treleani & Fabrizio Fabris (2015) Concomitant use of argatroban and warfarin during hemodialysis in heparin-induced thrombocytopenia, Hematology, 20:1, 48-49, DOI: 10.1179/1607845414Y.0000000157

To link to this article: https://doi.org/10.1179/1607845414Y.0000000157

Published online: 28 Feb 2014.

Case report

Concomitant use of argatroban and warfarin during hemodialysis in heparin-induced thrombocytopenia

Fabrizio Vianello[1], Lucrezia Furian[2], Maurizio Nordio[3], Martina Treleani[1], Fabrizio Fabris[1]

[1]Department of Medicine, Internal Medicine Unit, Padua, Italy, [2]Kidney and Pancreas Transplantation Unit, Department of Surgery and Organ Transplantation, University of Padua, Padua, Italy, [3]Nephrology and Dialysis Unit, Camposampiero District Hospital, Padua, Italy

Objective and importance: The use of argatroban during hemodialysis in a patient receiving warfarin is not established. We present a case of heparin-induced thrombocytopenia in a patient on hemodialytic therapy who successfully received argatroban concomitantly to warfarin during renal replacement therapy.
Clinical presentation: A 46-year-old male patient with autosomal dominant polycystic kidney disease presented with heparin-induced thrombocytopenia (HIT) arised during dialytic procedures.
Intervention: After the acute episode requiring argatroban and warfarin therapy, the patient continued to receive argatroban during the hemodialytic session concomitantly to warfarin.
Conclusion: The administration of argatroban in the dialytic circuit of a patient on oral anticoagulant therapy can be considered an effective and safe approach.

Keywords: Heparin-induced thrombocytopenia, Hemodialysis, Argatroban

A 46-year-old male patient with autosomal dominant polycystic kidney disease underwent unilateral nephrectomy for chronic pain. Two weeks later the patient was readmitted with abdominal pain and fever. Acute pancreatitis was diagnosed. Due to low urine output and worsening renal function, the patient underwent peritoneal dialysis and subcutaneous prophylactic dalteparin was started (2500 U). During the dialytic session respiratory distress and hypotension developed and the patient was transferred to intensive care unit. Peritoneal cell fluid count was consistent with secondary peritonitis and the patient was started on wide spectrum antibiotic treatment.

On day 5 from heparin prophylaxis, thrombocytopenia developed (from 397 to $54 \times 10^{9/L}$). Catheter-related internal jugular vein thrombosis was detected by duplex ultrasound (US). A high pretest clinical scoring system (4Ts) for HIT was calculated.[1]

Heparin-related IgG (H/PF4 Abs) were detected at high titre (3901 OD, n.v.<450 OD) using a commercial PF4/polyanion enzyme-linked immunosorbent assay (Genetic Testing Inc., GTI, Waukesha, Wisc., USA). The result was confirmed by visual examination of heparin-induced platelet activation assay. The patient was started on argatroban and switched to warfarin at complete platelet count recovery ($>150 \times 10^{9/L}$).

One month later the patient was readmitted with acute abdominal pain, vomiting, constipation, and gross hematuria due to cyst rupture. Warfarin was stopped and the patient underwent left nephrectomy. Reassessment of heparin-related Abs showed persistence of anti-heparin abs at a lower titre (523 OD) whereas US scan found residual thrombosis of the right upper limb and recent deep vein thrombosis (DVT) of the left upper limb. The patient was then started on argatroban maintaining aPTT at 1.5 to 3 times baseline. On day 15 from nephrectomy the patient was switched to warfarin.

Hemodialysis was then started on a three times a week schedule, using synthetic polysulfone membranes. Blood flow rate ranged from 150 to 250 ml/minute with a bicarbonate dialysates at a flow rate of 2000 ml/hour. Argatroban was administered in the dialytic circuit as a 125-μg/kg bolus followed by 1.5 μg/kg/minute. aPTT was measured before and

Correspondence to: Fabrizio Vianello, Internal Medicine Unit, Department of Medicine, Padova University School of Medicine, Padova 35128, Italy. Email: fabrizio.vianello@unipd.it

DOI 10.1179/1607845414Y.0000000157

during argatroban administration. The mean baseline aPTT (n.v. 22–32 seconds) before argatroban (while on warfarin only), was 35.4 seconds (range 26–40) whereas the aPTT during argatroban administration in the dialytic circuit was 50.7 seconds (range 39–60). The patient was then put in the kidney transplant list. Three months later the allograft became available and the patient was successfully transplanted with full renal function recovery. As in the pre-operative evaluation anti-heparin antibodies were not found, prophylaxis was carried out with fondaparinux.

Argatroban, a synthetic direct thrombin inhibitor with a relative short elimination half-life and predominant hepatic clearance, has been systematically studied in patients with HIT and thrombosis, demonstrating a safe and effective profile in this setting. As its pharmacokinetic and pharmacodynamic are not significantly affected by renal dysfunction, the use of argatroban has been successfully exploited in the setting of hemodialysis in end-stage renal disease. Several regimens of argatroban have been studied and found to be equally effective and safe in patients with end-stage renal disease during hemodialysis.[2] However, no data are available on the use of argatroban in the hemodialytic circuit in patients on oral anticoagulation.

Our case report is of interest as it describes an unaddressed clinical situation related to the use of argatroban during hemodialysis in a patient receiving warfarin for a recent episode of HIT and thrombosis. Of importance, the patient was at that time on a transplant waiting list.

The issue of administering argatroban in the dialytic circuit of a patient on oral anticoagulant therapy may be arguable. In fact, warfarin use as a sole anticoagulant during hemodialysis could have been considered. However, therapeutic or low-dose warfarin in renal replacement therapy has been reported to be associated to high rate of hemodialysis catheter failure[3] and clearly this was our major concern in view of the recent thrombophilic condition experienced by our patient.

Whether alternative methods of anticoagulation are preferable (including saline flushing, citrate) has not been systematically investigated.[4,5]

The dose of argatroban to be administered concurrently to warfarin was empirically chosen based on guidelines suggested for HIT.[5] In this setting, INR $\geq$ 4 is recommended based on the high risk of thrombosis at a lower INR in patients with HIT. As our goal was to avoid fibrin strands or sludging in the dialyzer circuit while minimizing the bleeding risk, argatroban was administered with the purpose to keep a therapeutic INR below 4 and an aPTT at about 1.5 the basal value. Although with all the limitations of a single experience, this protocol was successfull either in avoiding bleeding as well as in reaching a successful anticoagulation.

Finally, just a short comment on the choice to administer fondaparinux in the peri-transplant period. According to published guidelines, a short-time heparin course may have been considered in our patient as platelet factor 4/heparin antibodies were absent at the time of transplantation.[5] This reasoning comes from experiences in the different clinical scenario of the cardiopulmonary bypass.[5] In this setting, a restricted exposure to heparin to the operative period does not elicit HIT antibodies. However, exposure to heparin in our case would have been on a regular basis with the purpouse of hemodialysis, therefore jeopardizing the condition of HIT remission.

Argatroban can be safely considered in hemodialysis patients on oral anticoagulants with a recent history of HIT.

Disclaimer statements

Contributors FV wrote the paper. MN was responsible for the hemodialytic protocol. LF evaluated all laboratory and clinical data and followed up the patient. MT was responsible for anti-PF4/heparin assays. FF reviewed the case and all data.

Funding None.

Conflicts of interest None.

Ethics approval Not applicable.

References

1 Lo GK, Juhl D, Warkentin TE, Sigouin CS, Eichler P, Greinacher A. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. J Thromb Haemost. 2006;4(4):759–65.
2 Murray PT, Reddy BV, Grossman EJ, Hammes MS, Trevino S, Ferrell J, *et al.* A prospective comparison of three argatroban treatment regimens during hemodialysis in end-stage renal disease. Kidney Int. 2004;66(6):2446–53.
3 Bennett WM. Should dialysis patients ever receive warfarin and for what reasons? Clin J Am Soc Nephrol. 2006;1(6):1357–9.
4 O'Shea SI, Ortel TL, Kovalik EC. Alternative methods of anticoagulation for dialysis-dependent patients with heparin-induced thrombocytopenia. Semin Dial. 2003;16(1):61–7.
5 Warkentin TE, Greinacher A, Koster A, Lincoff AM. Treatment and prevention of heparin-induced thrombocytopenia: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(6 Suppl):340S–80S.