Letter to the Editor

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Prevalence of Heparin-Induced PF4-Heparin Antibodies in Hemodialysis Patients

Dear Sir,

Heparin-induced thrombocytopenia (HIT) associated with severe thrombotic events is a well-recognized complication of heparin therapy. The frequency of HIT varies widely in different reports and cumulative data suggest a prevalence of about 1–5% in patients treated with unfractionated heparin [1, 2]. In most cases HIT manifests with platelet counts below 100×10^3/ml within 5–10 days after heparin therapy. An immunological mechanism has been emphasized to be involved in the development of HIT and thrombosis [3, 4]. It has been proposed that heparin complexed to platelet factor 4 (PF4) is a target for IgG antibodies. The immune complexes generated consist of heparin, PF4 and IgG, bind to circulating platelets via the Fc receptor and induce a cycle of platelet activation and consumption. Paradoxically, thromboembolic complications may develop in some patients with HIT, possibly by in vivo platelet activation [5]. Based on this hypothesis, an enzyme-linked immunosorbent assay (ELISA) was recently developed to detect anti-PF4-heparin antibodies in the serum of HIT patients [3].

The available data on the frequency of HIT mainly concern patients receiving heparin during a relatively short period of time [2]. Since patients on hemodialysis are repeatedly exposed to heparin, one might expect a higher frequency of heparin-dependent antibodies associated with HIT in this group of patients. In the present study we investigated the prevalence of antibodies against PF4-heparin complexes in patients on regular hemodialysis. Patient characteristics are outlined in table 1. All patients were treated 3 times a week with unfractionated heparin consisting of a single intravenous bolus injection (1,000–5,000 IU) at the beginning of each dialysis session followed by continuous infusion (1,000–2,000 IU/h) for 4–5 h. Blood samples were collected at the beginning of a hemodialysis session for platelet counts. IgG antibodies to PF4-heparin complexes were detected by an ELISA as described by Amiral et al. [3]. The results are given as the optical density at 492 nm. Using healthy subjects ($n = 20$, $OD < 0.25$) and positive standards as controls, an $OD > 0.5$ was considered positive.

In only 1 of our patients was the platelet count $< 100 \times 10^3$/μl, but in this patient heparin-induced antibodies were not detected. However, anti-PF4-heparin IgG antibodies were found in 2 patients (OD 0.6 and 1.6) with normal platelet counts. None of the 2 patients had thromboembolic complications and no unexpected clot formation in dialyzers or extracorporeal circuits was observed during an observation period of 6 months following the blood sampling. In our study the prevalence of IgG antibodies to PF4-heparin complexes in patients with end-stage renal failure on chronic hemodialysis was 2.8%. The finding is consistent with a previous report [6], where the prevalence of heparin-dependent antibodies in hemodialysis patients was 2.3% and the presence of these antibodies was also not associated with the clinical picture of HIT.

The prevalence of HIT seems to be higher at the beginning of hemodialysis treatment. In 3.9% (6 of 154) of patients newly treated with hemodialysis, Yamamoto et al. [7] observed HIT with thromboembolic events within 60 days after initiation of treatment, and 5 of 6 patients had positive levels of anti-PF4-heparin antibodies. Similar observations were made in orthopedic patients who received low-dose heparin for prophylaxis against deep venous thrombosis [2]. In summary our data demonstrate that hemodialysis patients, who are repeatedly exposed to heparin over a long period of time, have a low prevalence of antibodies to PF4-heparin complexes. The clinical relevance of these antibodies is as yet unknown but their presence does not seem to be associated with the clinical picture of HIT. However, the detection of heparin-dependent antibodies seems to be relevant during the first weeks after initiation of hemodialysis [7, 8].

Table 1. Characteristics of hemodialysis patients

Number of patients	70
Sex	
Male/female	41/29
Mean age, years (± SD)	54 ± 13
Mean duration of hemodialysis, months (± SEM)	75 ± 9
Primary renal diseases	
Chronic glomerulonephritis	22
Polycystic kidney disease	11
Diabetic nephropathy	10
Interstitial nephritis	10
Nephrosclerosis	9
Others	8

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Announcement

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