

First report of renal replacement therapy using hemodialysis in a patient with severe hemophilia B in Uruguay: a clinical challenge

Primer reporte de terapia de reemplazo renal mediante hemodiálisis en paciente con hemofilia B grave en Uruguay: un desafío clínico

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Case presentation

Hemophilia B is an X-linked genetic bleeding disorder that results in a deficiency of coagulation factor IX. It has an estimated incidence of 5 cases per 100,000 male births, being much less frequent than hemophilia A¹.

Advances and greater availability of treatments for hemophilia have increased the life expectancy of these patients, which currently approaches that of the general population². This has led to a parallel increase in age-associated comorbidity, such as cardiovascular diseases, chronic kidney disease (CKD), and cancer³.

The increasing prevalence of CKD in patients with hemophilia is also associated with various risk factors (Table 1), making a multidisciplinary approach essential for its prevention⁴. In cases of end-stage renal disease, renal replacement therapy (RRT) in patients with hemophilia represents a unique challenge due to their hemorrhagic risk, the scarcity of available standardized clinical practice guidelines, and the complexity in selecting the dialysis modality, vascular access, and

administration of clotting factor before or after the procedure.

The objective of this article is to report the first case of a patient with severe hemophilia B and end-stage CKD requiring RRT by hemodialysis in Uruguay. This case offers us the opportunity to discuss the most important aspects related to the management of RRT in patients with hemophilia and to analyze strategies to minimize the development of complications.

A 54-year-old male from Montevideo, with a disadvantaged socioeconomic background, presented with severe hemophilia B (factor IX activity < 1%) without inhibitor. He was on prophylaxis with AIMAfix (plasma-derived factor IX) at a dose of 40 IU/kg, twice weekly, and had a history of insulin-dependent diabetes mellitus, arterial hypertension, cured hepatitis C, and porphyria cutanea tarda. He had diabetic nephropathy, with stage V CKD according to the KDIGO classification (glomerular filtration rate: 13 ml/min/1.73 m²).

Coordinated admission for RRT was planned. The patient presented with severe hemophilic arthropathy in

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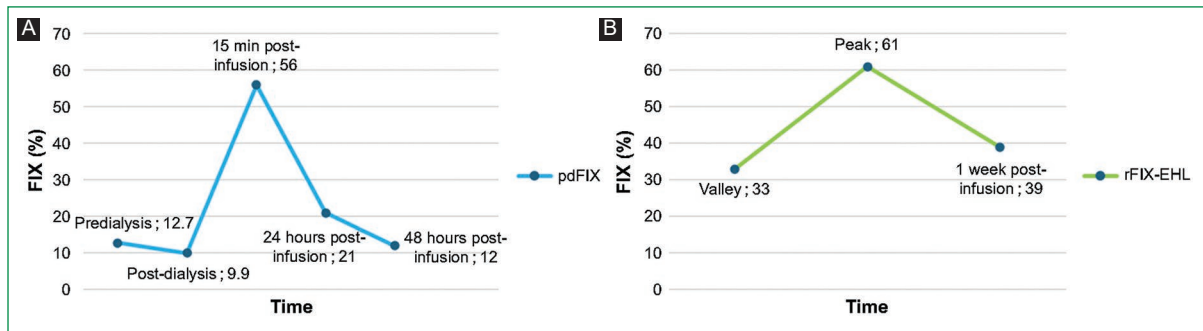


Figure 1. Pharmacokinetics of factor IX. **A:** treatment with plasma-derived factor IX (pdFIX). **B:** treatment with recombinant extended half-life factor IX (rFIX-EHL).

Table 1. Risk factors for developing chronic kidney disease in patients with hemophilia

Risk factor	Mechanism
Age	Loss of renal mass Decreased renal blood flow Decreased glomerular filtration rate Membranous nephropathy
Recurrent hematuria	Obstructive uropathy Anatomical sequelae in the urinary tract
Use of antifibrinolytics	Obstruction by clots (ureters, bladder) Direct nephrotoxic effect
Arterial hypertension	Nephroangiosclerosis
Diabetes mellitus	Diabetic nephropathy
Benign prostatic hyperplasia	Obstructive uropathy
HIV infection	HIV-associated nephropathy Drug-induced nephrotoxicity (ART, antimicrobials) Thrombotic microangiopathy Neoplastic infiltration (lymphoma, Kaposi's sarcoma)
Hepatitis B or C virus infection	Membranoproliferative Glomerulonephritis (immune complex-mediated) Mixed cryoglobulinemia
ITI in hemophilia B with inhibitors	Nephrotic syndrome

ITI: immune tolerance induction; ART: antiretroviral therapy;
HIV: human immunodeficiency virus.

the elbows that limited the range of motion and manual dexterity, hindering the implementation of peritoneal dialysis. Following multidisciplinary evaluation (hemotherapy, nephrology, and vascular surgery), hemodialysis via a tunneled jugular venous catheter was chosen,

avoiding the use of an arteriovenous fistula due to the risk of post-puncture hematomas.

Hemodialysis sessions were established three times a week, without using heparin, and plasma-derived factor IX was administered after dialysis (dose of 60 IU/kg). The pharmacokinetics of factor IX (Fig. 1) were analyzed using a one-stage coagulation assay based on activated partial thromboplastin time (aPTT), obtaining blood samples pre- and post-dialysis, and at 15 minutes, 24 and 48 hours after factor IX infusion. A trough level of factor IX pre-dialysis of 12.7% was observed, without significant variations compared to post-dialysis values, with a total session duration of 4 hours. After 3 months, albutrepenonacog alfa (extended half-life recombinant factor IX) was initiated as prophylaxis, at a dose of 40 IU/kg per week, maintaining trough factor IX levels at 33% (Fig. 1). Currently, after 15 months on hemodialysis, the patient has not experienced any bleeding related to the procedure.

Discussion

We report a case of hemophilia B and end-stage CKD that safely initiated RRT by hemodialysis with prophylactic factor IX replacement. This case illustrates the challenges of managing renal replacement therapy in patients with hemophilia.

As the life expectancy of patients with hemophilia increases, the frequency of cases of end-stage CKD requiring RRT also rises, necessitating careful selection of the safest and most effective dialysis modality. There is no general consensus to guide decision-making; therefore, the evidence derives primarily from case reports and expert opinions.

Peritoneal dialysis is often preferred in patients with hemophilia, as the risk of bleeding is lower compared

with hemodialysis^{5,6}. Administration of coagulation factors is usually required only at the time of catheter placement, and episodes of hemoperitoneum are infrequent^{5,6}. However, there is a greater risk of peritonitis and, in some cases, reduced efficacy in the clearance of small solutes^{5,6}. This modality was ruled out in our patient due to his disabling arthropathy, as motor limitation precluded self-administration of peritoneal exchanges.

Hemodialysis is considered a higher risk due to repeated vascular punctures, although more evidence is needed in this regard. The use of arteriovenous fistulas or permanent catheters is possible, but requires strict monitoring to prevent bleeding⁷⁻¹⁰. As demonstrated in this case, hemodialysis through a tunneled central venous catheter can be performed safely with appropriate strategies for coagulation factor replacement and limitation of anticoagulant use. The choice of a tunneled catheter prioritized safety aspects; however, long-term use of this type of device predisposes to the development of catheter-related infections.

Patients with hemophilia B require replacement therapy with coagulation factor IX when undergoing invasive or surgical procedures. Most dialysis membranes have pores that prevent the passage of albumin (69 kDa), and consequently, factor IX, with a lower molecular weight (55 kDa), could be removed during dialysis, making its administration necessary after each hemodialysis session⁸. This therapeutic strategy was safe and effective in the analyzed case, reinforced by the pharmacokinetic analysis, which demonstrated minimal intradialytic clearance of factor IX.

It is important to emphasize that trough factor IX levels above 10% were sufficient to prevent bleeding, validating the suggested minimum protocols⁴. The omission of systemic heparin use further contributed to reducing the risk of hemorrhagic complications, without thrombus formation in the extracorporeal circuit. The successful transition to extended half-life recombinant factor IX therapy allowed for higher trough factor IX levels, while reducing the infusion burden.

Finally, although CKD can generate platelet dysfunction secondary to uremia and potentially increase hemorrhagic risk, this is usually corrected with dialysis⁴. It has been observed that platelets tend to adhere to the artificial surfaces of dialysis membranes; therefore, periodic platelet count monitoring is recommended in patients with hemophilia on dialysis if increased bleeding is identified⁴.

Conclusions

The increase in life expectancy of patients with hemophilia is expected to lead to a rise in the prevalence of comorbidities, such as CKD. It is urgent and important to deepen the therapeutic approach for patients with hemophilia and end-stage renal disease, given the limited quality evidence currently available. The present case, the first reported in Uruguay, demonstrates that hemodialysis is a viable and safe method in patients with severe hemophilia B through a multidisciplinary approach focused on: 1) vascular access via long-term tunneled catheter to reduce hemorrhagic risk, 2) omission of systemic heparin, combined with post-dialysis administration of factor IX concentrate, and 3) serial pharmacokinetic monitoring for dose optimization. The stability of post-dialysis plasma factor IX levels supports that its high molecular weight significantly limits its clearance by the procedure.

Given the progressive aging of this population, it is imperative to develop standardized clinical practice guidelines that integrate the use of extended half-life factor IX concentrates and personalized management protocols for patients requiring RRT. This experience provides practical evidence for the management of this complex clinical scenario, whose prevalence will increase in the coming decades.

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Conflicts of interest

None.

Ethical considerations

Protection of human and animal subjects. The authors declare that no experiments were performed on human subjects or animals for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, have obtained informed consent from the patient, and have received approval from the Ethics Committee. The recommendations of the SAGER guidelines have been followed, according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence for the writing of this manuscript.

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