Use of fondaparinux for extracorporeal circuit anticoagulation in patients with heparin-induced thrombocytopenia type II (HIT II) on haemodiafiltration (HDF)

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Introduction

HIT II is a potentially fatal condition that could occur after exposure to unfractionated (UFH) or, less commonly, to low-molecular weight heparin (LMWH). Haemodialysis (HD) patients have increased risk of developing HIT II, due to prolonged exposure to heparin for anticoagulation of the extracorporeal circuit. If HIT II is diagnosed by detecting antibodies to complexes of platelet factor 4 (PF4) and heparin, exposure to UFH or LMWH must be discontinued. Alternative drugs for anticoagulation in these patients are limited due to the cost and/or absence of approval for use in HD patients.

Aim of the study

Aim of this prospective observational dose-finding study was to evaluate the feasibility, effectiveness and tolerability of fondaparinux for circuit patency in patients with HIT II on high-flux HD (HF-HD) and on-line Mixed HDF. Fondaparinux, a low-priced synthetic pentasaccharide with a molecular weight of 1728D, is a specific anti-Xa inhibitor which does not cross-react with PF4. Literature on its use is controversial in long-term diffusive dialysis techniques and very limited in convective techniques, which add a greater convective component to conventional HD, changing the pharmacokinetics of most anticoagulants.

Methods

Seven patients who developed HIT II after the start of thrice weekly chronic dialysis with Mixed HDF (n=6) or HF-HD (n=1) with helyxone high-flux dialyzers (FX CorDiax 800/1000, Fresenius Medical Care) and heparin as anticoagulant were shifted to fondaparinux at a dose of 0.03 mg/kg. Anti-Xa activity levels were measured at the beginning and at the end of the first three dialysis sessions to assess for accumulation and removal during treatment (dose reduction needed if postdialysis anti-Xa levels > 0.5 mg/L). Treatment failure (total/partial extracorporeal circuit clotting, loss in efficiency treatment, other side effects) were monitored for one month. Dose escalation was performed when significant clotting in the bubble trap and dialyzer membrane were observed.

Results

Patients were followed for one month and a total of 98 sessions. Their characteristics are shown in Table 1. The average predialysis anti-Xa level was <0.039 mg/L and the postdialysis one ranged from 0.040 to 0.3 mg/L, with a mean level of 0.11 mg/L. No dose reduction was performed, as no accumulation was detected. None of the patients experienced bleeding or other side effects associated with the drug. Partial dialyzer clotting was observed in the first session of three patients (one on HF-HD and two on Mixed-HDF), that required fondaparinux dose escalation up to 0.05 mg/kg; no further clotting was detected in these patients over extensive repeated administration.

Table 1.

Overview of patient and dialysis characteristics.

Number of patients	7
Age (years)	69 ± 8,6
Sex (M/F)	4/3
Body weight (kg)	64,9 ± 12
Dialysis session (min)	240
Dialyser type - dialysis technique	1 pz x FX CorDiax 80 - HF-HD 1 pz x FX CorDiax 800 - Mixed-HDF 5 pz x FX CorDiax 1000 - Mixed-HDF
Blood flow rate (ml/min)	379 ± 26
Dialysate flow rate (ml/min)	1 pz x 500 6 pz x autoflow factor of 1.5
Administration of fondaparinux	Intravenous
Predialysis anti-Xa (mg/L)	< 0,039
Postdialysis anti-Xa (mg/L)	0,11 ± 0,07

Conclusions

Fondaparinux provided adequate circuit anticoagulation for patients with HIT II on HF-HD and Mixed-HDF with high-flux dialyzers, without side effects during the treatment and the interdialytic interval. It is of simple and safe use and cost-saving with respect to other anticoagulants (argatroban, bivalirudin, etc..) and may be the indication of choice for alternative anticoagulation in patients with HIT II on convective dialysis techniques.

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