Managing dialysis with low systemic heparinization – An observational survey on the usage of the new Evodial® dialyzer

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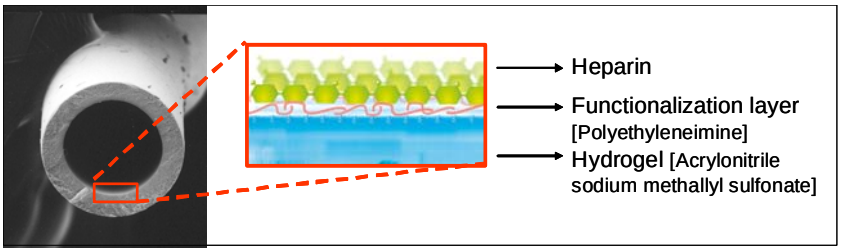
Introduction

Clotting may occur in the extra-corporeal dialysis circuit as a result of blood components interacting with materials and air in the dialyzer and tubing. Administrating an anticoagulant, like heparin, aims at preventing such events. However, when given systemically the effects of heparin go well beyond attenuating coagulation cascade activation in the dialysis circuit. A recurrent systemic administration of heparin represents a potential risk. A growing share of dialysis patients, old and suffering from diabetes, inflammation, and vascular disease, may benefit from the possibility to use less systemic anticoagulation [1,2]. In addition, conditions of increased bleeding risk often require that heparinization is minimized or even omitted.

The HeprAN™ membrane

The new Evodial dialyzer contains the innovative HeprAN membrane, originating from the well-established AN69ST membrane technology [3,4]. The blood contacting surface of the HeprAN membrane is in production made anti-thrombogenic by a multipoint ionic grafting with unfractionated heparin. Internally this surface heparinized membrane has a hydrogel structure and performance characteristics that closely resemble those of the AN69ST membrane. A clinical study in 2007 established product safety and key performances for the Evodial dialyzer, and gave initial indications that when using this dialyzer it may be possible to reduce the systemic heparin dose without affecting treatment delivery or dialysis dose [5,6].



Clinical survey

Following CE-marking and first introduction of the Evodial dialyzer for HD and HDF treatments, initial clinical experiences in France and Italy were collected. For this purpose a specially designed questionnaire was widely distributed to dialysis units known to use the Evodial dialyzer. The questionnaire focused on anticoagulation practices and issues related to treatment completion. Responses were voluntary. This paper presents the summary data of the responses, coming from 32 dialysis centers and covering 296 treatments with the Evodial dialyzer in 100 chronic HD patients. Of the patients 32% were stated to have diabetes and 24% to be in a state of high bleeding risk. Patient body weight was 70±15 kg. Sixty-eight per cent of the treatments used Evodial 1.6 (1.65 m^2 effective membrane surface area), while Evodial 2.2 and Evodial 1.3 were used for 31% and 1% of treatments respectively.

Using regular heparin

Eighty-nine treatments (82% HD, 18% HDF) were reported using unfractionated heparin, with treatment duration of 4.0±0.4 hour and a blood flow rate of 304±29 ml/min.

The total systemic heparin dose was 3463±2357 IU (50±37 IU/kg). For 52 treatments having a bolus and infusion approach the mean bolus dose was 1632 IU (22 IU/kg) and the mean infusion rate was 590 IU/h for 3.4 hours.

In 9 patients, the survey data suggested an approach to systematically lower the heparin dose while using the Evodial dialyzer. The data provided indicate that a 46±10% reduction from 4506±1477 to 2417±944 IU was feasible. One of these cases required premature rinseback when heparin was reduced by 43% from an initial 7000 IU.

An overall 93% of treatments were reported as successfully completed while six treatments (7%) were prematurely stopped between 3.5 and 4.7 hours after treatment start. These early stopped sessions typically had a

low heparin bolus dose given at treatment start (708±1005 IU). Clotting in the circuit was given as the main reason for an early stop, most notably in the drip chambers. Five of these early stopped treatments were run in postdilution HDF mode.

Heparin doses reported on in this survey are considerably lower than those indicated in the European Best Practice Guidelines [7]. These recommend as best practice a bolus of 50 IU/kg plus infusion of 800-1500 IU/h, implying a total dose in the range of 6500-9100 IU for a 70 kg patient.

89 sessions with UFH	3500 ±2400 IU	93% success
105 sessions with LMWH	3100 ±1400 IU	94% success
94 sessions heparin-free	-	97% success

Using low molecular weight heparin

One hundred and five treatments (90% HD, 10% HDF) in 46 patients used a low molecular weight heparin (LMWH) as anticoagulant. Treatment duration was 4.0±0.2 hour and blood flow rate was 305±40 ml/min.

Enoxaparin was the most commonly used LMWH, followed by dalteparin and nadroparin. With few exceptions, LMWH was administered as a single bolus dose at treatment start. The volumes given correspond to an overall LMWH dose of 3051±1427 IU.

In 4 cases the survey revealed a gradual reduction in LMWH dose from a presumed standard level. All were successful and indicated that in these patients a reduction from 4300 IU to 2200 IU was feasible.

Overall, 94% of treatments were reported as successfully completed while six treatments (6%) were reported as prematurely stopped between 3.5 and 4.0 hours after treatment start. Two of these six treatments were run in postdilution HDF mode.

Heparin-free treatments

Ninety-four heparin-free treatments were reported (85% in HD, 15% in HDF) in 28 patients. This is 32% of all Evodial treatments reported in the survey. As the questionnaire did not specifically ask for heparin-free treatments to be included it is assumed that these patients had a clinical indication to perform dialysis heparin-free; fourteen cases were characterized as high bleeding risk patients. Eight patients were reported to be on treatment with a vitamin K antagonist, five to be on aspirin medication, and two on other anti-platelet drugs. Actual treatment duration was 3.8±0.4 hour and blood flow rate was 304±36 ml/min.

Overall, 97% of heparin-free treatments were reported as successfully completed while three treatments (all in HD) were reported as prematurely stopped between 1.25 and 3.0 hours after treatment start due to clotting in the dialyzer and/or the venous drip chamber.

Concomitant ACE-I medication

ACE inhibitor drug therapy was indicated for 15 patients in this survey without any report of specific treatment reactions.

Comments and Conclusions

The current cross-sectional data obtained from an initial post-market survey show that the Evodial dialyzer is successfully used at heparin doses that on average are only about 50% of what is recommended by European clinical guidelines or by LMWH manufacturers. A few cases of gradually reduced heparin doses were reported; although generally successful, these cases should be viewed as preliminary and not as conclusive evidence that a heparin reduction is possible in each patient by converting to Evodial.

The data further indicate that the Evodial dialyzer can be successfully used when patients have a clinical indication for heparin-free dialysis and the treatment is closely supervised for clotting events.

This survey did not ask for information on which type of blood tubing was used. It is obvious, however, that blood lines may also add significantly to clotting events in the circuit, e.g. by exposing blood to an air interface. Thus, whenever attempting to approach a non-thrombogenic extracorporeal circuit for dialysis one should consider not only selecting the appropriate dialyzer but also search for the suitable blood lines.

While waiting for more controlled data on the potential to reduce the amount of systemic anticoagulation when using the Evodial dialyzer, we may conclude from this survey that the Evodial dialyzer can generally be used successfully in patients who require tight heparinization. One may hypothesize that the heparin-grafted HeprAN membrane is a key factor for this success.

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