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Case Report

Treatment of severe dialysis reactions with the AN69-ST membrane: biocompatibility does matter

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Abstract

Dialysis reactions with biocompatible membranes are rare, and complement activation has been suggested to be a culprit. We report here a case of an incident haemodialysis patient with asthma disease who experienced severe adverse reactions late into dialysis session, with different synthetic membranes (FX 80, Fresenius; Polyflux 17L, Gambro; FX 10, Fresenius; BLS 512, Bellco-Sorin). After replacing the dialyser by the surface-treated AN69 membrane (Nephral ST 500, Hospal), the dialysis sessions became uneventful. The case reinforces the need for biocompatible dialysers with high permeability and adsorptive capacity in susceptible patients experiencing severe dialysis reactions with synthetic membranes.

Keywords: biocompatibility; dialysis reactions; surface-treated AN69

Background

During haemodialysis, patients may experience a number of reactions that are a direct consequence of establishing the extracorporeal circuit, often referred to as dialysis reactions. The best-known classification system of such reactions is described by Daugirdas and Ing [1] where the reactions are divided into either Type A (hypersensitivity reactions) or Type B (non-specific reactions). Type B reactions are less understood compared to Type A reactions but are also thought to be related to complement activation [1].

The majority of dialysis reactions have been related to the use of either ethylene oxide sterilization, non-biocompatible membrane dialysers or the simultaneous use of AN69 membranes and angiotensin-converting enzyme (ACE) inhibitors [2]. Dialysis reactions with polysulphone membranes are rare and have been reported to be associated with the activation of complement [3]. Cross reactions between different types of membranes, like polimethylmetacrylate, polysulphone and polycarbonate, can also occur [3].

Herein, we report the case of an incident haemodialysis patient who experienced severe dialysis reactions while being treated with different synthetic membranes. After replacing the dialyser with the surface-treated AN69 membrane (AN69-ST), the dialysis sessions became uneventful.

Case report

An 84-year-old woman with diabetic end-stage renal disease and controlled asthma started haemodialysis therapy on 20 September 2009, via an arteriovenous fistula. The patient's medication comprised acid acetilsalicilic 150 mg o.d., sinvastatin 20 mg o.d., calcium carbonate 1 g b.i.d., formoterol/budesonide 4.5/160 μg b.i.d. and darbepoetin 20 μg/week. Intravenous iron therapy was not performed. Since her first treatment, she experienced recurrent episodes of acute respiratory distress with bronchospasm, dyspnoea, hypoxaemia, lacrimation and a burning sensation throughout her body approximately 45 min into haemodialysis in almost all dialysis sessions. During the acute episodes, the dialysis session was stopped, and the patient was immediately taken off the machine. Steroids (hydrocortisone 300 mg i.v.), antihistamines (clemastine 2 mg i.v.) and epinephrine (1 ml 1:1000 i.m.) were also administered. No other patients experienced dialysis reactions in the same outpatient clinic. She was dialysed with polysulfone membranes (FX 80, Fresenius, is a high-flux, biocompatible dialyser, with moderate–high adsorptive capacity, sterilized by steam). It should be noted that dialysers are not reused or preprocessed (outside of rinsing with normal saline) in our country.

On 21 October 2009, the patient was admitted to our nephrology department. Because the cause of her reactions was not apparent, it was decided to use the standard setup of our unit, with the Polyflux 17L, Gambro, dialyser to determine if her reactions would still occur at this location. The Poliflux 17L dialyser is a low-flux, biocompatible dialyser (with the polyarylethersulphone/polyamide membrane) which is ster-

ilized by steam. The circuit was double-rinsed just before her session. Within 45–60 min of treatment, she developed similar reactions with oxygen desaturation, cyanosis, bronchospasm, dyspnoea, lacrimation and burning sensation. Her blood work revealed leukocytosis with normal eosinophil count at the end of the dialysis. Her haemoglobin remained stable. As before, her symptoms improved gradually with supportive measures and dialysis interruption.

For the next treatments, the BLS 512, Bellco-Sorin and the FX 10, Fresenius, dialysers were used, and the circuits were double-rinsed just before the sessions. Both are low-flux and biocompatible dialysers (with polyethersulfone and polysulfone membranes, respectively). Surprisingly, she experienced essentially identical reactions.

The Nephral ST 500, Hospal dialyser was used on the next session on 27 October 2009, again with double-rinsing. She was symptom-free on this treatment. From that day, the patient was able to perform her 4-h dialysis sessions three times a week, without prophylactic measures and uneventfully.

Discussion

We report the case of a patient with a history of controlled asthma suffering from severe dialysis reactions late into therapy, with several biocompatible membranes. On many different occasions, she experienced the same constellation of symptoms, including dyspnoea and burning sensation. Although she fit the criteria for Type A reactions [1], the unusual late presentation seemed to resemble Type B reactions more. Furthermore, ethylene oxide is recognized as the most important aetiologic factor in Type A reactions, and she had never been on therapy with ethylene oxide-sterilized dialysers or blood tubing systems.

With these questions in mind, the less commonly reported causes of dialyser reactions were explored. In addition to ethylene oxide and bradykinin, acetate-containing dialysate, the use of heparin, dialysate contamination and complement activation have also been implicated [4]. No acetate-containing dialysate is used in our dialysis unit. Haemodialysis was performed without heparin. It has been demonstrated that endotoxin and other bacterial breakdown products can move from the dialysate compartment into the blood compartment and induce cytokine release [5]. Although synthetic high-flux membranes such as polysulfone and polyacrylonitrile (and the closely related AN69) are permeable, they also have a high capacity for the adsorption of bacterial fragments, resulting in lower levels of cytokine induction when compared to low-flux cellulosic membranes [4]. In our dialysis unit, the water supply used for dialysate production is regularly tested and conforms to the latest European Pharmacopeia water treatment standards. Furthermore, our current fleet of dialysis machines generates dialysate using dry bicarbonate powder.

Finally, activation of the complement via the alternative pathway is practically universal for all dialysis membranes, albeit to various degrees [6]. Because of the temporal profile of complement activation during haemodialysis, anaphylatoxin-mediated reactions are more likely to occur at 30 min or later rather than within the first minutes of the treatment [6]. Even though several studies have found no difference in reaction rates between membranes that readily activate complement and those that do not, a subset of patients (those with atopia and/or eosinophilia) seems to be more susceptible to dialysis reactions and experiencing recurrent symptoms [6].

Membranes that produce little interaction with blood components and the humoral components of plasma are described as being biocompatible. Poliacrylonitrile membranes activate complements to a lower extent than the other synthetic membranes [4]. Also, the ability to adsorb potentially harmful substances, including C3a, C5a and bradykinin, can affect biocompatibility [4]. The AN69 membrane is a copolymer of acrylonitrile and sodium methallyl sulfonate with a high adsorptive capacity [7]. Further neutralization of charged surface anionic sulfonate groups scattered over the polymer by polyethyleneimine, as in the AN69-ST membrane, significantly improves the binding of C3a, C5a [8] and Factor D [9], thus increasing its biocompatibility.

The Nephral ST 500 is a high-flux, biocompatible dialyser (with the AN69-ST membrane), with high adsorptive capacity. Interestingly, the use of the AN69-ST membrane led to the prevention of further dialyser reactions in our patient. By 27 October 2009, she no longer demonstrated any adverse reaction during dialysis. Further investigations including complement fragments (C3a, C5a, etc.) are needed to confirm if complement activation was indeed the cause of her dialyser reactions.

In conclusion, our case report suggests that high-flux membranes with high adsorptive capacity, like AN69-ST, are a useful alternative in susceptible patients experiencing severe dialysis reactions with synthetic, biocompatible membranes.

Conflict of interest statement. None declared.

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