Intestinal manifestations with a surface-treated AN69 membrane and ACEI during haemodialysis

Sir,

AN69-associated reactions in haemodialysed patients receiving angiotensin-converting enzyme inhibitors (ACEI) are well-documented [1]. The negatively charged AN69 membrane is thought to activate the bradykinin system. Moreover, ACEI reduces bradykinin inactivation. Surface-treated AN69 is considered to be safer in that regard. To our knowledge, only one case of anaphylactoid reaction induced by ACEI during haemodialysis with a surface-treated AN69 membrane has been reported [2]. We report here two patients who had a more subtle presentation with predominantly intestinal manifestations.

Case 1

A 54-year-old male with end-stage renal disease (ESRD) consequent to IgA nephropathy had been on chronic haemodialysis (4 h, three times per week) for 2 years. He was dialysed using a surface-treated AN69 membrane (Nephral ST® 500, Gambro) for 4 months. His medication included metoprolol, furosemide, amiodarone, calcium carbonate, sevelamer, allopurinol, oxybutinin, epoetin-α, calcitriol, warfarin and naproxen. On 8 November 2004, ramipril 2.5 mg once daily was initiated for hypertension and cardiovascular protection. At the next dialysis, the patient presented moderate abdominal cramping and diarrhoea during haemodialysis. These symptoms did not recur until 19 November. They were present on 22 and 24 November, when medical attention was first requested. At this time, the working diagnosis was viral gastroenteritis. However, by caution, the dialyser was changed for a cellulose membrane since the first dialysis treatment. His medication continued without any problem for many months. In the second case, ACEI not used concomitantly in this case was tolerated without any problem for many months. In the second case, ACEI and a surface-treated AN69 membrane used concomitantly seemed to have been well-tolerated at first, when compliance to enalapril was questionable. No other explanation was found for the abdominal symptoms in January than a reaction to the filter, since the symptoms suddenly ceased after the dialyser was changed. We felt that challenging this patient again with a surface-treated AN69 membrane would have been dangerous and unethical.

Even if surface-treated AN69 membrane was shown to be less electronegative, the coating of PEI may not cover perfectly all electronegative charges. Variability within dialysers or between fibres filaments is possible. These uncovered charges can activate the Hageman factor and consequently contribute to bradykinin generation. We can imagine a spectrum of bradykinin synthesis in this context ranging from mild non-specific symptoms to anaphylactoid reactions. Our patients were probably in the middle of this spectrum. Moreover, bradykinin is thought to be a mediator of gut sensitivity [5]. Interindividual differences in susceptibility to hypersensitivity reaction in patients haemodialysed with an AN69 membrane, while on treatment with an ACEI can be partly explained by different degrees of enzyme activity. However, bradykinin generation was not measured in our cases, and we cannot prove their exact role in the symptoms presented by our two cases.
In conclusion, the safety of surface-treated AN69 membrane used concomitantly with ACEI should be more formally evaluated. This may help to recognize and describe the spectrum of hypersensitivity reactions in this context. We recommend changing the dialyser when facing a new or suspect intestinal manifestation in patients dialysed with a surface-treated AN69 membrane and receiving ACEI, if any doubt is present.

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