Hypersensitivity reactions to acetate in the bicarbonate dialysate in a patient undergoing pre-dilution online hemodiafiltration

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Abstract A 63-year-old male patient first experienced recurrent hypotensive episode during the dialysis session just after switching the mode from hemodialysis to online hemodiafiltration (OL-HDF) with infusion in pre-dilution of the bicarbonate dialysate containing 9.2 mEq/L of acetate. Peripheral eosinophil count and serum IgE were both elevated to 16,440/ μ L and 2000 IU/L. The reactions promptly dissolved with substitution of acetate-free solution. This case illustrated that pre-dilution OL-HDF can induce an occult hypersensitivity to acetate in the standard bicarbonate dialysate.

Keywords Acetate · Dialysate · Allergy · Online hemodiafiltration

Introduction

Hypersensitivity reactions in relation to the use of acetate dialysate are rarely reported in patients undergoing regular hemodialysis (HD) [1–4]. These reactions are usually disappeared when acetate was substituted for bicarbonate buffer. We herein reported a case of acetate allergy whose reactions became first evident just after switching the mode from HD to pre-dilution online hemodiafiltration (OL-HDF).

Case report

The patient was a 63-year-old man with end-stage kidney disease due to diabetic nephropathy. He had been undergoing regular hemodialysis (HD) for 21 months using the bicarbonate dialysate (LinpackTA1[®], Nipro Pharma Co., Osaka, Japan) containing a small amount of acetate (9.1 mM) with polysulfone dialyzer membrane (APS15SA, Asahi Kasei Medical, Tokyo, Japan). His past medical record did not disclose any allergic problem. He had also not experienced any episode of anaphylactic shock.

At December 20, 2013, his dialysis mode was changed to pre-dilution online hemodiafiltration (OL-HDF) with the total fluid flow rate of 11 L/h (reinfusion fluid 8 L/h, dialysate 3 L/h) using a polysulfone hemodiafilter (ABH15F, Asahi Kasei Medical, Tokyo, Japan). At December 23, he suddenly experienced hypotensive episode at the first period of HD session. Despite the increment of dry weight and intravenous infusion of etilefrine hydrochloride, his systolic blood pressure (SBP) decreased to <90 mmHg every session (totally 5 sessions). At January 3, 2014, he experienced anaphylactic shock including hypotension (SBP 63 mmHg), flushing and disseminated wheezing at 30 min after the start of HD. Laboratory examination disclosed that white blood cell, eosinophil count and serum IgE were elevated to 25,140/ μ L, 16,440/ μ L and 2600 IU/L (normal range $\leq$ 173 IU/L). Drug-induced lymphocyte stimulation test (DLST) for the dialysate powder was negative.

We first suspected hypersensitivity reaction in association with OL-HDF therapy. We changed the dialysis mode to previous HD mode using the same dialysate at January 6. We next exchanged the dialysate to acetate-free citrate-containing solution (Carbostar[®], Ajinomoto Pharmaceuticals Co. Ltd, Tokyo, Japan) for the next 20 units.

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Table 1 Dialysis mode and hypersensitivity reactions in the dialysis sessions

Mode	Time on the mode	Treatment sessions	Dialysate buffer	Dialyzer	Sterilizer	Hypersensitivity reactions
HD	21 months	316	Bicarbonate	PS	γ ray	Negative
OL-HDF	17 days	7	Bicarbonate	PS	γ ray	Positive
HD	1 day	1	Bicarbonate	PS	γ ray	Negative
HD	7 weeks	20	Acetate-free	PS	γ ray	Negative
OL-HDF	14 months	211	Acetate-free	PS	γ ray	Negative

HD hemodialysis, OL-HDF online hemodiafiltration, PS polysulfone

Table 2 Cases of hypersensitivity reactions to acetate in the dialysate

References	Age/sex	Dialysis	Dialysate	Eosinophil/IgE	Disappeared with substitution
Ei et al. [1]	30/M	HD	Acetate	Elevated	Bicarbonate
Caravaca et al. [2]	35/F	HD	Acetate	Elevated	Bicarbonate
Papadakis et al. [3]	23/F	HD	Acetate	Elevated	Bicarbonate
Yang et al. [4]	46/F	HD	Acetate	Normal	Bicarbonate
Present case	63/M	OL-HDF	Acetate-containing bicarbonate	Elevated	Acetate-free

HD hemodialysis, OL-HDF online hemodiafiltration

Since any allergic symptom did not occur during the procedure. We re-introduced pre-dilution OL-HDF using acetate-free citrate-containing dialysate since February 19. He did not experience any hypersensitivity reactions until now (Table 1). His eosinophil count was also returned to within normal range. We diagnosed that the patient had latent allergy to dialysate acetate.

Discussion

Hypersensitive reactions related to acetate dialysate are rarely reported. To our best knowledge, there were only 4 cases in the literature (Table 2). Clinical symptoms were generalized skin itching, flushing, asthma, hypotension, and shock. All symptoms were resolved promptly after substitution for bicarbonate dialysate. Eosinophils and serum IgE levels were elevated during the use of acetate dialysate, and returned to normal range when bicarbonate dialysate was used.

It remains unknown how acetate dialysate causes anaphylactoid symptoms, but it seems dose-dependent reactions, since a small amount of acetate in the bicarbonate dialysate did not induce any reaction [1–4]. However, despite a small amount of acetate in the bicarbonate dialysis solution, a single HD increases plasma acetate levels from 22 ± 3 to $222 \pm 11 \mu\text{M}$ [5]. Given the considerable quantity of dialysis fluid directly re-infused, the transfer of acetate to the patient will be expected greater in patients on pre-dilution OL-HDF when compared with those on HD.

It is reported that pre-dilution OL-HDF with 40 L of filtered bicarbonate dialysate containing 3 mM of acetate resulted in an increase of plasma acetate level by about 10-fold (from 25 ± 2 to $316 \pm 14 \mu\text{M}$), whereas the plasma level of acetate remain in the normal range ($1\text{--}100 \mu\text{M}$) (from 33 ± 5 to $71 \pm 15 \mu\text{M}$) when using acetate-free dialysate [6]. A challenge test using a commercially available acetic acid showed that serum acetate level was increased to $800 \mu\text{M}$ during an attack of asthma due to acetate ingestion [1]. In this case, the bicarbonate dialysate contained almost 3-time higher amount of acetate (9.1 mM) compared to the previous ones [5, 6]. It is, therefore, likely that a greater load of acetate to the patient during pre-dilution OL-HDF may trigger hypersensitivity reactions to acetate in this case.

In summary, we experienced a case that developed to hypersensitivity reactions to acetate in the dialysate just after switching the mode from HD to pre-dilution OL-HDF. This case illustrated that pre-dilution OL-HDF could elicit an occult hypersensitivity to acetate in the bicarbonate dialysate despite the small amount.

Conflict of interest All the authors have declared no competing interest.

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