

Acetate-free blood purification can impact improved nutritional status in hemodialysis patients

Kazuhiro Matsuyama · Tadashi Tomo ·
Jun-ichi Kadota

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Abstract Effects of online hemodiafiltration (HDF) using acetate-free bicarbonate dialysis (AFD) fluid on microinflammation, resulting in improved nutritional status in hemodialysis patients, were examined and compared with conventional acetate-containing bicarbonate dialysis (ACD) fluid. A total of 24 hemodialysis patients were registered for a cross-over design study for a 6-month period. These patients were subjected to ACD for the first 3 months followed by AFD fluid for the latter 3 months. Blood variables of C-reactive protein (CRP), interleukin-6 (IL-6), leptin, neuropeptide Y (NPY), protein catabolic rate (PCR) and %creatinine (Cr) index were determined after the first and last 3-month period. The filters and the conditions of HDF and drug regimens including erythropoiesis-stimulating agents were unchanged throughout the cross-over study. Predialysis blood pH and bicarbonate were significantly higher in the AFD phase than in the ACD phase. Blood CRP and IL-6 levels were significantly decreased in the AFD group compared to the ACD group. Concerning nutritional evaluation, leptin and NPY were significantly lower and higher, respectively, in the AFD phase than in the ACD phase. PCR tended to be higher in the AFD phase than in the ACD phase. A significantly higher %Cr index level was observed in the AFD phase than in the ACD phase.

These results suggest that online HDF using AFD fluid contributes to alleviating bioincompatible events associated with microinflammation, leading to improvement in the nutritional status in hemodialysis patients.

Keywords Acetate-free blood purification · Biocompatibility · Microinflammation · Nutrition

Introduction

The strong association among malnutrition, inflammation and atherosclerosis (MIA syndrome) has been attracting close attention recently [1]. Many reports describe that hemodialysis patients exhibit a state of chronic microinflammation [2, 3]. The causes of microinflammation in hemodialysis patients include accumulation of uremic substances [4], hyperosmotic stress due to accumulation of low-molecular-weight materials [5], elevation of free radical activity and activation of adhesion factors during dialysis therapy, suggesting that hemodialysis therapy itself can also cause inflammation [6–8]. The biocompatible factors triggering the inflammatory process during dialysis therapy can mostly be found in the dialyzers (dialysis membranes) and dialysis fluid [9]. Some reports demonstrated that inflammatory responses were reduced by the introduction of synthetic high-molecular-weight dialysis membranes and/or highly purified dialysates [10, 11]. Besides such factors, the composition of the dialysate may also be a candidate for affecting biocompatibility.

A major question addressed here is what the problems with dialysate composition are. Many of the dialysis fluids currently used in Japan contain sodium bicarbonate as a buffer source. In the past, sodium acetate had been used as a buffer source because it is useful for avoiding the

K. Matsuyama (✉)
Matsuyama Clinic Oita Nephro Internal Medicine Department,
457-1 Tajiri, Oita, Oita 870-1143, Japan
e-mail: kazuhiro@matsuyama-iin.com

T. Tomo
Department of Nephrology, Oita University Hospital, Oita, Japan

T. Tomo · J. Kadota
Department of Internal Medicine II, Faculty of Medicine,
Oita University, Oita, Japan

precipitation of calcium or magnesium carbonate from the dialysis fluid (which is likely to emerge if sodium bicarbonate is used) [12]. However, the adverse effects of acetate in hemodialysis patients have been known for the past several years and can be associated with intradialytic hypotension and cardiovascular instability; therefore, the primary buffer is bicarbonate in standard hemodialysis [13]. Nevertheless, the bicarbonate-buffered dialysis fluids currently used in Japan contain small amounts of acetate (8–10 mEq/l) as an additive to prevent crystallization of calcium and magnesium within the dialysis fluid. Problems arising from such small amounts of acetate contained in the dialysis fluid have also been discussed.

Grandi et al. reported that the addition of 4 mmol/l acetate to acetate-free biofiltration liquid induced NO synthase expression in ventricular cardiomyocytes and might cause cardiac contractile impairment in unstable patients receiving conventional bicarbonate dialysis [14]. This observation is in good agreement with data drawn by Amore et al. from the comparison of conventional acetate-containing bicarbonate dialysis with acetate-free biofiltration, which suggests that acetate in dialysis fluid, even in low concentrations (4 mmol/l), enhances NO synthase activity in endothelial cells [15]. Higuchi et al. [16] also reported that cytokine production was minimal during acetate-free biofiltration (an acetate-free method of blood purification), but maximal during bicarbonate dialysis with a dialysis fluid containing small amounts of acetate. This tendency was observed in a study showing only a considerably limited elevation in superoxide production by neutrophils during acetate-free biofiltration compared with during bicarbonate dialysis [17]. These findings suggest that even small amounts of acetate in dialysis fluid in bicarbonate dialysis can induce microinflammation during blood purification therapy.

In 2007, acetate-free bicarbonate-buffered dialysis fluid was launched on the market in Japan. This dialysis fluid is characterized by the absence of acetate and a higher level of bicarbonate (35 mEq/l) than in the conventional bicarbonate dialysis fluids in Japan. Also, citrate is added to the dialysis fluid to prevent precipitation of calcium carbonate.

This study was undertaken to examine whether the composition features of the dialysis fluid, such as the removal of acetate (acetate-free bicarbonate-buffered dialysis fluid), would lead to alleviation of bioincompatible events, including microinflammation found during blood purification, resulting in improved nutritional status in stable patients undergoing maintenance hemodialysis. To this end, online hemodiafiltration (HDF) was carried out in these patients, and thereby the effects of acetate-free bicarbonate-buffered dialysis (AFD) fluid were investigated and compared with those of conventional acetate-containing bicarbonate-buffered dialysis (ACD) fluid.

Materials and methods

Patients

The study involved 24 maintenance hemodialysis patients who were receiving online HDF (13 males and 11 females, aged 58.2 ± 14.5 years, dialysis vintage = 10.0 ± 8.0 years) in stable clinical condition. Causes of renal failure were chronic glomerular nephritis in 20 patients, diabetic nephropathy in 2 patients, polycystic kidney in 1 patient, and nephrosclerosis in 1 patient.

The protocol and informed consent were reviewed and approved by the Medical Ethics Committee of Oita University Hospital. All patients signed written, informed consent prior to the start of the study. This research was carried out in accordance with the ethical principles of the Declaration of Helsinki.

Purification system for dialysis fluid

We used purified underground water for dialysis water. The underground water was deferrized and demagnetization followed, then it was treated with reverse osmosis (RO) through the respective exclusive machines. Then hypochlorous acid was added to the water in order to gain a final concentration of 0.3 ppm/l as chloride. The water obtained with the above-mentioned process was exclusively used for dialysis water. The original water was further purified by dialysis indoor RO, which consequently became the dialysis water. Finally, the purity and quality of the dialysis fluids were not more than 10^{-6} CFU/ml in terms of bacterial counts and not more than the detectable limit for the endotoxin level at the end of the dialysis circuit. The resultant dialysis fluid satisfied ISO requirements for ultrapure dialysis fluid, and compliance with the criteria was maintained throughout the study.

Conditions and procedure for online HDF

Online HDF was carried out in three sessions weekly for 4–5 h/session with predilution mode (12–21 l/h) at a blood flow rate of 200–350 ml/min and a dialysate flow rate of 500–700 ml/min. The compositions of ACD and AFD fluids approved and authorized in Japan were tested in this study and are presented in Table 1. The filter of the dialysis used in the present study comprised synthetic high-molecular-weight dialysis membranes. The filter material types were polysulfone, polyethersulfone polymer alloy and polyethersulfone. We show the dialysis membranes used and operational conditions of online HDF in Table 2.

The patients enrolled in this study, specified in the “Patients” section, were treated beforehand with ACD fluid for 1 month in the prestudy period (1 May–31 May

Table 1 Composition of dialysis fluids tested in the present study

	Na (mEq/l)	K (mEq/l)	Ca (mEq/l)	Mg (mEq/l)	Cl (mEq/l)	HCO ₃ ⁻ (mEq/l)	Acetate (mEq/l)	Glucose (g/l)
Acetate (-) dialysate ^a	140	2.0	3.0	1.0	111	35	–	1.5
Acetate (+) dialysate	140	2.0	2.5	1.0	114.5	25	8	1.5

^a Citrate 2 mEq/l is added

Table 2 Type of dialysis membranes used and operational conditions for online HDF

Case	Filter	Material	Blood flow rate (ml/min)	Dialysate flow rate (ml/min)	Substitution flow rate (l/h)	Dialysis time (h)
1	APS-15SA	PS	250	500	15	5
2	APS-15SA	PS	250	500	15	4
3	APS-15SA	PS	250	500	15	4
4	APS-18SA	PS	300	600	18	4
5	APS-18SA	PS	250	500	15	4
6	APS-18SA	PS	300	600	18	4.5
7	APS-25SA	PS	300	600	18	4
8	APS-21E	PS	250	500	15	4
9	APS-21E	PS	350	700	21	4
10	APS-21EL	PS	250	500	15	4
11	VPS-18HA	PS	250	500	15	4
12	VPS-21HA	PS	250	500	15	4.5
13	TS-1.8UL	PS	250	500	15	4
14	TS-1.8UL	PS	250	500	15	5
15	FDX-150GW	PEPA	200	500	12	5
16	FDX-150GW	PEPA	200	500	12	4
17	FDX-150GW	PEPA	250	500	15	4
18	FDX-180GW	PEPA	250	500	15	4
19	FDX-180GW	PEPA	250	500	15	4
20	FDX-210GW	PEPA	300	500	18	5
21	FDX-210GW	PEPA	250	500	15	4.5
22	FDX-210GW	PEPA	250	500	15	4.5
23	PES-210S α	PES	250	500	15	4
24	PES-210S α	PES	250	500	15	4

The filter material types were PS, PEPA and PES

Cases 1–12: products were APS and VPS series from Asahi Kasei Kuraray Medical Co., Ltd.; cases 13, 14: TS series from Toray Medical Co., Ltd.; cases 15–22: FDX series from Nikkiso Co., Ltd.; cases 23, 24: PES series from Nipro Corp.

PS polysulfone, PEPA polyethersulfone polymer alloy, PES polyethersulfone

2007). Thereafter, the patients were treated with ACD fluid for the first 3 months of the study followed by AFD fluid for the latter 3 months. During the 6-month study period, composed of the first 3 months (ACD phase; 1 June–31 August 2007) and the last 3 months (AFD phase; 1 September–30 November 2007), only the dialysis fluid was changed, and the following conditions were kept unchanged: (1) filters (membrane surface area, raw material), (2) settings for HDF, i.e., blood flow rate, dialysate flow rate, dialysis time, dry weight, pre-dilution mode and convective volume; (3) drug regimen including an erythropoiesis-stimulating agent (drug type, dosage). On the last Monday (for the Monday, Wednesday and Friday dialysis group) or the last Tuesday (for the Tuesday, Thursday and Saturday

dialysis group) of each 3-month period, blood samples were taken from each patient.

Measurements and analysis

Each blood sample was analyzed as follows: (1) C-reactive protein (CRP, FALCO biosystems Ltd.) and interleukin-6 (IL-6, R&D Systems, USA) as markers related to inflammation and (2) leptin (IBL, Japan), neuropeptide Y (NPY, BACHEM, USA) and albumin (Alb, FALCO Biosystems Ltd.) as markers related to nutrition. pH and HCO₃⁻ drawn before hemodialysis sessions were also analyzed. Furthermore, for nutritional evaluation, urea generation (GU) and body weight (BW) were measured, and the protein

catabolic rate (PCR) and %creatinine (Cr) index were calculated using the equations given below.

Interdialytic urea generation rate (GU) equation is [18]:

$$GU = (Kr + \alpha)[C0 - Ct\{(Vt + \alpha\theta)/Vt\}^{-(kr+\alpha)/\alpha}] / [1 - \{(Vt + \alpha\theta)/Vt\}^{-(kr+\alpha)/\alpha}]$$

In the above formula, Vt is the end dialysis volume; Kr is kidney urea clearances; Ct and C0 are the BUN concentrations at the end and beginning of a dialysis treatment; α is the rate of interdialytic volume expansion and is calculated by the total interdialytic weight gain divided by the length of the interdialytic interval, θ . The anthropometric volume of distribution of urea may be calculated by Watson formulae derived from stature, age and gender-specific estimates of total body water (TBW) in healthy subjects.

The Watson formulae are [18–20]:

$$[\text{Males}] : \text{TBW} = 2.447 - (0.09156 \times \text{age}) + (0.1074 \times \text{height}) + (0.3362 \times \text{weight})$$

$$[\text{Females}] : \text{TBW} = -2.097 + (0.1069 \times \text{height}) + 0.2466 \times \text{weight}$$

$$\text{PCR} = 9.35(\text{GU} + 1.2)/\text{BW}$$

$$\text{Cr index (mg/24 h)} = \text{dialysate (or ultrafiltrate)Cr (mg/24 h)} + \text{urine creatinine (mg/24 h)} + \text{change in body Cr pool (mg/24 h)} + \text{Cr degradation (mg/24 h)}$$

$$\begin{aligned} \text{Change in body Cr pool (mg/24 h)} \\ = & \left[\text{serum creatinine (mg/L)}_f - \text{serum creatinine (mg/L)}_i \right] \\ & \times [24/\text{h}/(\text{time interval between the } i \text{ and } f \text{ measurements})] \\ & \times [\text{body weight (kg)} \times (0.50 \text{ L/kg})] \end{aligned}$$

where *i* and *f* are the initial and final serum creatinine measurements, respectively. Body weight is the time-averaged body weight between the initial and final serum creatinine measurements [20].

$$\begin{aligned} \text{Cr degradation (mg/24 h)} &= 0.38 \text{ dL/kg/24 h} \\ &\times \text{serum creatinine (mg/dL)} \\ &\times \text{body weight (kg)} \end{aligned}$$

$$\begin{aligned} \% \text{Cr index (\%)} \\ = & (\text{actual Cr index value}/\text{standard Cr generation rate}) \times 100 \end{aligned}$$

Standard Cr generation rate (mg/24 h) is below [21].

$$[\text{Males}] : (140 - \text{age}) \times \text{body weight (kg)} \times 0.2$$

$$[\text{Females}] : (140 - \text{age}) \times \text{body weight (kg)} \times 0.2 \times 0.85$$

CRP, Alb, PCR and %Cr indexes were measured at the start of the 6-month study.

Statistical analysis

Data are expressed as mean \pm standard deviation (SD). Paired *t* test was employed for comparison between different dialysates. *P* < 0.05 was regarded as statistically significant.

Results

None of the 24 patients enrolled in this study developed any adverse events throughout the 6-month evaluation period (first and last 3-month periods). This study protocol was well tolerated by all patients, allowing the filters, settings for dialysis and drug regimen to remain unchanged as stated in the “Conditions and procedure for online HDF” section of “Materials and methods”.

Predialysis blood pH and bicarbonate levels were significantly higher in the AFD phase than in the ACD phase (Table 3).

AFD resulted in significant decreases in blood CRP and IL-6 levels, which are markers related to inflammation, compared to ACD (Tables 4, 3, respectively). For CRP level, no significant difference was observed between before and after the ACD phase (Table 4).

For markers related to nutrition, leptin was significantly lower in the AFD phase than in the ACD phase (Table 3), but NPY was significantly elevated in the AFD phase (Table 3). There was no statistically significant difference in blood Alb level and PCR between the ACD phase and AFD phase (Table 4). A significantly higher %Cr index level was observed in the AFD phase compared to the ACD phase, although there was no significant difference in the %Cr index between before and after the ACD phase (Table 4).

Table 3 Comparison between conventional acetate-containing bicarbonate-buffered dialysis and acetate-free bicarbonate-buffered dialysis

	ACD (<i>n</i> = 24)	AFD (<i>n</i> = 24)	<i>P</i> value
pH	7.368 \pm 0.033	7.381 \pm 0.036	<0.05
HCO ₃ ⁻ (mEq/l)	19.6 \pm 2.3	21.3 \pm 1.6	<0.01
IL-6 (pg/ml)	8.247 \pm 7.08	5.594 \pm 2.57	<0.05
Leptin (ng/ml)	3.28 \pm 10.79	2.57 \pm 9.24	<0.05
NPY (ng/ml)	0.363 \pm 0.086	0.408 \pm 0.109	<0.05

Data are expressed as mean \pm SD of 24 patients

P values are shown at a statistically significant level for comparison between ACD and AFD by paired *t* test

Predialysis blood was sampled at the end of AFD and ACD phases during their respective 3-month periods

ACD conventional acetate-containing bicarbonate-buffered dialysis, AFD acetate-free bicarbonate-buffered dialysis

Table 4 Comparison between the start and end of conventional acetate-containing bicarbonate-buffered dialysis and the end of acetate-free bicarbonate-buffered dialysis

	Pre-ACD (<i>n</i> = 24)	Post-ACD (<i>n</i> = 24)	Post-AFD (<i>n</i> = 24)
CRP (mg/dl)	0.093 ± 0.081	0.096 ± 0.089	0.055 ± 0.016* [#]
Alb (g/dl)	3.68 ± 0.21	3.67 ± 0.23	3.71 ± 0.28
PCR (g/kg/day)	0.92 ± 0.154	0.921 ± 0.148	0.926 ± 0.149
%Cr index (%)	106.3 ± 26.2	106.1 ± 26.5	110.8 ± 27.9* [#]

Data are expressed as mean ± SD of 24 patients

For other comparisons, no significant differences were observed (paired *t* test)

Predialysis blood was sampled at the start (the first point) of ACD and at the end of ACD and AFD phases during their respective 3-month periods

Pre-ACD at the start (the first point) of conventional acetate-containing bicarbonate-buffered dialysis, *Post-ACD* at the end of conventional acetate-containing bicarbonate-buffered dialysis, *Post-AFD* at the end of acetate-free bicarbonate-buffered dialysis

* *P* < 0.05 significantly different from pre-ACD (paired *t* test)

[#] *P* < 0.05 significantly different from post-ACD (paired *t* test)

Discussion

Adverse effects of acetate-buffered dialysis fluids resulting from acetate intolerance have been reported to be associated with higher cardiovascular risks, thus leading to the widespread use of bicarbonate-buffered dialysis fluids [13]. Many of the commercially available dialysis fluids in Japan are bicarbonate buffered; these contain some acetate (8–10 mEq/l) to prevent salt precipitation. The AFD fluid contains no acetate, but instead a greater amount of sodium bicarbonate (up to 35 mEq/l) to enable effective correction of metabolic acidosis, which is common in individuals with chronic renal failure. The present study was designed to explore the effects of online HDF therapy with AFD fluid on the prognostic factors for bioincompatible events including microinflammation and its concerned nutritional status in hemodialysis patients when compared with those with conventional ACD fluid.

In predialysis analysis of blood pH and bicarbonate levels, effective correction of metabolic acidosis was observed in the AFD phase, evidenced by a significantly higher pH and bicarbonate level. From this data, it can be suggested that the effects depend on the relatively high concentrations of bicarbonate (35 mEq/l) contained in the AFD fluid. Lower predialysis blood levels of bicarbonate have been acknowledged to be associated with a higher risk of mortality for hemodialysis patients, and therefore it is recommended that the predialysis or stabilized serum should be maintained over 22 mEq/l by the K/DOQI guidelines [22]. In the present study, the predialysis blood bicarbonate level was 21.3 ± 1.6 mEq/l in the acetate-free bicarbonate dialysis phase, which seems to fail to meet the K/DOQI guidelines. However, the values obtained in this study are the data collected on Monday or Tuesday, after an interdialytic interval of 2 days, whereas the criteria

given in the K-DOQI guidelines pertain to the predialysis level obtained after an interdialytic interval of 1 day. Therefore, one could conceive that if the blood samples in our study were drawn after an interdialytic interval of 1 day, the values would satisfy the criteria specified in the K-DOQI guidelines.

Both CRP and IL-6, indicators of inflammatory responses produced during ACD, decreased significantly after being replaced by AFD. In the present study, the purity and quality of the dialysis fluids at the end of the dialysis circuit were consistently maintained below 10^{-6} CFU/ml in terms of the bacterial count and below detectable limits for endotoxin throughout the 6-month evaluation period. Furthermore, the conditional background for online HDF therapy, including the filter (membrane material, surface area), oral medication and erythropoiesis-stimulating agent (drug type, dosage), and settings for HDF was well maintained, indicating that such situations are unlikely to affect CRP and IL-6 levels. Higuchi et al. [16] reported that cytokine production was significantly reduced during acetate-free biofiltration therapy compared with during ACD. In view of these findings, the decreases in CRP and IL-6 observed in this study seem to reflect the influence of the absence of acetate in dialysis fluid. IL-6 can induce CRP [23], while the converse is also true, that is, in response to the reduction in IL-6, CRP production was downregulated in the present study. Both CRP and IL-6 have been reported to serve as predictors of the survival rates in maintenance hemodialysis patients, and lowered CRP and IL-6 levels can contribute to better prognosis, including survival advantage, and improved clinical status [24].

In the analysis of biomarkers related to nutritional status, leptin and NPY levels were significantly decreased and increased in the AFD, respectively. Leptin is known as a peptide that suppresses the appetite through its central

regulation [25], and its elevation observed in hemodialysis patients was reported to be positively correlated with inflammation [26, 27]. Given this viewpoint, the reduced level of leptin seen in the present study might be attributable to mitigated inflammatory responses. Conversely, some investigators indicated negative findings concerning the relationship between leptin and inflammation in hemodialysis patients [28]. Further studies are needed on this topic. On the other hand, it has been reported that no correlation was observed between leptin and acid-base balance; if any, the leptin level was increased after correction of metabolic acidosis in patients with renal failure [29, 30]. Therefore, it seems unlikely that correction of metabolic acidosis can be responsible for the reduction in leptin observed in the present study. NPY is a peptide that plays an important role in the stimulation of appetite and is counter-regulated by leptin via hypothalamic arcuate nuclei in the brain [31]. In the present study, it seems possible, therefore, that the reduction in leptin induced the activation of the hypothalamic neurons, resulting in elevation of the NPY level. The report that the NPY level was not changed during acetate-buffered dialysis but elevated during ACD suggests the involvement of the absence of acetate [32]. Although there are some unresolved questions concerning the cause of changes in leptin and NPY, it is expected that the reduction in leptin and elevation in NPY act to stimulate the appetite and thus favorably affect the nutritional status of the living body.

In the present study, AFD failed to affect the blood Alb level or PCR, which are well known as typical nutritional markers in hemodialysis patients [33]; however, a significantly higher blood Alb level during AFD might be overwhelmed by an increased Alb leak through highly permeable dialysis membranes resulting from elevated filtration pressure related to increased viscosity of blood, depending upon raised hematocrit levels [34]. However, AFD was effective for the %Cr index. An increased %Cr index is interpreted as reflecting increased muscle mass, suggesting improvement in nutritional status [35]. It seems that the increased %Cr index observed in this study also depends upon alleviation of inflammatory responses as evidenced by Kaizu et al. [36], who indicated that IL-6 affected the nutritional indicators (albumin, Cr, body weight, arm muscle area) in hemodialysis patients. This issue has been supported by the fact that IL-6-induced skeletal muscle protein breakdown (increased tyrosine and 3-MeHis) and muscle atrophy have been reported by experimental and clinical studies [37, 38]. Our study showed that a reduction in the IL-6 level may lead to promoting greater muscle mass. The effectively changed PCR and %Cr index might result from increased appetite following a reduction in leptin and elevation in NPY [31]. Significant elevation in predialysis blood pH and HCO_3^-

levels should be noticed in the AFD. It has also been reported that correction of metabolic acidosis is associated with suppressed protein catabolism and improved nutritional status [39–41], but we cannot rule out that efficient correction of metabolic acidosis was also involved in the elevation of the %Cr index observed in the present study.

Limitations in this study are the small number of subjects (24 patients) and inability to design a complete cross-over study (ACD → AFD → ACD). Furthermore, our data stem only from patients receiving online HDF; therefore, studies in hemodialysis patients need to be implemented. The sample size in our study had to be limited because it was relatively difficult to keep steady conditions such as dialysis settings and drug regimens for 6 months. Also, the inability to execute a complete cross-over study can be explained by the domestic aspect that a central dialysis fluid delivery system (CDDS) has been introduced in many Japanese medical facilities; namely, if the dialysis fluid were changed for a cross-over study, patients other than the subjects of this study would also be involved. It should be considered that 8 of the 24 patients enrolled in our study strongly refused to resume ACD after AFD.

Our evaluation is based on the comparison between ACD and AFD regarding data obtained after 3 months of online HDF with ACD and AFD fluids, respectively. When the data drawn at the start of the study (at the start of online HDF with ACD fluid) were added to the evaluation, no significant difference in CRP levels was observed between before and after online HDF with ACD fluid, whereas the CRP level was significantly decreased 3 months after online HDF with AFD fluid (Table 4). Similar favorable changes were noted in the %Cr index (Table 4). These results strongly suggest that the changes in the CRP and %Cr index observed 3 months after online HDF with AFD fluid represent specific effects of the AFD fluid but do not reflect the effects of long-term online HDF therapy per session.

Conclusion

The results obtained in this study indicate that online HDF therapy with AFD fluid can significantly alleviate micro-inflammatory responses as compared to ACD fluid, and is accompanied by significantly greater alleviation or improvement of nutritional markers. Our data also suggest that even minimal amounts of acetate contained in the dialysis fluid can be bioincompatible for blood purification. Acetate-free blood purification therapy would be expected to open a promising therapeutic avenue for improving biocompatibility over conventional acetate-containing bicarbonate blood purification, thus leading to improvement in nutritional status, and possibly MIA syndrome, in hemodialysis patients.

Conflict of interest None declared.

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