

Acetate-Free Biofiltration Versus Online Acetate-Free Hemodiafiltration in Patients at High Risk of Hemodialysis Intolerance



Clara Apter¹, Bruno Seigneuric¹, Amandine Darres¹, Nathalie Longlune¹, Nassim Kamar^{1,2,3}, Olivier Cointault¹ and Stanislas Faguer^{1,3,4}

¹Department of Nephrology and Organ Transplantation, University Hospital of Toulouse, Toulouse, France; ²National Institute of Health and Medical Research, UMR 1291, INFINITY, Toulouse, France; ³University Paul Sabatier – Toulouse 3, Toulouse, France; and ⁴National Institute of Health and Medical Research, UMR 1297, I2MC, Toulouse, France

Correspondence: Stanislas Faguer, Department of Nephrology and Organ Transplantation, University Hospital of Toulouse, 1, avenue du Pr Jean Poulhès, 31059 Toulouse Cedex, France. E-mail: stanislas.faguer@inserm.fr

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KEYWORDS: acetate-free biofiltration; dialysis; hemodynamic tolerance; hypotension

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Intradialytic hypotension (IDH) is one of the most frequent^{1,2} and worrying issues in chronic hemodialysis.^{3,4} Systolic blood pressure (BP) <90 mm Hg has the strongest association with mortality in patients receiving chronic kidney replacement therapy (CKRT).³ IDH results from the combination of excessive ultrafiltration rate, membrane bio-incompatibility, and inappropriate hemodynamic response (heart rate and contractility, vascular tone).⁵ Modulation of the dialysate composition can improve tolerance, but standard bicarbonate dialysis remains associated with frequent IDH in patients at high risk. Online high-volume hemodiafiltration (HDF) was proposed to improve hemodynamic tolerance but was also associated with IDH in a subset of patients.

Bicarbonate dialysis requires the acidification of the dialysate to avoid carbonate precipitation, but this can contribute to IDH because of the toxicity of the acid used (e.g., acetate-induced vasoplegia and cardiac dysfunction), acidosis-induced neutrophils activation, or carbon dioxide loading during the session.^{6,7} Avoiding dialysate acidification using acetate-free biofiltration (AFB), a technique characterized by bicarbonate-free and acid-free dialysate with postfilter bicarbonate reinjection, was thus proposed in the 1980s to reduce the incidence of IDH. However, AFB did not find widespread use at that time because of technical pitfalls or uncertainty regarding its benefits.

In this study, we aimed to reassess whether AFB performed with modern monitors reduces hemodialysis intolerance in CKRT patients prone to IHD and is well tolerated.

We retrospectively reviewed the dialysis sessions of all the CKRT patients who received AFB at the University Hospital of Toulouse between January 2019 and January 2021 ($N = 23$). Hemodynamic parameters were collected before, during, and at the end of each dialysis session during the 3 months that preceded the start of AFB and during the first 3 months of AFB use (thus totaling 1656 dialysis sessions analyzed in this study). The primary outcome was the frequency of IDH. To increase the robustness of the findings, 3 definitions of IDH were used: Kidney Disease Outcomes – Quality Initiative classification (decrease of either 20 mm Hg for systolic BP or 10 mm Hg for mean arterial BP with symptoms), European Renal Best Practice classification (IDH with symptoms and intervention like stopping ultrafiltration, saline infusion), and UK guidelines (any BP decrease leading to intervention).⁵ Target weight and mean ultrafiltration were considered, as well as biological data related to the quality of euration and systemic inflammation (hemoglobin, C-reactive protein, and B2-microglobuline, Kt/V Daugirdas). Discontinuous variables were given as numbers and percentages and compared with Fisher exact test. Continuous variables were given as the mean \pm SD of each 3-month period and compared with the Wilcoxon matched-paired nonparametric test after evaluation of their distribution using the D’Agostino and Pearson and the Kolmogorov-Smirnov tests.

During the study period, 23 patients (male sex $n = 17$ (74%); mean age 68 ± 16) who had been requiring CKRT for a mean time of 6.3 ± 5.5 years switched from HDF to AFB (3 sessions per week). Most patients had

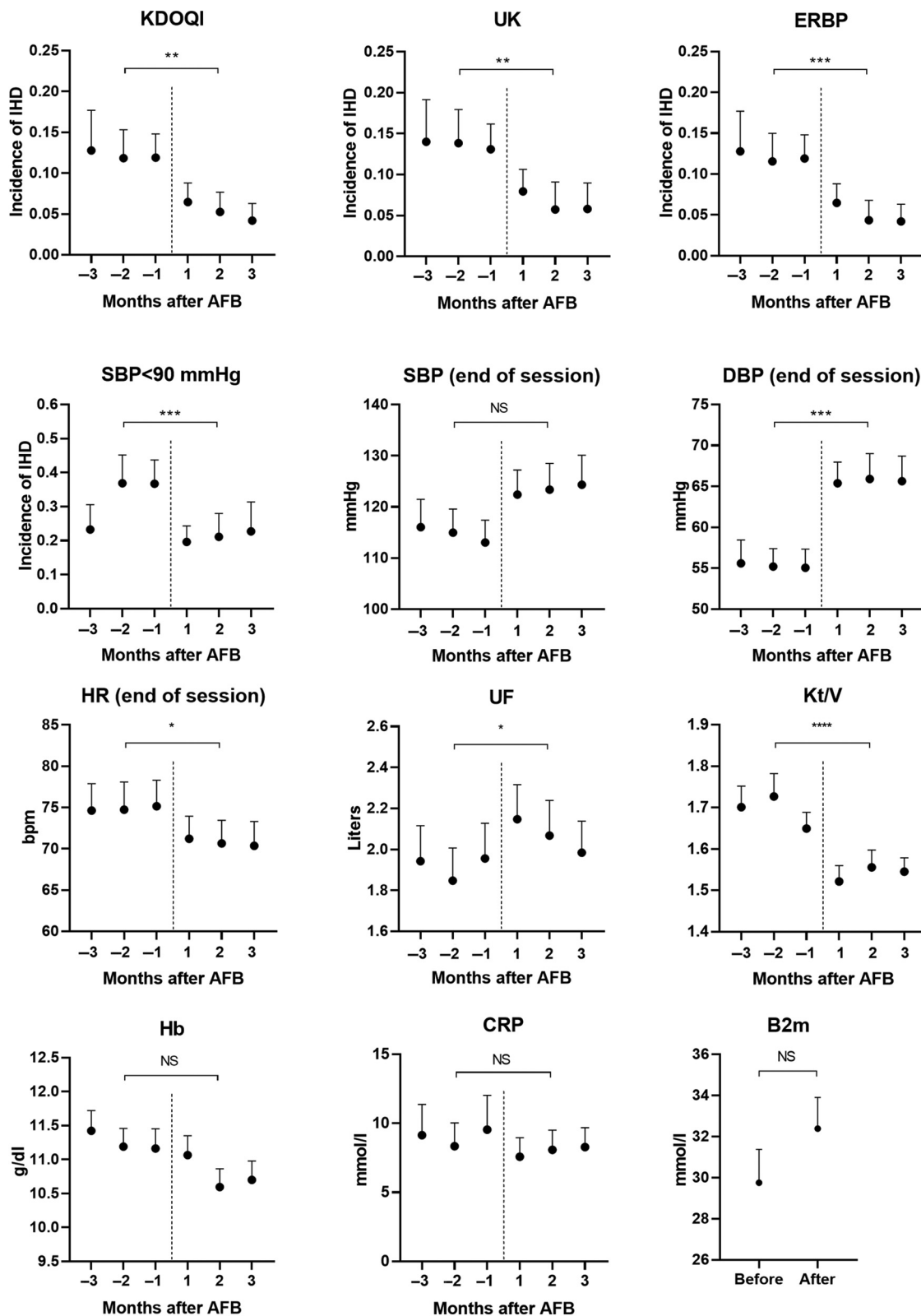


Figure 1. Hemodynamic and biological parameters before and after the switch from bicarbonate-based hemodialysis to AFB. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. AFB, acetate-free biofiltration; B2m, B2-microglobulin; bpm, beats per minute; CRP, C-reactive protein; DBP, diastolic blood pressure; ERBP, European Renal Best Practice; Hb, hemoglobin; HR, heart rate; IHD, intradialytic hypotension; KDOQI, Kidney Disease Outcomes - Quality Initiative; NS, not significant; SBP, systolic blood pressure; UF, ultrafiltration; UK, United Kingdom.

Table 1. Characteristics of the 23 patients included in the study

Characteristics	Cohort N = 23	
	Before (HDF)	After (AFB)
Age, yr, mean ± SD	63 ± 16	
Male, n (%)	6 (26)	
Time on CKRT, yr, mean ± SD	6.3 ± 5	
Diabetes mellitus, n (%)	10 (43)	
Cardiac disease, n (%)		
Ischemic	6 (26)	
Valvular	3 (13)	
LVEF <50%	4 (17)	
Atrial fibrillation	9 (39)	
Hemodynamic parameters before the session		
Heart rate, bpm, mean ± SD	75 ± 12	74 ± 12
SBP, mm Hg, mean ± SD	128 ± 19	133 ± 21
Diastolic blood pressure, mm Hg, mean ± SD	60 ± 11	71 ± 13
Intradialytic hypotension, %, mean ± SD		
KDOQI	11.8 ± 15	5.5 ± 9
UK	13.1 ± 16	6.2 ± 12
ERBP	11.7 ± 15	4.8 ± 9
SBP < 90 mmHg	33.5 ± 31	20.8 ± 25
Total ultrafiltration, ml, mean ± SD	1.91 ± 0.7	2.1 ± 0.7
Hemodynamic parameters after the session		
Heart rate, bpm, mean ± SD	75 ± 14	71 ± 13
SBP, mm Hg, mean ± SD	117 ± 24	122 ± 23
Diastolic blood pressure, mm Hg, mean ± SD	57 ± 13	65 ± 12
C-reactive protein, mg/l, mean ± SD	13.6 ± 14	10.8 ± 8.5
B2-microglobulin, mg/l, mean ± SD	29.8 ± 6.9	32.4 ± 6.8
Hemoglobin, g/dl, mean ± SD	11.2 ± 1.2	10.9 ± 1.5
Kt/V, mean ± SD	1.7 ± 0.2	1.54 ± 0.2

AFB, acetate-free biofiltration; bpm, beats per minute; CKRT, chronic kidney replacement therapy; ERBP, European Renal Best Practice; HDF, hemodiafiltration; KDOQI, Kidney Disease Outcomes - Quality Initiative; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure; UK, United Kingdom.

diabetes mellitus, ischemic heart disease, atrial fibrillation, or left ventricular ejection fraction <50%. A total of 11 patients (48%) had hypertension. At the time of the switch, all patients except 1 received high-volume HDF (>20 l per session) with high cutoff membrane and chloride acid-based dialysate acidification. Parameters of AFB were as follows: Artis Physio monitor (Baxter, Maurepas, France), Safebag dialysate (Baxter), blood flow 300 to 350 ml/min, dialysate flow 500 ml/min, bicarbonate reinjection 2 to 2.3 l/h, Elisio 21H filter (Nipro Pharman Authon-du-Perche, France), and decreasing potassium profile.

As shown in Figure 1, the incidence of IDH dramatically decreased after the switch from HDF to AFB, whatever the IDH definition used. Mean percentage of dialysis sessions with at least 1 BP <90 mm Hg was significantly higher during the HDF period (32%) compared with the AFB period (21%) ($P < 0.01$). During the AFB period, mean diastolic BP at the end of the session dramatically increased owing to significant increase in diastolic BP (57 vs. 65 mm Hg, $P < 0.0001$). Target weight and total ultrafiltration were similar

between the 2 study periods. Accordingly, heart rate at the end of the session significantly decreased. The BP measured before the start of the session was higher, suggesting maintained positive effect of AFB on hemodynamic status beyond the dialysis session. After the switch to AFB, serum levels of C-reactive protein, B2-microglobulin, and hemoglobin were stable (Table 1). Kt/V was significantly lower with AFB compared with high-volume HDF but remained >1.2 in all patients. Throughout the study period, no adverse events related to these techniques occurred.

AFB was developed 40 years ago to reduce the toxicity of dialysates with a high amount of acetate,^{8,S1,S2} and some preliminary studies suggested a higher hemodynamic tolerance compared with conventional bicarbonate dialysis,^{S3,S4} but some technical pitfalls precluded its widespread use. Here, we reported a significant decrease in IDH incidence after the switch to AFB in patients prone to IDH (long history of CKRT, underlying cardiovascular diseases, high incidence of IDH), although patients received optimized high-volume HDF and acetate-zero dialysates. The superiority of AFB over HDF was thus confirmed in the patients the most at risk of IDH, even when compared with HDF performed with acetate-zero dialysate, a new finding that is complementary to older studies.

Some limitations of this study should be stated. First, the number of patients is small, but hemodynamic parameters were collected for a total of >1600 dialysis sessions. Throughout the study, standard-of-care was applied to patients, and the switch from HDF to AFB was the only significant change. Second, because of its retrospective design and the short follow-up, our study cannot conclude whether improved hemodynamic tolerance with AFB will ultimately translate into better survival and lower cerebral or cardiac morbidity. Third, the mechanisms that underlie better hemodynamic tolerance remain elusive. AFB led to an increase in diastolic BP, suggesting reduced hemodialysis-induced vasoplegia. The main difference between HDF and AFB is the strong release of carbon dioxide from the dialysate with bicarbonate dialysis and HDF compared with reduced carbon dioxide loading with AFB,⁷ which may activate inflammatory cells and promote nitric oxide release within systemic circulation,^{6,S5} 2 mechanisms contributing to vasoplegia. Fourth, the patients included in this study were highly selected and had a strong intolerance to HDF. Fifth, the use of a decreasing potassium profile may also have contributed to the better tolerance of AFB. The “real-life” design of the study reinforces the interests of the technique, which was easily implemented in our center. Further prospective controlled

studies will have to identify patients who will benefit from the switch to AFB.

In conclusion, in a cohort of patients at high risk of CKRT, the switch from HDF to AFB was associated with a dramatic improvement in hemodynamic tolerance.

DISCLOSURE

SF received travel support from Sanofi-Genzyme, consulting fees from Abionyx Pharma, and symposium fees from Asahi and Vifor Pharma (all outside the scope of this study). All the other authors declared no competing interests.

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ETHICAL CONSIDERATION

This study was conducted according to the Declaration of Helsinki, as revised in 2004. According to the French law regarding retrospective studies, the Institutional Review Board of the University Hospital of Toulouse waived the need for written informed consent.

AUTHOR CONTRIBUTIONS

SF, OC, and CA designed the study. All the authors followed the patients included in this study. CA collected the data. SF performed the statistical analyses. SF and CA wrote the first draft of the paper, and all coauthors approved the last version of the manuscript.

SUPPLEMENTARY MATERIAL

[Supplementary File \(PDF\)](#).

[Supplementary References](#).

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