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Original article

Comparison of the hemodynamic tolerance and the biological parameters of four acetate-free hemodialysis methods

George Kosmadakis *, Enrique Da Costa Correia, Julie Albaret, Frédéric Somda, Didier Aguilera

Hemodialysis Unit–pôle métabolique, centre hospitalier Jacques-Lacarin, 54, boulevard Denière, 03207 Vichy, France

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ABSTRACT

Purpose. – Acetate in hemodialysis solutions exerts inflammatory, vasodilatatory and cardio-depressive effects. Citrate has been proposed as an optimal substitute. The aim of the present trial was the comparison of the hemodynamic and biological parameters on a group of patients dialysed consecutively with 4 acetate-free haemodialysis techniques.
Methods. – In a prospective crossover manner, we measured the hemodynamic and biological effects of four acetate-free hemodialysis methods: the acetate-free biofiltration with variable potassium (AFBK) and three methods with a citrate buffer: conventional hemodialysis (HD), on-line hemodiafiltration (HDF) and on-line hemofiltration (HF). Fourteen chronic hemodialysis patients (9 males mean age 72.21 ± 11.21 years old) underwent 6 four-hour dialysis sessions for 2 weeks on each of the 4 studied techniques.
Results. – The AFBK technique presented less intradialytic hypotensive episodes (1 in 84 sessions) compared to the other techniques (HD: 29/84, HDF 22/82 and HF: 14/78; $P < 0.001$). The blood pressure after one, two, three hours of dialysis and at the end of the hemodialysis session was significantly higher in the AFBK technique. On AFBK the net ultrafiltration (UF) ($P < 0.001$) and the UF as a percentage of the dry weight ($P = 0.005$) were significantly higher. A significant correlation between the prevalence of hypotensive episodes and the change of serum potassium levels ($P = 0.002$) during the first hour of dialysis was detected.
Conclusions. – AFBK is associated with a better intradialytic hemodynamic tolerance and could be an optimal method for frail hypotension-prone hemodialysis patients.

1. Introduction

From the early stages of the hemodialysis era, the physico-chemical mechanisms of diffusion, filtration (osmosis) and absorption were tried in various combinations in order to achieve the maximal clearance of the broader uremic toxins' molecular weight spectrum, without a serious loss of substances necessary for the physiological functions. In the mean time, financial and quality of life purposes are pressing for shorter dialysis duration with the maximal efficacy and with the best hemodynamic tolerance possible. This task is even more complicated by the rise of the mean age and comorbidity burden of the dialysis population [1].

Acetate was used as a dialysis buffer since the early stages of the hemodialysis era and its serious secondary effects led to the introduction of bicarbonate-containing dialysate [2].

Nevertheless, in the context of the so-called conventional bicarbonate dialysis, the acid phase of the dialysate still contains 4–8 mmol of acetate. On-line hemodiafiltration requires the production of large volumes of ultrapure dialysate produced from the same acetate-containing concentrate. That leads to a significant mass of acetate being infused in the patient exposing him to its proinflammatory, vasodilatatory and cardio-depressive effects [3].

Citrate hemodialysis is a hemodialysis technique firstly proposed by Ahmad et al. in which the acetate is substituted by citrate [4].

Citrate is an acetate substitute but at the same time it is antagonising calcium which is a central coagulation factor participating in multiple stages of the coagulation cascade [5].

* Corresponding author.
E-mail address: George.kosmadakis@gmail.com (G. Kosmadakis).

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In non-inferiority studies, it has proven a safe alternative to acetate-containing bicarbonate dialysis and on-line hemodiafiltration without significant hypocalcemia or clinically important coagulation issues [6,7].

Acetate-free biofiltration with potassium profiling (AFBK) is a technique proposed with the Hospal/Gambro® dialysis machines that includes an acetate-free biofiltration method with a profiling of dialysate potassium concentration. The module without potassium profile has been proposed since 1982 by Zucchelli et al. [8] and the addition of potassium profiling has improved the arrhythmogenic potential of the dialytic process [9] as well as the intradialytic hemodynamic tolerance [10].

The aim of the present study is the comparison of the hemodynamic and the biological parameters of 4 acetate-free hemodialysis techniques in a sample of patients dialysing 4 hours 3 times a week.

2. Patients and methods

We performed a prospective crossover study of the hemodynamic as well as biological effects of four acetate-free hemodialysis methods: the AFBK, and three methods with a citrate buffer, the conventional hemodialysis (HD), on-line hemodiafiltration (HDF) and on-line hemofiltration (HF).

Fourteen chronic hemodialysis patients (9 males/5 females mean age 72.21 ± 11.21 years old) underwent 6 four-hour dialysis sessions for 2 weeks on each of the 4 studied techniques on a random order. AFBK is a hemodiafiltration technique with infusion of the bicarbonate final solution in the form of 3 L bags post-filter (9 L in total) and the concentrate of potassium in a 4 L bag with a regulated variable intradialytic concentration. The very high flux polysulfone Toraysulfone TS 1.8® dialyser was used. Apart from the potassium profiling adjusted for a mean intradialytic concentration equivalent to 2 mmol/L with the AFBK, the rest of dialysate parameters were common for all the techniques with conductivity and estimated osmolality equivalent to a Na concentration of 140 mmol/L, calcium concentration at 1.5 mmol/L, glucose 1 g/L, magnesium 0.5 mmol/L and bicarbonate at 32 mmol/L. The dialysate temperature for all dialysis techniques was set at 36.5 °C, the blood flow was set at 350 mL/min and the dialysate flow (except in HF where there was no dialysate) at 600 mL/min. For the non-AFBK techniques, the citrate concentration was 3 mEq/L and the dialysate potassium concentration was 2 mmol/L. On HDF and HF, the volume of reinfusion was between 22 and 25 L per dialysis session (6 L/h) and for AFBK a total of 13 L per session (three 3 L 1.4% bicarbonate bags and a 4 L potassium containing bag per session).

The study was prospective and partially single-blinded as the patients could identify the use of different dialysis machines during the AFBK period (Hospal Evosys®) but could not understand the difference between the other three techniques practiced on the same model of dialysis machine (Fresenius 5008 HF®).

During these 6 dialysis sessions on every method, we studied the intradialytic hemodynamic parameters including the number of sessions with hypotensive episodes, the systolic and diastolic blood pressures registered on an hourly basis throughout the dialysis session as well as the maximal and minimal intradialytic tensional values. A hypotensive episode was defined by a reduction of systolic arterial pressure of at least 25 mmHg associated with diaphoresis, cramps or lack of conscience, necessitating a medical or paramedical intervention with reduction of the ultrafiltration (UF) rate to 0 mL/min, the infusion of a 100–200 mL bolus of 0.9% NaCl or 10 mL of 10% NaCl intravenously as well as the positioning of the patient in a Tredelenburg position [11].

We also studied the difference in the dry weight and the indices of UF per method of dialysis. The state of hydration as well as the body composition were measured with the Blood Volume Monitor (BVM)® Fresenius Medical Care, Bad-Hamburg, Germany. Finally, we studied a series of biological parameters that were measured on the fifth session of each dialysis method in order to avoid the influence between methods.

The Kt/V was used to quantify the dialysis adequacy and by using the second generation single pool Daugirdas formula $(Kt/V = -\ln(R - 0.03) + [(4 - 3.5) \times R) \times (UF/W)]$, where R = post-dialysis BUN/pre-dialysis BUN, UF = net ultrafiltration, W = weight, K = dialyzer clearance of urea, t = dialysis time, and V = patient's total body water [12]. The nPCR for the patients' nutritional status was estimated using the formal urea kinetic modelling [13]. Regarding the biological parameters, we measured haemoglobin levels and serum sodium, potassium, calcium, phosphate urea, alkaline reserve, creatinine, uric acid, beta-2-macroglobulin and magnesium concentrations at baseline, serum potassium on every hour during the dialysis session and serum urea as well as beta-2-macroglobulin levels at the end of the dialysis session.

The patients were clinically stable adults without any acute illnesses or hospitalisations since at least 3 months, mentally capable to give consent for participating in a study and literate enough to read and understand the French language. An informed consent form was signed by the participating patients at least a week after being given an information sheet and explained the details of the study. Out of the 20 patients proposed and given the study information sheet, 14 accepted to participate in the study and signed the informed consent form. The hypertensive treatment of the patients was not modified during the study period.

All four methods of dialysis are routinely used in our centre and in centres all over the world and the prescriptions were aimed at offering the best complication-free dialysis. The current patient group was on on-line HDF before the study and presented the same hemodynamic profile as the one observed throughout the on-line HDF period during the study.

3. Data and study protocols, statistical analysis

This prospective crossover single centre study was approved by the local standards ethics committee and took place under continued medical surveillance.

Hemodynamic data were obtained throughout the six dialysis sessions per method. In this non-superiority study, the null hypothesis is that the clinicobiological parameters do not differ significantly between the 4 methods. The primary end-point is the number of hypotensive episodes and the secondary end-points are the hemodynamic and biological parameters studied.

We compared the levels of the studied parameters in the four methods and between the four methods throughout the study period. Values are given as mean ± SD. Statistical analysis was performed using the SPSS® Version 21.0 (SPSS Inc., Chicago, IL, USA). The x^2 was used for the comparison of categorical data (the number of hypotensive episodes per method). Analysis of variance (ANOVA) was performed to evaluate the overall significance in the rate of change for the studied parameters during the treatment period. A post-hoc analysis (Bonferroni analysis) was performed to compare the differences between the four groups in the studied parameters at every specific time-point throughout the study. A multivariate analysis took place on the search for multiple variables correlations (one-way MANOVA). P-values < 0.05 were considered to be significant. It is important to note that we made an alpha correction (Bonferroni) to account for multiple ANOVAs being run. As such, in this case, the statistical significance was $P < 0.025$.

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