Effects of dialyzer reuse on dialysis adequacy, anemia control, erythropoieting-stimulating agents use and phosphate level

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Submitted: 29 October 2013
Accepted: 30 October 2013

Arch Med Sci 2016; 12, 1: 219–221
DOI: 10.5114/aoms.2016.57599

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Almost 50 years have passed since the first time the concept of dialyzer reuse in hemodialyzed patients was introduced for primarily economic reasons [1]. Hemodialyzers are labeled by the Food and Drug Administration (FDA) and European Medicines Agency (EMA) as single use only. In recognition of the widespread practice of reuse in the United States, in 1996 the FDA required manufacturers to label dialyzers for multiple use and to back up this claim with data showing that the performance of the dialyzer is sustained over multiple uses [2]. In Poland there is also a tendency to stop the reuse of dialyzers. There are three major concerns with reuse: the risk of infection; biochemical and immunologic effects; and loss of performance with impairment in clearance and/or ultrafiltration [3].

The aim of our study was to assess the dialysis adequacy, anemia control, erythropoieting-stimulating agents (ESA) use as well as phosphate control in 68 patients from a single center before and 1 year after stopping reuse of dialyzers. In addition, together with single use of dialyzers, all the patients were switched to high-flux dialyzers (Fresenius, Bad Homburg, Germany).

We conducted a prospective study. Sixty-eight hemodialyzed patients (33 females) with overall mean age of 65 ±16 years were included in the study. Mean time on dialysis was 51 months. The causes of end-stage renal disease varied between diabetic nephropathy (n = 7), chronic glomerulonephritis (n = 20), autosomal dominant polycystic kidney disease (ADPKD) (n = 5), hypertensive nephropathy (n = 15), nephrolithiasis (n = 5) and others or unknown (n = 12). All the dialyzed patients met the following criteria: a stable clinical state, C-reactive protein (CRP) below 6 mg/l (using a qualitative method for screening), no oral contraception in women of child-bearing age, stable and no more than twice the normal glutamic-oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT) activities, no evidence of blood loss other than that related to dialysis during the last 6 months, and no other than renal cause of anemia. None of the patients investigated had received blood transfusions for at least 1.5 months and no drugs known to affect platelet function and coagulation were administered for at least 2 weeks prior to the study (except heparin during the hemodialysis session). The study was approved by the Ethic Committee. All the patients were on chronic maintenance hemodialysis (three times a week for 4–4.5 h per hemodialysis

procedure). All HD patients were receiving treatment with low-flux cuprophane (Bellco, n = 17) or polysulfone membranes (F5 n = 10, F6 = 32, F8 = 9) and bicarbonate-based dialysate with heparinization (low-molecular-weight heparin (LMWH) = 3, unfractionated heparin (UFH) = 61). All the dialyzers were reused. Blood was drawn both in the morning between 8.00 and 9.00 a.m. to avoid circadian variations before the switch of the dialyzers and stopping reuse before the start of the midweek dialysis session (and before heparin administration), and after hemodialysis from the arterial line of the hemodialysis system, immediately before discontinuation of the extracorporeal circulation (only for urea concentration necessary for Kt/V determination, used as a marker of adequacy of dialysis). The following biochemical parameters were assessed: hemoglobin, serum iron, total iron binding capacity, urea before and after HD, phosphate by means of standard laboratory methods in the central laboratory. Then high-flux single-use polysulfone dialyzers were introduced (F50, F60 or F80 respectively) in all the patients. ESA used was Eprex (Jannsen-Cilag, Switzerland), and iron used was iron sucrose (Venofer, Ferrum Lek, Ljubljana, Slovenia).

Data were expressed as means ± SD. The data given were analyzed using Statistica 10.0. computer software (Tulsa, OK, USA). The examination of the distribution normality of variables was done using the Shapiro-Wilk W test.

The biochemical and clinical data are presented in Table I. One year after the switch to single use high flux dialyzers use of ESA (both weekly and per kg dry body weight) dropped significantly in the study group, with a significant increase in hemoglobin, whereas the iron supplementation did not change. A significant fall in serum phosphate was also observed. We also observed a better dialysis adequacy as reflected by significantly lower urea after the HD session, and a highly significant rise in urea reduction ratio was observed, together with a tendency to rise in Kt/V.

In our pilot, single center study, we found a better dialysis adequacy as reflected by significantly higher urinary reduction ratio, lower urea after HD and a tendency of increased Kt/V. There are a few reports on dialysis adequacy in regard to dialyzer reuse and after switch to single use dialyzers. Mitwalli *et al.* [4] prospectively studied reuse of hemodialyzers in 10 HD patients for 3 months. The urea reduction ratio was maintained between 73 ±5% at baseline and 71.2 ±9.03% (p = 0.53) at the maximum reuse. We studied a much larger population of 68 patients for a much longer period of time, i.e. 1 year vs. 3 months. On the other hand, the negligible effects on urea, creatinine, and phosphorus removal with cellulose membranes were reported previously [5]. However, reprocessing dialyzers may compromise delivery of the prescribed dialysis dose, i.e. measured Kt/V for urea during dialysis with a low (mean 4th reuse) and a high (mean 14th reuse) number of reuses [6]. The Kt/V was significantly lower in the high number of reuse treatment (1.05 vs. 1.10 early in the sequence). Why this occurs is unclear, but it could be related to the progressive intradialytic loss of fiber bundle volume (FBV) and effective surface area that is not detected during postdialysis FBV measurements made on the reprocessing machine [7]. We also found a favorable effect on serum phosphate in our patients, indicating better phosphate control including removal during HD. As

Table I. Some biochemical parameters before and after switch to non-reuse and polysulfone dialyzers

Parameter	Before change	After change	Value of p
Urea before HD [mmol/l]	24.01 ±6.35	24.24 ±6.90	
Urea after HD [mmol/l]	7.40 ±2.41	6.64 ±2.15	< 0.05
Urea reduction ratio (%)	69.34 ±6.79	72.54 ±4.73	< 0.001
Kt/V	1.46 ±0.54	1.54 ±0.17	
HD time weekly [h]	11.71 ±2.27	12.34 ±1.54	< 0.05
ESA weekly dose [IU]	3485 ±2179	2846 ±2706	< 0.01
ESA dose per kg dry body weight	55.12 ±38.41	45.42 ±45.56	< 0.01
Serum iron [nmol/l]	12.07±4.38	13.76 ±5.99	
TSAT (%)	32.34 ±19.02	34.64 ±17.77	
Iron *i.v.* weekly [g]	54.76 ±71.84	53.73 ±67.03	
Hb [mg/dl]	10.74 ±1.61	11.14 ±1.50	< 0.06
Phosphate [mmol/l]	1.87 ±0.55	1.73 ±0.51	< 0.05

TSAT – transferrin saturation.

hyperphosphatemia still remains an important issue in dialyzed patients and the dietary approach as well as phosphate binders use are suboptimal, our finding merits further evaluation. It might also be of clinical importance in patients with inadequate adherence to the diet and medications. It might also be relevant to the clearance of uremic toxins other than phosphate known to be associated with mortality [8]. Dialyzer reuse is practiced in more than 75% of the patients and dialysis units in the United States [1] and in other countries, including Poland. As shown by Okechukwu *et al.* [9] on the basis of the data source from the Dialysis Mortality and Morbidity Study, Waves 1, 3, and 4 of the US Renal Data System no reuse was more likely in larger units and in not-for-profit and hospital-based units. Although the bundle system was introduced in Poland several years ago, there were still some units reusing dialyzers, including chains. Costs of ESA and iron are included in the bundle in Poland. As shown for kidney transplant recipients, comorbidities and treatment play a role in cost-effectiveness [10]. We looked at whether the reuse and the switch to single use and more compatible polysulfone membranes affected ESA requirements and iron supplementation. In our population studied hemoglobin increased significantly whereas ESA use decreased significantly (both weekly dose and dose per kg dry body weight). At the same time, intravenous iron use remains stable. Yokoyama *et al.* [11] studied the effects of recombinant human erythropoietin (r-HuEPO) administration on adequacy of hemodialysis during single-use versus multiple-reuse of hemophan hollow-fiber dialyzers, assessed in 16 stable end-stage renal disease patients. When dialyzer reprocessing was performed, the r-HuEPO dosage and hemoglobin level remained unchanged compared with the subgroup treated with single-use dialyzers. However, they did not report weekly iron doses. The iron metabolism plays a crucial role in the pathogenesis of anemia in chronic kidney diseases [12]. We studied a much larger population and used much lower weekly doses of ESA (3485 vs. 4500 IU).

In conclusion, we are fully aware of the limitations of our study, being single center, non-randomized, without hard end-points. However, we had a unique opportunity to study the effect of switching from reprocessing dialyzers to single use, more biocompatible polysulfone membranes from only one company. We found a significant beneficial effect on anemia control as well as phosphate levels. It also provided more economical and efficient dialysis. It might also be relevant to the better control of blood pressure; however, the target value for the kidney population is still a matter of debate [13] with all its consequences [14, 15].

Conflict of interest

The authors declare no conflict of interest.

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