Journal of Trace Elements in Medicine and Biology 36 (2016) 52–56

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.com/locate/jtemb

Clinical studies

Impact of dialyzer membrane flux on metal clearance in hemodialysis patients

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ARTICLE INFO

Article history:
Received 18 January 2016
Received in revised form 4 April 2016
Accepted 6 April 2016

Keywords:
Metal ions
Low flux membranes
High flux membranes
Hemodialysis patients

ABSTRACT

Deficiency of essential trace elements (such as Cu or Zn) and accumulation of potentially toxic trace elements (as Cd or Pb) are both known to have adverse effects in hemodialysis (HD) patients. Up to our knowledge, no studies about the permeability of low and high flux polysulfone membranes on metal ions during hemodialysis are available. Therefore, the aim of the present study was to address this issue. Forty one hemodialysis patients (19 were using high flux polysulfone membrane while the remaining were using low flux one) participated in the study. Blood levels of Cu, Zn, Cd and Pb were determined by graphite furnace atomic absorption spectrometry among HD patients, before and after dialysis session, as well as among matched 40 healthy persons. Blood concentrations of Cu and Zn in the whole hemodialysis group was significantly lower than those of the healthy control group, on the other hand the toxic metals (Cd and Pb) levels were observed to be significantly higher among HD patients compared to the normal persons. Among the hemodialysis group, there were no significant differences between the low and high flux dialyzer groups in terms of pre-dialysis blood levels of Cu, Zn, Cd and Pb. In addition, significantly decreased levels of all metal ions were observed after dialysis sessions using either low or high flux membranes. An exception was Pb which did not show any difference between pre-dialysis and post-dialysis values in the low flux groupIn conclusion Zn and Cu deficiencies should be considered in the treatment of these patients. High flux membranes are more efficient than low flux ones in removing excess Cd and Pb. Therefore, when high flux membranes are used, chelation therapy might not be required for Cd and Pb overload.

1. Introduction

Hemodialysis (HD) patients are at risk of deficiency of essential trace elements (such as Cu and Zn) and overload of toxic metals such as Cd and Pb; both of which can affect health [1,2]. Zn deficiency is associated with delayed wound healing, reduced immunity, erythropoietin resistance, dysgeusia and erectile dysfunction [3–5]. Cu insufficiency was assumed to play a role in the pathogenesis of anemia and growth retardation of HD patients [6]. Blood Pb and Cd concentrations have been reported to be elevated in HD patients [7]. Cd exposure could induce lipid peroxidation [8,9], as well as increased oxidative stress in tissues [10,11]. Hsu et al. [12] reported that Cd exposure is significantly associated with malnutrition, inflammation, and protein-energy wasting in maintenance HD patients. In another study [13], there was a correlation between serum Cd levels and risk of atherosclerosis in long-term HD patients. High Pb levels have been associated with increased mortality in adults, both in peritoneal [14] and HD patients [15]. Previous studies also demonstrated that blood Pb level is related to hemoglobin level, blood pressure, and parathyroid hormone levels in HD patients [16–18].

Hemodialysis membranes are composed of semi-permeable materials, allowing the diffusion of certain types of molecules or ions between the blood and dialysate. Classical membranes are made up of modified cellulose. Subsequent membranes were produced from more synthetic polymers such as polyacrilonitryl and polysulfone [19]. Polysulfone-based membrane has been used in HD and it is incessantly improved to ensure its applicability [20]. Polysulfone dialysis membranes modified by polyvinylpyrrolidone have excellent biocompatibility in clinical use, and are capable of being prepared in low-flux or high-flux form [21]. High-flux mem-

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http://dx.doi.org/10.1016/j.jtemb.2016.04.004
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Table 1
Characteristics of the study population.

	Hemodialysis patients		Control group
	Low flux group	High flux group	
Number	22	19	40
Age (years)	39.7 ± 14.8	46.5 ± 12.5	41.4 ± 11.6
Gender	11 males, 11 females	11 males, 8 females	22 males, 18 females
Duration of Hemodialysis (years)	8.9 ± 2.1	9.3 ± 2.4	–
Serum creatinine (mg dL^{-1})[a]	10.8 ± 3.1 [4.1 ± 1.2]	10.7 ± 1.6 [3.9 ± 1.4]	0.8 ± 0.1
Serum sodium (mmol L^{-1})[a]	138.1 ± 2.0 [137.8 ± 2.4]	138.2 ± 2.6 [138.0 ± 1.8]	137.8 ± 1.8
Serum potassium (mmol L^{-1})[a]	4.8 ± 0.8 [3.5 ± 0.5]	5.2 ± 0.9 [3.4 ± 0.6]	3.4 ± 0.5

Data are expressed as Mean ±S.D.
[a] Values in brackets were after hemodialysis sessions.

Table 2
Analytical results for Cu, Zn, Cd and Pb in certified reference materials.

Certified reference materials	Metal ions	Certified value	Acceptable range	Found value[a]
Seronorm Trace Elements Whole Blood L-1 (μg L^{-1})	Cu	680 ± 140	410–950	618 ± 26
	Zn	4400 ± 200	4000–4800	4530 ± 228
	Cd	0.36 ± 0.02	0.32–0.40	0.34 ± 0.02
	Pb	10.2 ± 2.1	6.0–14.4	10.7 ± 1.8
Seronorm Trace Elements Whole Blood L-2 (μg L^{-1})	Cu	1330 ± 270	790–1870	1274 ± 172
	Zn	6500 ± 300	5800–7200	6608 ± 417
	Cd	5.8 ± 0.2	5.4–6.2	5.7 ± 0.2
	Pb	310 ± 62	186–434	325 ± 49

[a] Mean ± SD of five independent determinations.

Table 3
Blood concentrations of Cu, Zn, Cd and Pb in males compared to females of the studied population.

Blood level (μg L^{-1})	HD patients		The controls	
	Males	Females	Males	Females
Cu	698.8 ± 50.4	724.0 ± 32.1	915 ± 52.4	930 ± 44.9
Zn	4290.7 ± 259.5	4380.4 ± 148.9	5612 ± 198.5	5490 ± 210.4
Cd	2.0 ± 0.4	1.9 ± 0.5	0.94 ± 0.2	0.91 ± 0.2
Pb	81.6 ± 7.8	78.5 ± 10.5	57.5 ± 5.9	52.9 ± 4.6

branes have the ability to eliminate larger molecules, such as beta-2 microglobulin (11,800 Da) [22].

To the best of our knowledge, there are no studies concerning the permeability of low and high flux polysulfone membranes for metal ions during HD. Therefore, the aim of the present study is to compare both low and high flux polysulfone HD membranes regarding their efficiency for removal of some metal ions during the HD session.

2. Material and methods

2.1. Study population and sample collection

This study was conducted at the Urology and Nephrology Center, Mansoura University, Mansoura, Egypt. Forty one end-stage renal disease patients participated in the study. All patients were on regular HD for more than 6 years using polysulfone membrane dialyzers. Among them, 19 patients were using high flux polysulfone membrane while the remaining patients were using low flux polysulfone membranes.

Blood samples for metal analysis were collected into polypropylene tubes containing lithium heparin as anticoagulant and stored at −20 °C. Plasma samples obtained after centrifugation (3000 g, 10 min) were used for determination of creatinine, Na^+ and K^+. Blood samples were also obtained from matched 40 healthy persons who served as a control. All study subjects were non-smokers with no history of occupational exposure to metals. The characteristics of the study population were summarized in Table 1.

2.2. Apparatus

Analysis of metal ions was carried out by means of a Perkin Elmer® AAnalyst™ 800 atomic absorption spectrophotometer (Shelton, CT, USA) with a longitudinal Zeeman background correction equipped with a transversely heated graphite atomizer. The wavelengths used for monitoring Cu, Zn, Cd and Pb were 324.8, 213.9, 228.8 and 283.3 nm, respectively. The spectral bandwidth was 0.7 nm for all metal ions. Digested sample solutions were injected into the atomizer using AS-800 autosampler. The system was equipped with winLab 32 software. Digestion of the samples was carried out via a CEM MDS 2000 microwave system (Matthews, NC, USA). Plasma levels of creatinine, Na^+ and K^+ before and after dialysis sessions were determined using the Architect c4000 system (Abbott Diagnostics, Wiesbaden, Germany). Hemoglobin was measured using a hematology analyzer (Sysmex XT-1800i, Sysmex Corporation, Japan).

2.3. Reagents and glassware

Reagents used in the study were of analytical grade purchased from Sigma–Aldrich (St. Louis, MO, USA), Fluka (Buches, Switzerland) or Merck (Darmstadt, Germany). Ultrapure water (UPW) that had been obtained from Milli-Q water purification system (Millipore, Billerica, MA, USA) was used throughout the study. The laboratory glassware was kept overnight in 10% v/v HNO_3 solution. Before its use, the glassware was washed with UPW and dried in a dust free environment. Accuracy of the method was assessed by analysing the certified reference materials: Seronorm™ Trace