Saudi J Kidney Dis Transpl 2011;22(3):576-580

Saudi Journal of Kidney Diseases and Transplantation

Renal Data from the Arab World

Effect of the Quality of Water Used for Dialysis on the Efficacy of Hemodialysis: A Single-Center Experience from Morocco

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ABSTRACT. The quality of the water used for dialysis has been suggested as a factor causing inflammation in patients on hemodialysis (HD). We therefore conducted this study to identify the effect of quality of the water on nutritional state, inflammation and need for human recombinant erythropoietin (EPO) in patients undergoing HD at Agadir, Morocco. This prospective study included patients on HD for at least one year. The water treatment was done according to the standard protocol, which was followed by additional enhancement of ultrafiltration using an additional polysulfone filter (diasafe, Fresenius, Bad Homburg, Germany) before the dialyser. Water was monitored regularly during the study period to ensure acceptable levels of bacterial count as well as endotoxin levels. Various parameters including dry weight, systolic and diastolic blood pressure (PA) before and after an HD session, need for human recombinant EPO, levels of hemoglobin (Hb), albumin, ferritin, C-reactive protein (CRP), and the dose of dialysis delivered (Kt/V) were measured first at the beginning of the study and thereafter, in the third, sixth and 12th months of the study. The study involved 47 patients, and after 12 months of the study, an improvement in median dry weight (1.2 kg, P = 0017) and a simultaneous median reduction of 20.7 IU/kg/week of EPO, with an in-crease of the median level of Hb, was noted. The results of our study suggest that by improving the biocompatibility of HD with the use of good quality water, patients acquire a better nutritional, inflammatory and hematologic status.

Introduction

Each week, approximately 400 L of treated water comes into direct contact with the blood-stream of patients on chronic hemodialysis (HD), through a semi-permeable membrane.[1] This underlines the importance of water purification before its use in dialysis and the need for continuous and rigorous monitoring of the quality of water used for dialysis.

The process of HD is associated with a state of chronic inflammation which may lead to malnutrition, anemia of various causes [reduction of erythropoiesis, resistance to recombi-

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Table 1. Characteristics of the study patients at recruitment.

Characteristics		Number	Percentage (%)	95% CI
Gender	Male	28	59.6	(45.3–72.4)
	Female	19	40.4	(27.6–54.7)
Age	<30 years	4	8.5	(3.4–19.9)
	30–50 years	14	29.8	(18.7–44.0)
	50–70 years	20	42.6	(29.5–56.7)
	>70 years	9	19.1	(10.4–32.5)
Duration on hemodialysis	<5 years	25	55.6	(41.2–69.1)
	5–10 years	15	33.3	(21.4–47.9)
	>10 years	5	11.1	(4.8–23.5)
Cause of end-stage renal disease	Diabetes	14	30.4	(19.1–44.8)
	Vascular	5	10.9	(4.7–23.0)
	Lithiasis	2	4.3	(1.2–14.5)
	Unknown	25	54.3	(40.2–67.8)

95% CI: confidence interval at 95%

nant human erythropoietin (EPO)] and accelerated atherosclerosis.[1-4] This inflammation is the result of a permanent activation of monocytes, leading to the secretion of cytokines such as interleukin-6 (IL-6), 1ß and tumor necrosis factor α (TNFα), an elevation of C-reactive protein (CRP) and a decrease in albumin.[3,5-7]

Generally, the technical components of HD are incriminated in the genesis of this inflammation (membranes, tubing, and dialysate). While many authors have studied the role of membranes in inflammation in HD, few have studied the effects caused by the dialysate.[1]

It appears that the quality of dialysate is an independent factor for inflammation in patients on HD.[8,9] A low concentration of endotoxin and other bacterial products has been shown to help in reducing inflammation in HD patients.[2,3] Bacterial contamination of water is therefore an important issue to be considered, in order to reduce the inflammatory status associated with HD.[3,9]

The aim of this study was to test the effect of using an additional dialysate ultrafiltration filter (diasafe filter) on the nutritional and inflammatory status, as well as the need for EPO in a group of patients on chronic HD.

Patients and Methods

Patient characteristics

The patients included in this study were all on chronic HD covered by the health insurance of the Moroccan Royal Armed Forces and on dialysis at the Agadir HD center (AHC).

Characteristics of water treatment at the AHC

The water treatment system includes pretreatment with sand filter, particulate filters 50 and 10 µm, a softener, an activated carbon filter and two microfilters 5 and 1 µm, followed by final purification with double reverse osmosis and a hydraulic closed circuit without dead space. Ultrafiltration is further enhanced by the use of an additional polysulfone filter (diasafe, Fresenius, Bad Homburg, Germany), before the dialyser.

Disinfection of the water plant is carried out twice per quarter with *Sporotal* (sodium hypochlorite/sodium hydroxide/silica/potassium salt) and *Puristeril* (hydrogen peroxide/per acetic acid).

HD sessions were conducted using 4008 S machines (Fresenius); the duration ranged between three and five hours, the blood flow was maintained between 200 and 300 mL/min, the dialysate flow was maintained at 500 mL/min, and all patients were on dialysis using a synthetic low-flux membrane (Helixone, polysulfone, Fresenius).

Method of study

The study was prospective and involved patients on HD at AHC for at least one year. Before the commencement of the study, patients received conventional dialysis where the

Table 2. Bacteriological analysis of the water used for dialysis.

Months	0	3	6	12
Endotoxin (IU/mL)				
Check loop	0.057	0.033	0.05	0.037
Back loop	0.062	0.066	0.129	0.052
Final dialysate	<0.03	<0.03	<0.03	<0.03
Bacteria (CFU/mL)				
Check loop	15	10	1	3
Back loop	19	13	3	5
Final dialysate	3	1	0	0

dialysate was not ultrafiltered.

Patients were followed up in a regular manner during the 12 months study period. The parameters studied were measured first at the beginning of the study and subsequently at three, six and 12 months. These parameters included the dry weight, systolic and diastolic blood pressures before and after an HD session, the need for EPO therapy, the levels of hemoglobin (Hb), albumin, ferritin, CRP, and parathyroid hormone (PTH). The dose of dialysis (Kt/V) was measured by ionic dialysance.

Bacteriology of dialysate

Samples of water used for HD were collected quarterly at entry and exit from the extracorporeal circuit as well as in the final dialysate after the diasafe filter. The determination of bacterial endotoxins was done by kinetic chromogenic study and enumeration of total bacteria was done by membrane filtration.

The maximum levels of bacteriological contamination were defined as those recommended by the European Pharmacopoeia to a threshold of less than 100 bacteria colony forming units (CFU)/mL and an endotoxin concentration of less than 0.25 Endotoxin Unit/mL.

Statistical Analysis

The data were analyzed by statistical software SPSS 11.5. The quantitative variables were expressed as mean ± standard deviation and qualitative variables were expressed as a percentage. The comparison of mean values from baseline (screening) was performed using analysis of variance (ANOVA) with repeated measurement. All comparisons were bilateral with $P < 0.05$ considered as the threshold for statistical significance.

Results

Patient characteristics

The study involved 47 patients admitted to the HD center from 14 October 2007 and followed for one year; 51.6% were males and 40.4% were females. The mean age was 53.4 ± 15.3 years, ranging from 17 to 80 years. About 27% of the patients had associated hypertension. The characteristics of the study patients are shown in Table 1.

Bacteriology of dialysate

The results of the bacteriological analyses of water after treatment (reverse osmosis) are shown in Table 2. The results are in accordance with the international recommendations (including the European Pharmacopoeia).

Dose of dialysis

The Kt/V measured by ionic dialysance [Online Clearance Monitoring (OCM)] remained constant and satisfactory during the study period. Table 3 shows the evolution of averages.

Nutritional status and inflammatory markers

After 12 months of care, an improvement in the estimated average dry weight of patients, with an average gain of 1.2 kg, was noted. This difference between the dry weight at initial screening and after 12 months was statis-

Table 3. Evolution of mean values of Kt/V during the study period.

Month	0	3	6	12	*P*
Kt/V	0.93 ± 0.32	1.09 ± 0.26	1.02 ± 0.22	1.19 ± 0.41	≤0.0001

Table 4. Evolution of the average dry weight, serum albumin and C-reactive protein levels during the study period (mean ± standard deviation).

Parameter	Value	Duration on dialysis with ultrapure water			P
		3 months	6 months	12 months	
Dry weight (kg)	62.4 ± 13.3	62.5 ± 13.4	62.4 ± 13.4	63.6 ± 13.6	0.001*
Albumin (g/L)	39.0 ± 1.0	39.5 ± 1.2	40.1 ± 0.7	38.5 ± 1.5	0.47
CRP (mg/L)	8.1 ± 2.1	10.3 ± 2.4	7.0 ± 2.3	5.6 ± 1.3	0.09

*Statistically significant.

tically significant ($P = 0.017$).

However, our study did not show a significant difference in other nutritional and inflammatory markers (Table 4).

Need for erythropoietin and hemoglobin and ferritin levels

During the study, there was an average reduction of 20.7 IU/kg/week in the dose of EPO required after 12 months of care; this was associated with an increase in the average level of Hb (Table 5).

Discussion

Unlike the chemical contaminants whose maximum permissible concentrations are well defined,[11,12] there are differences between the recommendations on the level of bacteriological contamination of water allowed for HD,[2] as well as the validated testing methods.[2,3,11]

Our study is the first in Morocco to look at the effect of quality of water used for HD. Although we had no control on the bacteriological quality of water during dialysis prior to its arrival at our center, after starting HD at our center, the dialysate was closely monitored twice per quarter, from samples collected before and after the diasafe filter.

The inflammation caused by bacterial contamination of the dialysate appears to be an independent factor among the other causes such as nature and permeability of membranes, HD lines, etc.[1] Usage of dialysis water with a low concentration of endotoxin (0.1 CFU/mL and 0.03 IU/mL of endotoxin) has been suggested to reduce inflammation and its late complications such as malnutrition, amyloidosis related to β2-microglobulin, resistance to EPO and loss of residual renal function.[2,6,8,10,13] Beyond the need to conform to international standards,[11,12] it was suggested that additional ultrafiltration of the dialysate is able to make ultrapure dialysate.[2]

In our study, we obtained a statistically significant increase in the average dry weight in our patients. Similar findings have been reported by other workers.[13,14] In two prospective studies, Schiffli et al demonstrated that patients receiving HD using an ultrapure dialysate for one year showed a significant increase in dry weight, a decrease of CRP levels and IL-6, and a reduction in the dose of EPO, when compared with those using conventional dialysate.[14,15]

In our study, the mean value of CRP decreased but was statically insignificant ($P = 0.09$). Using an ultrapure dialysate, some studies showed a decrease in CRP,[6] while some others were not conclusive about the effect of the dialysate on the decrease of CRP.[3,16] These discordant results may partly be due to the permeability of membranes.[17] Additionally, our patients showed an increase in their Hb levels

Table 5. Evolution of the dose of erythropoietin needed and the hemoglobin and ferritin levels during the study period (mean ± standard deviation).

Parameter	Value	Duration on dialysis with ultrapure water			P
		3 months	6 months	12 months	
Dose of EPO (IU/kg)	88.5 ± 7.4	77.7 ± 5.8	65.0 ± 6.8	67.7 ± 6.7	$<10^{-4}$*
Hb (g/dL)	9.8 ± 0.2	10.8 ± 0.3	12.2 ± 0.3	11.4 ± 0.2	$<10^{-4}$*
Ferritin (ug/L)	422.3 ± 55.7	380.3 ± 36.2	444.2 ± 38.8	463.5 ± 41.0	0.23

*Statiscally significant.

associated with a reduction in the requirement of EPO. Similar observation has been noted in other studies as well.[15]

Our study is not randomized or controlled. Further studies are needed to confirm these results. Also, the impact of the additional cost of adding diasafe filter was not studied in this report.

Quality of water used for HD is an independent factor of biocompatibility, which may reduce inflammation, improve nutrition and contribute to the correction of anemia in patients on HD. Standardization of the quality of water used for dialysis will help in offering good and efficient dialysis to the patients. The cost-effectiveness of the use of ultrapure dialysate for routine HD has to be resolved and further studies are needed to clarify this point.[16]

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