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The essential role of water treatment system (WTS) in the quality of water for hemodialysis

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INTRODUCTION

During hemodialysis (HD), dialysis fluid (DF) contaminants pass through the dialyzer to patient's blood. Some of them accumulate, and may sometimes causes acute and/or chronic toxicity. These contaminants, which are classified as chemical and microbiological, come from water treated for HD, concentrates and other solid solutes, and the hydraulic circuits of HD monitors. Ideally, DF would have to meet the quality criteria for fluids for intravenous infusion, and if this requirement is not met is because of financial reasons. It is obvious that contaminant toxicity should be prevented. The question is: What are the safe limits of contaminants in DF? Where does contaminant overload or accumulation end and contaminant toxicity start? Most current recommendations, such as the Guidelines for Quality Management of Dialysis Fluid of the Spanish Society of Nephrology,[1] mention two quality levels. A first level, that we will call standard, marks the maximum levels of contaminants in water and DF that can be admitted when performing HD. The other level, much more demanding, corresponds to ultrapure water and DF and is the one currently recommended for any type of HD. The main determinant factor for achieving high quality DF is availability of a modern water treatment system with dual osmosis, on-line water production without a storage deposit, automatic sterilization system of the water distribution ring and direct connection to monitors. Modern continuous flow monitors should also be available. The second determinant factor is a standardized, rigorous control methodology.[2] In this same issue of *Nefrología*, Sobrino Pérez et al.[3] publish an article about the operation of a treatment or purification system for hemodialysis water and the control methods used for 5 years. It is a system that may be considered as "modern" and that provides very good results. In this editorial, I will try and make clear the basis for such statements.

The chemical contamination to which HD patients are subjected has significantly decreased over the years.[4-8] While subacute aluminum intoxications with neurological and bone clinical signs previously occurred, we now monitor how many patients have high Al levels in blood,[6] e.g. 2.1% of 1,410 and 2.5% of 117,000 samples in the United States, and proportions have decreased every year. This has been due to widespread use of reverse osmosis for water treatment, in an increasing number of cases using a dual stage. While dialysis water is the main source of trace elements (TEs), these may come from contamination of solutes used for DF preparation, and this aspect requires control in the OL-HDF era. In a study[4] with a low Al level, 15 µg/L, in the water supplied, the level in biosmotized water was only 3.3 µg/L, but reached 5.4 µg/L in DF and reinfusion fluid. Significant increases in blood levels of some metals such as aluminum, lead, mercury, and cadmium may be seen with hemodialysis.[7,8] Environmental factors also have an influence, of course.[8] Other contamination sources, such as pumps in centralized DF manufacturing systems, should always be considered.[5] New contaminants added to water, such as perchloroethylene, are regularly reported.[10] On this subject, we may conclude that availability of a good water treatment with dual osmosis (RO) or deionizer (DI) plus an osmosis that maintains the recommended conductivities (1) (maximum conductivity should be 4.3 µS.cm-1 at 20 ºC for purified water, and 1.1 µS.cm-1 for highly purified or ultrapure water), combined with water aluminum controls (atomic absorption spectrometry, 0.01 mg/L (10 µg/L) at least every six months, gives us a very high assurance that adequate levels exist of the other chemical contaminants (table I). Authorities responsible for water supply should inform dialysis units about any changes made or detected in water.

Control of biological contamination is more difficult.[2,12-14] The presence of biofilm in the pipes[14] and the existence of bacterial strains resistant to antibiotics[16] are aspects requiring preventive action. Once these have appeared, they are very difficult to remove. They are usually related to high bacterial contamination levels, higher than 1,000 CFU/mL, and to contamination recurrence early after disinfection.[1] Prevention is therefore essential. The two main factors for such prevention include water of a high chemical quality and regular effective disinfection. They both are easily achieved with a modern water treatment system (WTS). The relationship of WTS quality and age and age of the hemodialysis unit to the degree of bacterial contamination is well

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Table I. Maximum limits admitted of contaminants by quality level of water treated for hemodialysis

	Standard water	Ultrapure water	Recommendations
Conductivity corrected for temperature	4.3 µS.cm-1 at 20 ºC	1.1 µS.cm-1	Conductivity should be kept stable (continuous reading)
Aluminum	0.01 mg/L (10 µg/L)	0.01 mg/L (10 µg/L)	< 0.005 mg/L (5 µg/L)
Bacteriology CFU/mL R2A	< 100	< 10 CFU/100 mL	With 50 mL, corrective action should be taken
Endotoxins EU/mL (LAL-KC)	< 0.25	0.03	

known.[13,14,16,17] A multicenter study conducted in 95% of Quebec centers showed a lower degree of bacterial contamination in units with DI+RO.[16] Epidemiological studies conducted in all dialysis centers in Greece[13] stressed the influence of water storage deposits, as well as WTS seniority, in poor water quality. Highly purified or ultrapure water is currently recommended for any type of hemodialysis (table I).

What may be considered as a modern WTS? The differential facts may be summarized as follows:[1] If water is stored, it should be untreated, as occurs in hospital tanks requiring rigorous maintenance. Pretreatment with dual elements of adequate size for the flow rate, from which duration and good treatment performance will depend. Dual reverse osmosis or on-line DI+RO, with no storage deposit for treated water. A ring or loop water distribution system made of pharmaceutical grade stainless steel, or failing this of PEXa. A programmable automatic sterilization system, if possible by water steam, and finally, direct connection of the ring to the HD monitors.[1] We recently concluded a study[18] reporting the degree of bacterial contamination and TE levels of treated water and DF in the HD unit of the HGUGM from January 1997 to March 2007 and examined the factors on which it had depended. A modern WTS such as the one previously described was available in the latter period. A total of 2,822 bacteriological samples and 100 TE samples were tested. It was concluded that contamination of water treated for dialysis depends to a great extent on the type of treatment system available. This contamination has an influence on monitor contamination, with some monitors being more prone to get contaminated than others. TE levels are related to bacterial contamination.

A good WTS is not enough, however; a good quality control is also required. First, a sufficiently sensitive system for detecting bacterial contamination and pyrogenic substances should be available.[2,19-23] Marked differences exist in sample culture procedures.[24] Several of these studies compared the TSA and R2A culture media, incubation temperatures of 35 ºC and 23 ºC, and short times, 48 hours, versus 5-7 days. Based on these studies, R2A, 23 ºC, and early and late readings should be used. This procedure will allow for a high sensitivity. R2A is not more expensive than TSA or standard agar. Some guidelines recommend as culture medium TGEA (tryptone glucose extract agar) (ISO-2007), which would be partly, like R2A, a nutrient-poor culture medium.[2] There are also differences in the sampling procedure.[25] Samples should always be taken as close as possible to the water intake by the monitor and at the end of the distribution ring, in the return. Endotoxins must be measured using the LAL test. For standard water, a standard Gel-clot will suffice. For ultrapure water, a more sensitive method, such as kinetic-chromogenic (KC) LAL, will have to be used. There is a need for a standardized method that allows for comparison of results.[26] The Spanish Society of Nephrology could lead a group for this purpose.

Contamination should be prevented by regular disinfection.[2,27-29] At least monthly disinfections are recommended. With modern WTS, one or two programmed weekly disinfections are enough. Special care should be taken with rinsing of chemical disinfectants[30] after a general disinfection. UV lamps may be of value in certain WTS.[31]

In home HD, one cannot renounce to having ultrapure water and regular disinfections.[32-35]

CONCLUSIONS

There is increasing evidence of the clinical value of using a hemodialysis fluid with the lowest possible amount of contaminants.[36-45] Treated water is its essential component. The main guarantee for quality of water for HD is availability of a modern WTS with an automatic disinfection system. In order to control its function, procedures with adequate sensitivity for detecting quality levels of ultrapure water should be used.[1,2]

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KEY CONCEPTS

1. A hemodialysis fluid with the least possible amounts of contaminants should be used. If possible, fluid should be obtained with ultrapure water.

2. The main guarantee for quality of water for HD is availability of a modern WTS with an automatic disinfection system.

3. In order to control its function, procedures with adequate sensitivity for detecting quality levels of ultrapure water shoud be used. A 100 mL sample, R2A as culture medium (or, failing this, TGEA), incubation temperature 23 °C, late readings a 5-7 days.

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