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Monitoring on-line treated water and dialysate quality

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SUMMARY

Introduction: On line-treated water has been designed to obtain ultrapure water. This quality of water is obviously necessary to obtain ultrapure dialysate, although this is not the only condition. To keep the quality of the process, is necessary the continuous monitoring of the water treatment, dialysate and haemodialysis machines.

Method: After the installation of a water treatment with these characteristics, we developed a protocol to follow up its quality. The measures included in the protocol were:

a) Microbiologic, endotoxin and chemical controls of the water on different stage: before and at the end of the treatment, pre-treatment and network of distribution. The chemical analysis included analytical and colorimetric measures.
b) Control of specific mechanical functions of the facilities.
c) Microbiologic and endotoxin analysis of the dialysate produced by haemodialysis machines.
d) Control and maintenance of haemodialysis machines, according to the technical indications.

Results: We analyse the initial five years of water treatment with the aim to evaluate quality parameters and efficiency. We explain the reasons of the modifications introduced in the system. During this period we have not any episodes of global or partial contamination. We refer here some incidents related with the quality of raw water supply before the treatment, but in any case it was necessary neither to stop the water supply or to reduce the water quality. We observed a persistent contamination of one haemodialysis monitor due to the port used to get the samples.

Conclusions: On line-treated water is at present the most appropriate system to obtain high quality water for haemodialysis. The process must be continuously monitored through specific protocols developed to evaluate the raw water's characteristics and the treated water.

Key words: *Ultrapure water. Ultra filtered dialysate. Non ultra filtered dialysate. Ultrapure dialysate. Reverse Osmosis (RO). SDI (Silt Density Index). «On line» water treatment.*

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RESUMEN

***Introducción:* Los tratamientos de agua «on line», están diseñados para obtener agua de gran calidad, condición indispensable, aunque no única, para conseguir LD ultrapuro. Para mantener ésta calidad es precisa la monitorización continua de la calidad del tratamiento del agua, del LD y de los monitores de diálisis.**

***Método:* Tras la instalación de un tratamiento de agua con estas características, implementamos un sistema de monitorización que incluía:**

a) Análisis microbiológicos, endotoxinas y químicos (analíticos y colorimétricos) en el agua en sus diferentes estadios (antes de ser tratada, en diferentes fases del tratamiento y en la red de distribución).
b) Control de los parámetros mecánicos de funcionamiento del tratamiento.
c) Análisis microbiológico y de endotoxinas del LD.
d) Control y mantenimiento de los diferentes monitores de hemodiálisis, según las indicaciones técnicas de los mismos.

***Resultados:* Tras cinco años de funcionamiento se ha evaluado su eficacia y la utilidad de las modificaciones introducidas a lo largo del tiempo. En este periodo no se han registrado contaminación global o parcial del agua después de ser tratada. Los incidentes registrados no han supuesto cortes de suministro o merma de la calidad que haya supuesto la paralización de la unidad de hemodiálisis, pese a los problemas derivados de las malas condiciones en que en ocasiones se encuentra el agua antes de ser tratada. Solo se registró una contaminación persistente en un monitor, que con gran certeza venía originada por el propio puerto para toma de muestras.**

***Conclusiones:* Los tratamientos de agua «on line» para hemodiálisis son los más adecuados para obtener agua de gran calidad. Han de ir acompañados de una monitorización basada en estrictos protocolos de seguimiento creados específicamente para evaluar las características del agua a tratar y tratada.**

Palabras clave: Agua ultrapura. Líquido de diálisis ultrafiltrado. Líquido de diálisis no ultrafiltrado. Líquido de diálisis ultrapuro. Osmosis Inversa (OI). SDI o Índice de Densidad de Suciedad. Tratamiento de agua on line.

INTRODUCTION

A new water treatment unit was implemented in December 2002 in the Hemodialysis Unit of de La Princesa University Hospital (Madrid, Spain). The chosen system comprised the most advanced technological solutions available at the time for the treatment of water for hemodialysis, with the purpose of obtaining ultrapure water and of eliminating the risks of contamination. The following principles were established: Non-storage of treated water, the use of non-degradable and inert materials, system design without dead point or ends, a double osmosis stage, and continuous water flow throughout the distribution network – including the ports reaching the monitors. It was considered essential to maintain ultrapure water quality to afford an ultrapure dialysate, since this is the key element with which dialyzer exchange is carried out.[1-22]

We considered ultrapure dialysate quality to be necessary for two fundamental reasons:

I. The increasingly generalized use of dialyzers allowing the passage of large molecules, with a high ultrafiltration coefficient in conventional hemodialysis and a high retrofiltration probability.
II. The implementation of high diffusive and convective transport hemodialysis techniques, such as on-line hemodiafiltration, in which the dialysate prepared by the monitor is directly infused in the patient. Such considerations apply despite the fact that these dialyzers are able to retain all or part of the endotoxins present in the dialysate via adsorption.[17-37]

On the other hand, it is necessary to guarantee a permanent supply of water even if some part of the system were to fail. Non-storage of treated water means that any failure of the different water-treating elements can lead to a lack of water supply to the monitors – though it also implies the elimination of elements vulnerable to malfunctioning and contamination (pumps, deposits, ultraviolet lamps, ultrafilters, etc.).

In order to reach these objectives, protocols were developed for the control, maintenance and monitorization of the new water treatment system, in addition to or complementing those indicated by the manufacturer. In addition to following the known general guidelines,[20,21] these were adapted to the water destined for treatment, the working dynamics of the unit, and the configuration of water treatment. With these global measures and the maintenance and control of the monitors, we have established the basis for securing and maintaining ultrapure dialysate quality. During five years, we have registered all the quality data regarding both the water and the dialysate, and well as the operational parameters of all the different system components. This period of time is sufficiently large to allow presentation and evaluation of the results obtained, beyond the mere preliminary results, which obviously must be expected to be positive.[21]

The main reference document used for such follow-up and interventional activities has been the Dialysate Quality Management Guide *(Guía de Gestión de Calidad del Líquido de Diálisis)*[21] to which we have fully adhered.

MATERIAL AND METHODS

Objectives

To obtain ultrapure water and ultrapure dialysate. Standardized technology has been used to determine whether the ultrapure quality standards for water and dialysate have been maintained over 5 years, in accordance with the specifications of the Spanish Society of Nephrology (*Sociedad Española de Nefrología*, SEN).[21]

To maintain such quality over time.

To guarantee a constant supply of water adequate for hemodialysis.

The definitions of purified water for hemodialysis, ultrapure or highly purified water, ultrafiltered dialysate, non-ultrafiltered dialysate, ultrapure dialysate, reverse osmosis, pretreatment, SDI (Silt Density Index), on-line water treatment and ultrafilter (for dialysate) are provided in Annex 1.

Design

In the consecutive sequence of elements through which the water circulates, the original design comprised the following:

- Double raw water supply input
- Prefiltration
- Decalcifier
- Carbon filters.
- Five-micron filters
- Double stage reverse osmosis
- Water distribution via a primary ring and secondary rings that emerge from the latter to reach the monitor.

Description of the facilities

For increased clarity, the facilities are divided into four blocks: Water supply, pretreatment, reverse osmosis equipment, and treated water distribution.

a) *Raw water supply and reserve*
   - Double water supply system: 1.- Individualized supply system for water treatment, composed of a pressure unit and individual supply. The water supply is taken directly from the deposits. The system operates as a priority water supply. 2.- Drawing of water from the internal general distribution network of the hospital. This serves as a reserve water supply. The water reserve is approximately 250 m^3.

- Water supply malfunction alarm system. This allows switching among water supply points before treatment is left without water.

b) *Pretreatment*
- Safety alarm system with water input interruption in case of flooding.
- Prefiltration with 105 µm self-cleaning filter and two multilayered sand filters operating in parallel, and with an individualized bypass system. Nocturnal counter-washings controlled by an automatic headpiece.
- Double decalcifier with automatic volume control. When one unit regenerates after completing its operating phase or is in standby phase, the other supplies decalcified water until its own operating phase is completed.
- Carbon filters (two) with nocturnal counter-washings for sponging, controlled by an automatic headpiece. Each has a volume of 100 liters, and the activated carbon presents a density of two liters per kilogram. Dual configuration is allowed: in operation or standby (with dry carbon) – or both functioning in series. Each alone is able to retain all the chlorine currently contained in the water. The carbon load is replaced after one year in operation.
- Five-micron filter. This serves as the last filtering element before reverse osmosis.

b) *Reverse osmosis equipment*
Double reverse osmosis staging, the principal characteristics of which are detailed below:
- Programmable Logic Controller (PLC), allowing non-automatized operation in the event of failure of the PLC.
- Independent regulation for each of the permeation and rejection flows, with full recovery of rejection corresponding to the second stage. Rejection of the first stage is recovered/discarded according to the PLC program.
- Independent pumps for each stage, with activation according to water demand (energy saving mode).
- Possibility of working with a single stage in the event of an emergency, controlled by the PLC or manually, depending on the anomaly involved.
- On-line cleaning of the first reverse osmosis stage through flow reversal. The water is circulated through the osmosis membrane in a direction opposite to the usual direction, for a brief period of time (15 sec.), and on a regular basis (≈15 min.). This reduces the risk of contamination, and can help avoid or reduce membrane silting.
- Absence of dead spaces throughout the system, including membrane housings. In the latter, water input, concentrate output and permeate take place in the upper part of the membrane housing.
- High-quality stainless steel construction of the entire reverse osmosis system (316 liters).
- Nominal production capacity of 1,050 liters/hour at a water temperature of 6 ºC. Under normal operating conditions, the production exceeds 1,500 liters/hour.
- The maximum demand for which the system was designed corresponds to 24 hemodialysis units, where 50% of the latter can operate at a dialysate production rate of 750 ml/min, and the rest at 500 ml/min – thus establishing a maximum water consumption rate of 900 l/h.
- In addition to affording high quality water, the operating characteristics of this reverse osmosis system allow important savings in raw water (more than 8000 liters per day with respect to the old plant).

d) *Distribution system*
- High-quality stainless steel principal distribution ring (316 liters).
- The junctions throughout the principal ring are made by orbital welding in the absence of oxygen. This type of welding prevents posterior oxidation of the junctions once they come into contact with water. These characteristics make it possible to avoid irregularities such as pits or sharp points, and the presence of glues or solvents, etc., in the distribution network.
- The surplus distributed water is returned to the reverse osmosis equipment and treated again.
- Each dialysis unit (24 in total) is served by a secondary ring emerging from the principal ring and reaching the monitor – eliminating the water outlet tube of the latter. The water always circulates to the monitor, even when turned off or disconnected from the water mains or network, thanks to the insertion of a pressure gradient system between impulsion and return of the secondary ring.
- The connecting system between the secondary ring and the monitor comprises male-female connections (both with self-sealing valves), thus eliminating the need for cutoff keys. This design in turn implies automatic closing down of both the monitor and the ring at the time of disconnection.
- Thermal disinfection of the distribution network. This is of a preventive nature. Disinfection is performed automatically on a weekly basis upon suggestion by the manufacturer. The duration of the process is two hours at a temperature of 80 ºC, with the possibility of varying these parameters. The presence of personnel is not needed for disinfection. The disinfection process does not affect the input and output water sampling points of the distribution ring. Therefore, possible contamination in the reverse osmosis unit or at the start and end of the distribution network would not be occulted by this preventive system.

Incidents and corrective measures

Carbon filters: The described system was selected because of the undesirable variability of the amount of chlorine and chloramines in the raw water when the equipment was designed.[13,14,21]

On the other hand, there was a risk of contamination of the second-positioned filter if the chlorination level was not very high and was entirely eliminated by the first filter. At the end of the first year in operation, contamination was detected in the second carbon filter; however, this did not affect posterior quality of the water, following passage through the reverse osmosis unit. Due to this situation, and the permanent stabilization of the chlorination level, we decided to keep a single carbon filter in operation – the other remaining with the carbon load under dry conditions. At the end of the service life of the active filter, established as one year, the functions of both filters are inverted.

The main incident recorded was premature saturation of the first osmosis stage, i.e., loss of volume production rate in this stage, requiring periodic decrustation of the unit. This production loss in no case implied system collapse, thanks to the established control protocols, which have made it possible to adopt the necessary measures in advance.

Silting of the reverse osmosis membrane is prevented and controlled by measuring the Silt Density Index (SDI), which establishes a direct correlation between increased silting and the loss of membrane production. The optimum value established by the manufacturer is SDI = 3, though some sources accept SDI values of under 5.[38-42] In general, the SDI is about 5 after pretreatment, and in rare instances remains stable at lower values. Higher values are recorded on a point basis – the cause having been shown to be totally unrelated to the facilities of the water treatment plant and hospital.

As corrective measure for partially lowering the SDI value, 1 mm filters have been installed after the carbon filter, substituting the original 5 mm filter.

On a point basis, with a very brief duration and no relation to the SDI value, we have found an elevated presence of iron – detectable only by colorimetric methods. This presence of iron may be directly related to the characteristics of the water distribution facilities in the city of Madrid. As a preventive measure, a filter for the elimination of iron has been placed before feeding the water to the osmosis system.

Another incident has been the high temperature of the water mains in the summer months, reaching over 23 ºC during this period in the year 2005. One monitor model did not allow a temperature of over 25 ºC; as a result, on attempting to lower the water temperature by means of the reverse osmosis unit, discarding a larger amount of water, a block resulted due to the excessive temperature of the raw water. The corrective measure was to insert a heat exchanger in these monitors, thereby allowing admission of a water temperature of up to 30 ºC, as in most hemodialysis monitors.

The final configuration established is shown in figure 1.

Controls of water mains and of operation of the water treatment plan

Periodic controls were created or adapted and monitored by the technician of the Unit, applied to the pretreated water and different stages of pretreatment (fig. 2), at three levels:

1) Water supplied to the Hospital by the supplying company in Madrid, Canal de Isabel II (CYII) (Quality Control Department of Canal de Isabel II).
2) Internal storage and distribution system of the Hospital.
3) Hemodialysis water treatment plant.

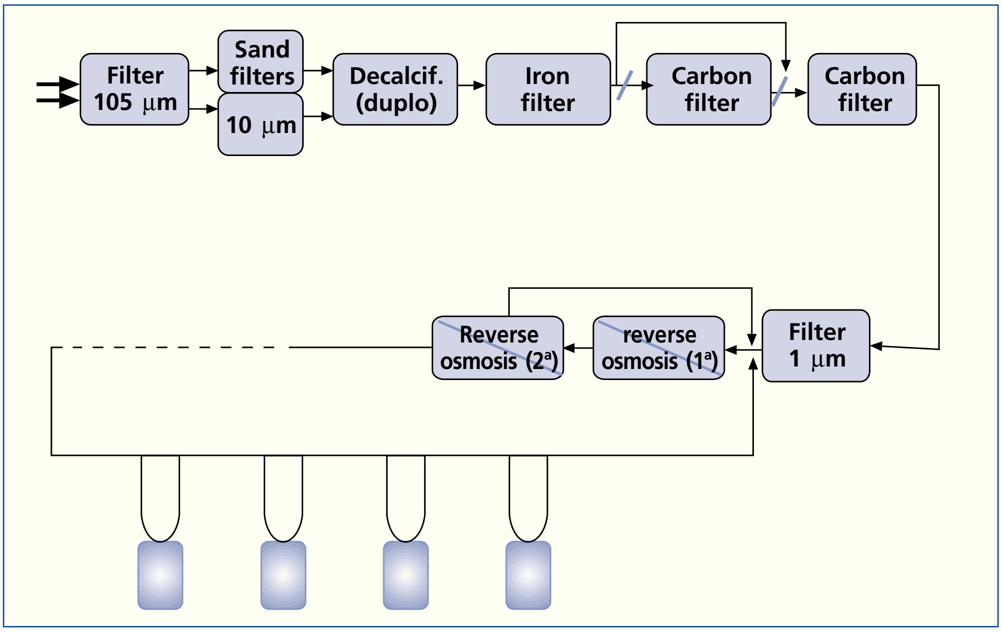


Figure 1. Schematic representation of the water treatment process.

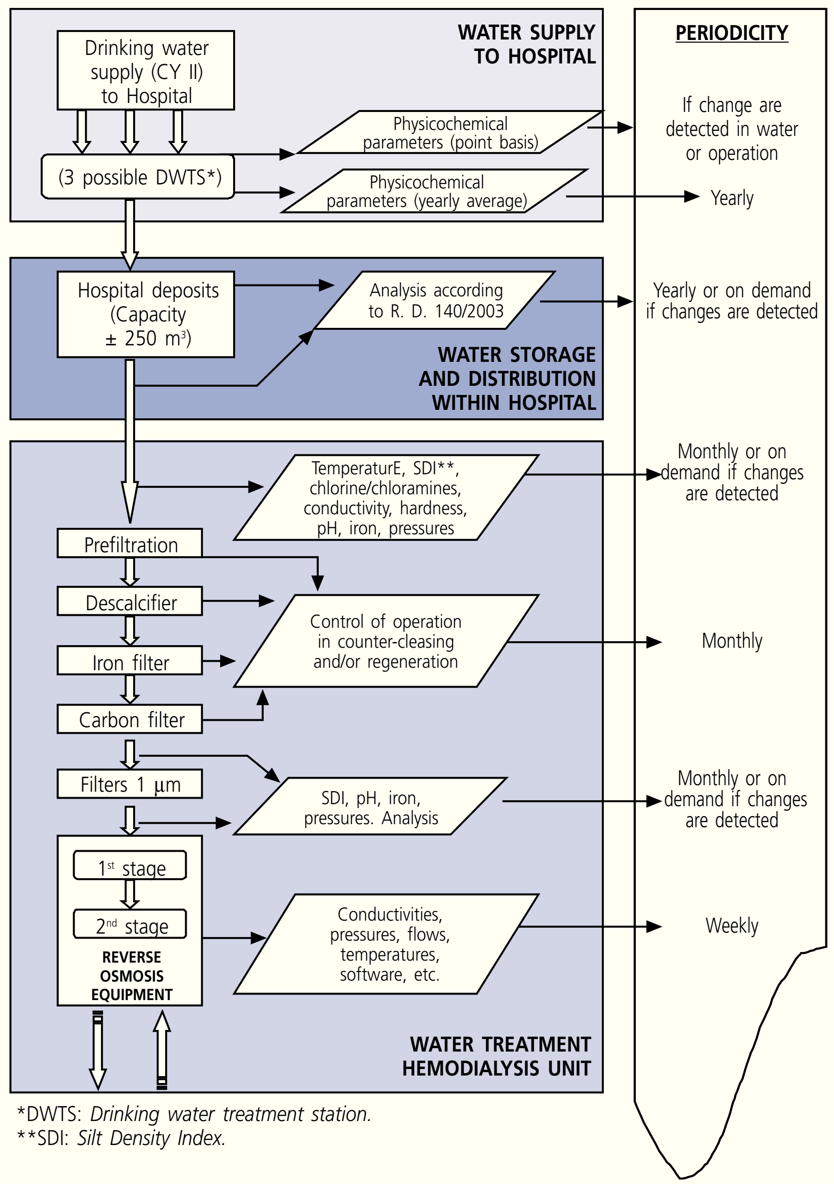


Figure 2. Flowchart of follow-up and control of the different parameters corresponding to water supply → pretreatment → final treatment (osmosis).

The physical/chemical analyses of the raw water prior to admission to the Hospital deposits are performed by Canal de Isabel II. Once in the Hospital deposits, the analyses are made by external laboratories upon request from the Hospital, in compliance with Spanish Royal Decree (RD) 140/2003, and upon demand from the Services of Nephrology and Maintenance. Where considered necessary, analyses of this kind are also performed at intermediate points of the pretreatment process.

The analyses corresponding to Royal Decree 140/2003, relating to the physicochemical criteria of the quality of water for human consumption, are carried out and evaluated by the Services of Maintenance and Preventive Medicine of the Hospital, since the water is distributed throughout the center. The technician of the Unit collaborates in the sampling process and in interpretation of the results, as well as in the control and configuration of drinking water distribution within the hospital. These controls establish the operational status of the system and make it possible to anticipate anomalies.[18-21] These controls have been individualized and modified over time according to the working experience gained.

The analyses and controls applied to the global water treatment plant are documented and evaluated first by the technician of the Unit, and are subsequently contrasted where necessary with the company supplying the equipment.

The reverse osmosis operational parameters are registered in electronic format for posterior analysis (including graphic representation), and comprise the following: pressures at 6 control points, conductivities, water flow at four points, water temperature, and SDI.

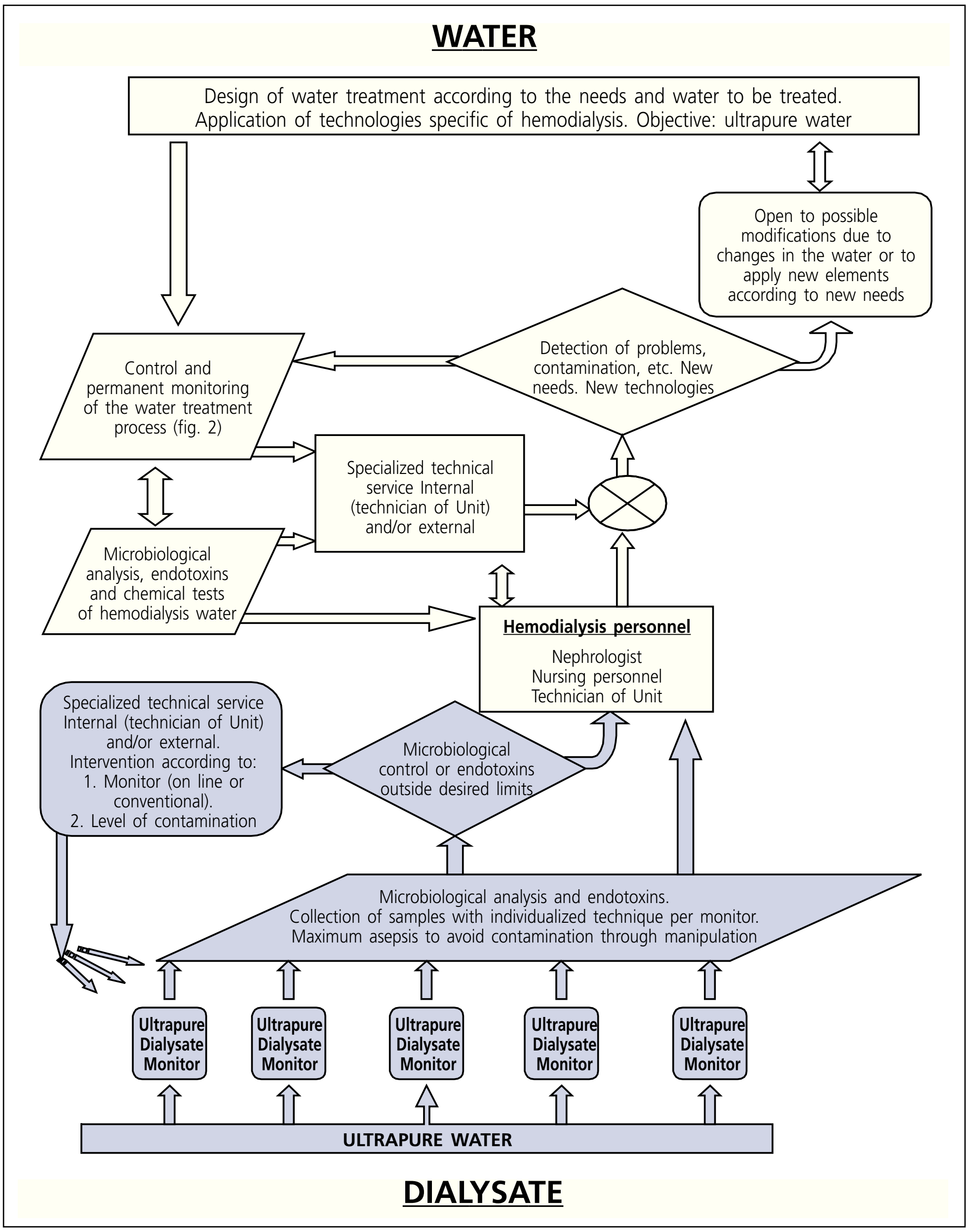


Figure 3. Schematic representation of the monitorization of the quality of treated water (white) and dialysate (gray).

Quality control of hemodialysis water and dialysate

During these five years, the analyses and controls have been adjusted as far as possible to the guidelines of the SEN «*Dialysate Quality Management*»,[21] and to the basic norms applicable in Spain (UNE 111 301 90). A flowchart of the working procedure used for quality control is shown in Figure 3. It can be affirmed that optimum dialysate quality is fundamented upon water quality, since the latter not only represents 96-97% of the dialysate but moreover also serves as the element for disinfection and posterior clearance. In addition, the water is retained within the monitor during standby periods; as a result, any water contamination will lead to contamination of the monitor.

Colorimetric and conductivity tests

Measurements are made and recorded on a daily basis, corresponding to water chlorine content, hardness and conductivity at different points of the system, based on reactive colorimetric techniques. At least once a month, measurements are also made of iron and pH at different points of the system.

Chemical

Tests are made following osmosis, according to norm UNE 111 301 90 and the SEN guidelines,[21] involving the analysis of up to 30 elements. On a point basis, tests of the pretreated water (i.e., before osmosis) are also made. The tests are made by external laboratories (Echevarne and Reference).

During the first trimester of 2003, testing was performed monthly, and then on a semestrial basis following the starting phase.[21]

Microbiological parameters and endotoxins

Sampling method

1. *Sampling conditions:* The samples are collected early in the morning, immediately before connecting the first patient shift, in search of the most favorable situation possible for the presence of microorganisms, i.e.: the monitors on standby all night, and water treatment in nocturnal model (water- and energy-saving mode).

The sampling points for both water and dialysate are previously disinfected: in the case of the water samples by flame application, and in the case of the dialysate by using a disinfectant. Posteriorly, a part of the liquid is discarded to avoid interaction between the disinfectant and the test sample.

The place and time of sampling of each monitor has been analyzed individually per model, in search of the ideal location, and selecting the point closest to the Hansen dialyzer connectors – attempting to avoid sampling elements that are vulnerable to external contamination. In some monitor models these considerations even led us to reject the ports established for sampling, since in some instances they were found to be susceptible to contamination.

Sampling is performed by the technician of the Unit, in cooperation with a staff member of the Service of Preventive Medicine, and using a mask and sterile gloves during sampling. Attempts are made to process the samples as soon as possible, to avoid contamination due to handling, and to prevent excessive delays in testing.

2. *Sampling times:* The samples for testing are collected at the same time for both types of sample (water and dialysate). The process is carried out on a monthly basis. During the starting and validation period (January-March 2003), sampling was performed weekly. By definition, ultrapure water must contain less than 10 CFUs/100 ml. This means that extreme care is required during handling of the samples to avoid contamination.

3. *Number and types of samples:* Collected on a monthly basis for microbiological and endotoxin controls:

1) *Water:* One sample at the reverse osmosis (RO) system outlet, and another at the point of unused water return, corresponding to the start and end of the distribution ring. Both sampling points are unaffected by the periodic thermal disinfection procedure applied. In this way we discard the possibility that potential RO system contamination may be masked by preventive disinfection of the distribution ring. A sample is also collected from an intermediate port of the distribution ring.
2) *Dialysate:* A sample is obtained from each monitor performing the on-line dialysis technique. At least one sample is collected from each model of monitor regularly operating in the Unit; in this case the monitors undergo rotation.
3) Samples of pretreated water are occasionally collected. Sampling from the monitor drainage points[21] was discarded due to the following reasons:
   - The monitor drains are transparent rubber tubes that measure over two meters in length.
   - The tubes remain open at one end, i.e., permanently exposed to the environment.
   - The dimensions and characteristics of the rubber drains imply that full tube liquid circulation along the entire length of the drain cannot be guaranteed.
   - The monitors are internally isolated from the rubber drainage tube when turned off.

In view of the above, we consider that the drainage ports are susceptible to contamination – though this does not necessarily imply contamination of the monitor. False alarms therefore could result.

4. *Determinations:*

a) *Microbiological controls and cultures,* performed by the Service of Microbiology of the Hospital, with the purpose of determining the number of viable bacteria present in the water.

Method: Culture of a known amount of water or dialysate in culture medium, with counting of the number of visible colonies in solid medium (agar plate). The results are dependent upon the composition of the medium, the temperature and the incubation time (detection sensitivity).

Standardized volumes of 0.1, 0.5 or 1 ml of the submitted samples are collected under aseptic conditions and seeded onto Petri plates. The plate medium used may be TSA, chocolate agar or blood agar. The samples are also seeded in enrichment medium (TG or BHI) to recover possible microorganisms in the event of scant plate growth – thereby facilitating their identification.

The spread plate technique is used.

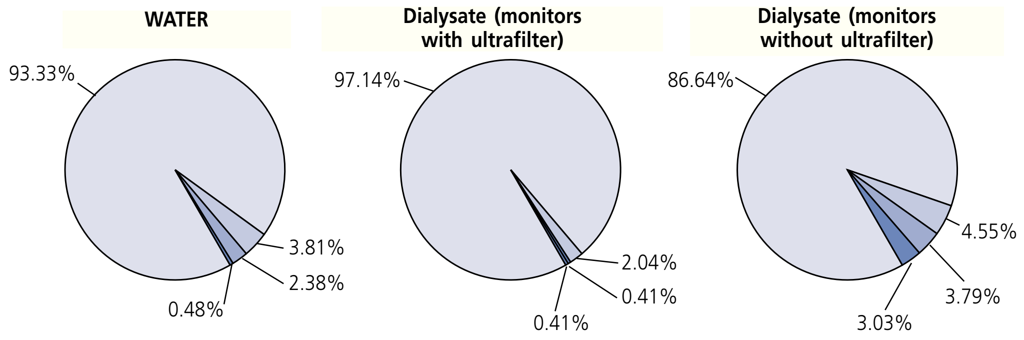
The plates are incubated at 37 ºC for 7 days, followed by the counting of colonies after 48, 72 and 168 hours.

Colony count: The number of colonies obtained is expressed as colony forming units (CFUs) per milliliter.

The identification of the isolated microorganisms is based on the usual laboratory methods.

The same methodology is applied to each sample. The entire process is performed on a monthly basis.

It should be pointed out that the count parameter for ultrapure water is expressed as CFUs/100 ml. We have carried out the process expressing the results in the form of CFUs/ml, though employing a more selective method than for non-ultrapure water or liquid. In this way we have avoided the need for shipment to an external laboratory, which in addition to increasing the regular costs would involve a



	Negative growth	Growth in enrichment medium	Growth (< 100 CFUs/ml)	Growth (> 100 CFUs/ml)	Total samples
WATER	196	8	5	1	210
Dialysate with ultrafilter	238	5	1	1	245
Dialysate without ultrafilter	117	6	5	4	132

Figure 4. Microbiological analysis. Interpretation: *Negative growth* ⇒ Ultrapure quality. *Growth in enrichment medium* ⇒ Non-ultrapure water, but of quality superior to simply purified water. Ultrapure dialysate. *Growth < 100 CFUs/ml* ⇒ Considered valid for purified water (non-ultrapure). Dialysate with ultrafilter is considered contamination. Standard quality dialysate. *Growth > 100 CFUs/ml* ⇒ Always considered contamination. In the case of dialysate, could be valid as standard liquid, provided 1,000 CFUs/ml is not exceeded. In any case, the types of growth must be evaluated in the context of the groups of collected samples. Growths have appeared sporadically; we reasonably believe they may represent contaminations during sampling or posterior manipulation.

greater risk of contamination secondary to sample manipulation.

b) *Determination of endotoxins* by an external laboratory (J. Chisvert), using the Limulus Amebocyte Lysate (LAL) chromogenic kinetic test at endpoint.

RESULTS

The reported results correspond to a period of five years (January 2003 to December 2007).

There have been no interruptions in water supply requiring suspension of the hemodialysis sessions. There have been minor delays as a result of incidents that have been resolved as soon as the situation was attended by someone with the minimum required knowledge of water treatment. These incidents corresponded to variations in the quality of the input water, with sudden collapse of the 1 mm filters that had to be replaced immediately as a result.

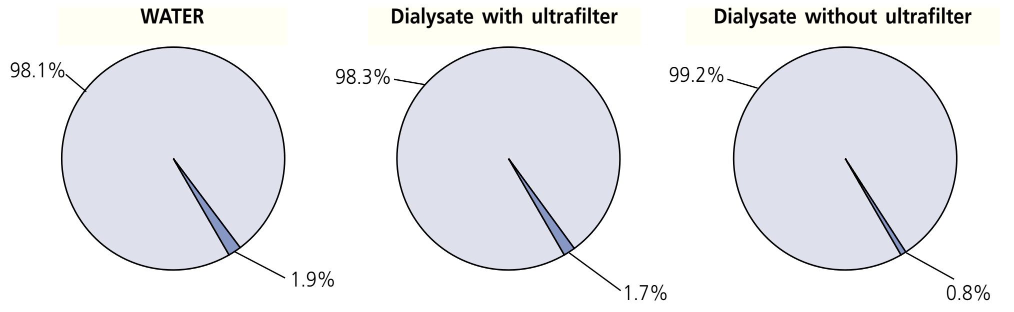
In December 2007, the membrane of the first osmosis stage was two years old, and had been subjected to decrusting approximately once every three months. Two membranes had been previously replaced, due to the need to analyze them with the purpose of determining the reason for rapid production loss attributable to water silt. The second membrane is five years old, i.e., as old as the system itself. This membrane has never required decrusting.

Colorimetric and conductivity tests: The values have always been within the ranges indicated by the norms and guides, with < 0.1 mg/l for free chlorine and total chlorine, and water hardness equivalent to zero French degrees.

Only conductivity has shown variations (between 0.7-1.5 micro-Siemens), which in the case of the highest value falls outside the range indicated by the SEN guidelines for ultrapure water conductivity (1.1 micro-Siemens). The most common values were 1-1.3 micro-Siemens. It must be taken into account that water conductivity can be modified by a number of factors,[21] (Appendix 1), without losing the microbiological and chemical properties required for ultrapure water destined for hemodialysis.

Chemical analyses: All the elements were found to be below the maximum limits specified by both UNE 111 301 90 and the SEN guidelines.[21] These chemical elements have not been represented, due to their diversity (as many as 30). In our case, aluminum must be regarded as a reference element, since its value in untreated water shows broad variation, and the osmosis membranes are unable to eliminate 100% of its presence. In the study period we have registered values in raw water of between 30 mg/l and 133 mg/l. The test results of the water supplying company indicate values of up to 200 mg/l – the maximum limit established for drinking water. The levels in treated water have always been < 5 mg/l, and < 2 mg/l as of 2004 (as a result of laboratory reduction of the detection margin).

Microbiological parameters and endotoxins: Figure 4 shows the collected samples of treated water, dialysate with ultrafilter and dialysate without ultrafilter – specifying the samples in which some type of growth was seen, along with the corresponding percentages. In the course of 2007, a total of 7 samples of water were sent to an external laboratory. The aim was to determine whether the count in CFUs/100 ml was < 0.1 CFU/ml. The samples were shipped in two groups (January and June). All the results were < 0.1 CFU/ml, with the exception of a single reading of 0.19 CFUs/ml. Figure 5 reports the evolution of the endotoxin levels.



	< 0.03 EU/ml	Value between 0.03 y 0.06 EU/ml	Total samples
WATER	158	3 (1.8%)	161
Dialysate with ultrafilter	227	4 (1.7%)	231
Dialysate without ultrafilter	125	1 (0.79%)	126

Figure 5. Levels of endotoxins. The few samples that have exceeded the specified limits for ultrapure water and dialysate are much closer to the level for pure water (< 0.03 EU/ml) than simply purified water (< 0.25 EU/ml).

Samples that have not been registered: Microbiology: Two water samples corresponding to the validation period, which were sent to an external laboratory and yielded < 10 CFUs/ml (without specifying the exact value). Three dialysate samples that were repeated tests of previous growths detected in two monitors.

Endotoxins: Two water samples corresponding to the validation period, in which the laboratory only reported < 0.05 EU/ml. Two water samples in this same period in which the laboratory was not informed of the margin in which the water quality could be found; as a result, the measurement method was not adequately adjusted, and yielded values of 0.1 and 0.09.

In only one monitor without ultrafilter did we record persistent contamination, even after repeated disinfection. This problem was resolved after eliminating the samples port of the monitor.

DISCUSSION

The creation and development of the SEN Dialysate Quality Management Guide coincided with the selection and installation of this water treatment system. In this context, it was our aim to establish the quality criteria defined in the mentioned Guide. At the same time, we aimed to guarantee the supply of highly purified water over long periods of time. We believe that the established protocols have made it possible to reach these objectives, maintaining quality despite all the problems derived from raw water. The sum of all the control elements makes it possible to predict problems in the water treatment system, and to resolve them before they give rise to alterations in terms of water quality.

The microbiological analyses require careful sampling to avoid contamination during manipulation. For this reason, when positive samples are observed, the analysis of the point that yielded the positive result is immediately repeated, regardless of the actions taken. The only exception to these measures is when contamination occurs in enrichment medium only, and the sample corresponds to dialysate from monitors without an ultrafilter – since the dialysate produced by the latter cannot be regarded as ultrapure, because of the lack of the mentioned filter.[21] In only one monitor without ultrafilter did we record persistent contamination, even after repeated disinfection. This problem was resolved after eliminating the samples port of the monitor.

The scant difference in results (microbiological and endotoxins) between the monitors with and without an ultrafilter are effectively minimal, and suggest that such a filter is not needed provided excellent quality water is available from the start. It should be remembered that monitors are actually large dead-end spaces where the water may be retained for long periods of time, and that they contain points within the hydraulic circuit that are never disinfected. As a result, the use of these filters is essential for guaranteeing the purity of the dialysate. On the other hand, drums of hemodialysis concentrate are still used that are permanently open, and which may constitute a source of contamination. As regards the results in terms of endotoxins, it should be mentioned that only five of the more than 500 samples analyzed yielded a value slightly above 0.03 EU/ml, without ever reaching even 0.06 EU/ml.

There is generalized concern over the fact of not storing treated water. It must be taken into account that storing water is no guarantee against ever being left without a water supply, since working in this way moreover implies the installation of elements that can also suffer anomalies (deposits, pumps, ultrafilters, UV lamps, etc.). On the other hand, the non-utilization of water deposits for storage implies an important saving of space, and obviates the need of structural facilities for housing such deposits. The elimination of deposits and the design of the circuit favor the avoidance of contamination throughout the treatment process (endotoxins, biofilm, etc.).

Measure of Silt Density Index (SDI) and iron: In certain periods far higher values of these parameters are recorded – making it necessary to shorten the time interval between decrusting procedures. Malfunctioning of the pre-treatment process as a possible cause for the increase in SDI has been discarded, since such treatment reduces the index 70-80% versus the raw water. The precise composition of the elements causing this rise in SDI is not clear, despite the multiple analyses made. On a point basis, very high iron values have appeared in the water supply. This elements adheres to the osmosis membranes, and has been detected in the analysis of silt retention by the reverse osmosis membrane. A possible explanation for the presence of iron, provided by the company in charge of supplying water to the Hospital, is that the drinking water distribution network of the center of the city of Madrid is very old and composed of iron tubing that occasionally may leach the element into the water. The measures adopted in an attempt to reduce this problem have been the placement of a filter for iron coagulation and elimination, and the placement of 1 mm filters instead of 5 mm filters immediately anterior to the osmosis stage. Despite these measures, however, we continue to occasionally register high SDI levels after the 1 mm filters.

During the limited periods of time during which the SDI remains below 3, before administering the water to the reverse osmosis stage, no variations in water production capacity are observed. When the index is between 3 and 5, a slow and gradual loss is observed, requiring periodic decrusting operations of the first membrane. Lastly, when SDI > 5, the production capacity decreases rapidly – requiring more frequent decrusting and even replacement of the first reverse osmosis membrane. The highest SDI values have always coincided with periods of drought, the summer months, or periods of torrential rainfall. The possible explanations are:

- Lowering of the water level in dams (as during drought) increases silt concentration in the lower water levels.
- During the summer months, stratification of the dam water levels occurs. When dam water is tapped in stratified layers, the presence of silt increases.
- Torrential rainfall exerts a drag effect with the accumulation of materials of all kinds.

Since November 2007, the SDI values have been seen to be higher on a permanent basis. In raw water, the index has been seen to exceed 45, without being able to establish an exact or even approximate value, due to the difficulties posed by measuring values of such levels. At the end of this study we are actively trying to determine the element or elements in the raw water responsible for this high SDI, considering that we have ruled out the possibility that failure of some water treatment system element may be at fault.

In conclusion: The new dialysis techniques with high diffusive and convective transport, and high-permeability dialyzers characterized by the presence of retrofiltration, require the availability of high-quality water. Water treatment of the characteristics described above is able to offer excellent water quality for hemodialysis. To this effect, it is essential to implement measures for the control, follow-up, maintenance, analysis and registry of all the system and water data in the different stages of the process, in a systematized manner and sustained over time.

ANNEX 1

Definitions

Purified water for hemodialysis: From the microbiological perspective, the requirements are < 100 CFUs/ml, and < 0.25 EU/ml.

Ultrapure water or highly purified water: The SEN guide (in its section 3.1.2) defines ultrapure water as water meeting the following requirements: Chemical contaminant contents according to the tables in the Annexes; maximum conductivity 1.1 _S cm (see Appendix 1 of the guide), measured at 20ºC; maximum total organic carbon 0.5 mg/l; maximum nitrates 0.2 ppm; bacterial contamination < 10 CFUs/100 ml, determined by membrane filtration, with at least 200 ml of highly purified water, and < 0.25 EU/ml. The SEN guidelines consider that the level of endotoxins should be < 0.03 EU/ml.

Ultrafiltered dialysate: The dialysate already prepared by the monitor at the programmed temperature and concentration, passed through an ultrafilter (similar to a dialyzer) installed in the monitor, prior to input to the dialyzer.

Non-ultrafiltered dialysate: Dialysate not passed through an ultrafilter prior to input to the dialyzer.

Ultrapure dialysate: Dialysate preferentially produced with highly purified or ultrapure water, containing < 1 CFU/ml and < 0.03 EU/ml of endotoxins, and which has been passed through an ultrafilter immediately before input to the dialyzer.

Reverse osmosis (RO): Water purification by filtering through a semipermeable membrane under the application of hydraulic pressure, with rejection of the ionic concentrate. The process eliminates ions and organic contaminants with a molecular weight of over 100 Daltons.

Pretreatment: This term refers to all the treatment elements for water destined for hemodialysis, located anterior to the reverse osmosis stage. It comprises the following: prefiltration, iron filter, decalcifier, carbon filter, microfiltering, etc.

Silt Density Index (SDI): This parameter is used to determine the degree of silt in water. The maximum SDI accepted for osmosis membranes is 3 or 5, depending on the manufacturer, though the general recommendation is SDI < 3, in order to preserve the membranes.

Briefly, the technique for measuring SDI involves the collection of a certain volume of water, previously passed through a 0.45 mm filter at a pressure of 2 kg, and measuring the time taken to collect that volume. Posteriorly, and after allowing the water to run through the mentioned filter during 15 minutes under the same pressure conditions, the determined volume is again collected, and the time is measured once more. Based on the two recorded time values, the global time and the application of a formula, the corresponding SDI is calculated (38-41).

On-line water treatment: Treatment of water destined for hemodialysis (in our case reverse osmosis), in which the water thus produced is immediately distributed to the hemodialysis monitors, without intermediate storage.

Ultrafilter (for dialysate): This is a sub-micron filter positioned immediately anterior to the point of dialysate input to the dialyzer, in the hemodialysis monitor, and which is able to retain endotoxins, among other elements.

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