

## Twelve Years Experience in Management Evolution to Improve Dialysis Water Quality

Piergiorgio Bolasco

Piergiorgio Bolasco, Territorial Department of Nephrology and Dialysis, ASL, Cagliari, Italy

Correspondence to: Piergiorgio Bolasco, Territorial Department of Nephrology and Dialysis, ASL, Cagliari, Italy.

Email: [pg.bolasco@tin.it](mailto:pg.bolasco@tin.it)

Telephone: + 390706097340 Fax: + 390706097332

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### ABSTRACT

**Methods:** The present editorial attempts to illustrate the positive experience produced over a 20-year period on progressive optimization of materials and procedures in the production of dialysis water in five dialysis units in Sardinia. In fact a significative improvement was observed in microbiological quality of dialysis because of regular samples, ranging from using PVC distribution rings and mono-osmosis (SRO), since introduction of steel circuits INOX AISI 316L and/or PEX. Further fundamental steps have been: bacterial controls improvement, use of bi-osmosis (TRO), daily overnight heated disinfection, validate new protocols of microbiological culture methods as recommended by the most important guidelines. **Conclusions:** Today dialysis water mustn't viewed by the Nephrologist like a simple good ultrapure water to perform high quality of dialysate/infusate but rather how a real drug exerting a demonstrable positive impact on micro-inflammation of hemodialysis patients. The use of PVC should be abandoned and ratio quality/costs is better using PEX piping than steel. By now it's mandatory the use of TRO devices. During this long time our actions result in a unexpected and sure quality improvements of hemodialysis and/or hemodiafiltration water.

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**Key words:** Quality Dialysis water; Reverse Osmosis; Dialysis Piping

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### INTRODUCTION

The hemodialysis patients treated with standard diffusive hemodialysis treatment sessions last 4-6 hours are exposed to 20.000 L of dialysis fluid yearly. Instead in hemodiafiltration procedures, dialysis water is administered in the form of infusate up to 6.500 L i.v. plus dialysate exposition<sup>[1]</sup>. In the last year in Italy and Europe is rapidly rising tendency to use on-line hemodiafiltration with high infusion volumes; these procedures implies therefore the potential presence in distribution piping rings of microbial, fungal, and chemical substances which should be carefully monitored, as provided for in specific guidelines<sup>[2,3]</sup>. Moreover it is mandatory that samples should be tested by certified laboratories using only specific analytical procedures for environmental water; this analytical procedures are very different from those applied to test human blood and secretions<sup>[4]</sup>. Numerous undesirable substances originate from polluted water or infiltrations in the drinking water supply network. Humans are the major culprits, contaminating waterworks through ineffective or wrong measures to kill bacterial and/or correct chemical pollutant. Paradoxically the majority of toxic contaminants derive from municipal waters, thereby suggesting that these are not always safe for direct use in hemodialysis applications<sup>[2]</sup>. Another iatrogenic effect is an unmonitored dialysis water treatment facility, an inefficient system for the distribution of dialysis waters to monitors, or a scarce regularity in disinfection causing inlet in piping of harmful or fatal substances. Thus, the main parameters to be applied in the treatment of waters destined for use in hemodialysis procedures, should be underlined especially to build and organize new hemodialysis centres<sup>[4,5]</sup>.

### Water purification processes

Water utilized in hemodialysis applications is prepared by different purification processes<sup>[6]</sup>.

(a) **Reverse osmosis:** it needs to prefer double reverse osmosis (TRO) and to eliminate single reverse osmosis (SRO); avoid deionization because mixed bed deionizers contain both cationic and anionic resins but these do not remove microbiological contaminants and to avoid inevitable cationic resins and anionic resins exhaustion<sup>[7-9]</sup>. In TRO it's necessary to use high pressure to force water across a semi-permeable membrane to form a permeate thereby rejecting 95 to 99 percent of ionic contaminants and > 95 percent of non-ionic contaminants. An TRO system membrane is a formidable barrier against microbiological contaminants, bacteria, viruses, and endotoxins. This procedure is mandatory for use in on-line hemodialytic methods with high convective volume fluxes<sup>[7]</sup>.

**(b) Pre-treatment procedures:**

**Filters:** A variety of filters may be utilized, at the beginning of pre-treatment for main tap water to remove coarse particulate and at the end of pre-treatment to protect RO membranes from fine particles washed out of carbon beds.

**Chlorination and dechlorination:** the use of these techniques is mandatory in new machinery and in area with it is usual to use superficial water contained in catch basins. Good quality proportional pumps should be applied to guarantee optimal chlorine concentration (0.5-1 ppm) but a complete water dechlorination should be ensured upstream of osmosis membranes to prevent inadvertent exposure of patients to chloramine as the capacity of the carbon is exhausted and so it is suitable to use two carbon filters in series<sup>[10]</sup>.

**Softeners:** Resin beads inside the tanks swaps bivalent cations (especially calcium and magnesium) present in the feed water with sodium ions exchange also to prevent RO membranes from fouling by calcium and magnesium salts. Dechlorinators and softeners represent a good "pabulum" for bacterial growth; at the moment it is impossible to disinfect this devices with a specific products; therefore these equipments represent the "unavoidable true weak point".

**(c) Optimal water piping distribution and discharge: the optimal characteristic are:** Little diameter distribution ring to avoid sluggish segments by better and faster "shear stress" on internal piping surface; the distribution system must be always designed as a closed ring. The use of PVC have to be eliminated and prefer materials such as INOX AISI 316L, PEX, and PVDF used to construct piping.

**(d) Storage:** This aspect is frequently underestimated. Tanks should be opaque, made of plastic for foodstuffs, and not be located in a "stagnant" corner of the circuit, but it should guarantee a constant flow of water.

**(e) Optimal:** Bacteriological and endotoxins periodic controls with appropriate procedures in sampling and transportation, in inoculation of the dialysis water sample in culture medium and in the accurate interpretation of results not taking into account merely mesophiles from the environment, but furthering observation to evaluate the presence of bacteria or mycetes<sup>[11]</sup> for this reason is required to evaluate culture to environmental temperature for mesophiles at 22°C but in hot climate area and/or periods culture test must be incubate at human temperature (37°C).

## EXPERIENCE HISTORY

Based on these premises therefore we showed a progressive practice and numerous changes by assessing the quality of water in five dialysis units over about 20 years; our experience have made an progressive evolution directing our choices toward different implemented methods used for disinfection, monitoring and improvements of several different used equipments. Obviously we

follow main specific guidelines<sup>[4,5]</sup> and we added further ameliorative suggestions.

The evolution regards materials, equipments, new analytical systems, disinfection.

### Use of PVC (Polyvinyl chloride) piping

**We used PVC piping in two successive periods:** (1) An "ancestral" period when we used irregular/occasional microbiological controls and chemical disinfection and SRO in polyamide; (2) A second period when we used a regular microbiological controls and chemical disinfections; (3) The banish of dangerous and cancerogenic use of PVC was discarded and replaced with PEX rings and/or AISI 316L steel rings.

### Use of AISI INOX 316L piping

**We used high corrosion resistance stainless steel piping in four successive periods:** (1): Use of INOX AISI 316L steel distribution ring with irregular/occasional microbiological controls and chemical disinfection and SRO in polyamide; (2) Use of INOX AISI 316L steel distribution ring with regular microbiological controls and chemical disinfection and SRO in polyamide; (3) Use of INOX AISI 316L steel distribution ring with regular microbiological controls and daily overnight pulsed thermal disinfection by means of TRO; (4) We recently abandoned use of steel because expensive and the "weak point" remains the weld joints in spite of use of specific techniques as Tungsten Inert Argo Welding. After few years in the weld area ferritic steels and porosity make aberrations over inner surface and offer "home" to bacterial biofilms<sup>[12]</sup>.

### Use of PEX (polyethylene thermoplastic polymer)

**We used PEX piping in three successive periods:** (1) Use of PEX distribution ring with irregular microbiological controls and occasional chemical disinfection and SRO in polyamide; (2) Use of PEX distribution ring with regular microbiological controls and SRO in polyamide; (3) Use of PEX distribution ring with regular microbiological controls and daily overnight pulsed thermal disinfection by means of TRO in polyamide. It's fundamental to avoid welds in the junction points causing circular bumps and fluid turbulence. In centers under construction it should use a unique piping PEX circuit without a break.

## BRIEF CHARACTERISTICS OF MATERIALS AND OPERATIONS

### Pre-treatment

(a) double water softeners. Softeners cubic foot of resins corresponds to 30,000 grains of hardness exchange capability. Softeners are daily invariably regenerated with concentrated sodium chloride solution (brine).

(b) dechlorination. The tanks contain approx. 400-500 L granular activated carbon which has never been regenerated. In the our "ancestral" period the carbon beds were not replaced, but in the last 10 years activated carbon was changed on a yearly basis and daily back-washing.

(c) SRO. Thin film RO membranes are made from polyamide and spiral wound around a permeate collecting tube. This material is compatible with peracetic acid used in disinfection.

(d) Thermal bi-osmosis (using TRO polyamide membranes) adopted over the last years doesn't require use of chemical disinfection products. Thermal disinfection of piping system provides for an automated nocturnal thermal disinfection with alternative

**Table 1** Results of Ishihara pseudo iso-Chromatic plates Test with DR stratification.

	Tap Water		Refined water post-osmosis (start and end of ring piping)		Final dialysate for standard hemodialysis		Non pyrogenic dialysate for hemodialysis/hemodiafiltration	
	Maximum allowable level	Frequency	Maximum allowable level	Frequency	Maximum allowable level	Frequency	Maximum allowable level	Frequency
CFU/mL bacterial, 22°C (*)	< 100	Every six months	< 100	Monthly	< 100	Every four months	<0.1; before infusion i.v.	Every four months for each on-line dialysis monitor
CFU/mL mycetes, 22°C	-	-	< 10	Every six months	< 10	for each dialysis monitor	0	
Endotoxns, EU/mL	-	-	< 0.25	Monthly	< 0.25		< 0.03	

(\*) : in hot climate: research pathogen bacteria at 37°C with same range and timetable. Identify bacteria.

thermal pulses from 60°C to 90/95°C. Polyamide TRO membrane continue disinfection bimonthly with peracetic acid.

**(e) Piping:** Designed as a closed ring. The optimal inner diameter in dialysis room is about 18.0 – 20.0 mm; all dialysis posts are connected with piping by steel AISI 316 L connection. The dialysis monitor can be programmed to thermal program with disinfection of both piping-monitor segment and circuit machine. In this segment use of a mesh tube has been definitely prohibited. A mesh tube constitutes an ideal pabulum for the growth of bacteria, mycetes, and algae. Approximately 15 days later swabs were obtained from the inside of mesh tubes, yielding dangerous results for microbiological load.

Drainage circuit: there are no contraindications to building this circuit in PVC, although drainage pipes from monitors should be of the anti-reflux gooseneck type.

## MICROBIOLOGICAL AND ENDOTOXIN CONTROLS

### Sampling

Sampling is carried out with a sufficient aliquot of water to be obtained for analysis (generally 100 mL). It is fundamental that during sampling procedures contamination should be avoided using bottles and vials to collect samples for microbiological analysis; these containers should never be washed at time of sampling. Water should be left to run long enough to eliminate disinfectants prior to sampling in order to not alter the chemical quality of water or produce false negative results.

Both taps and the inside of collars should be cleaned and residues, dust, mucilage, detergents and disinfectants, and other substances should be removed. It should be used in cleansing 10% solutions of commercially available sodium hypochlorite. In addition to the mandatory cleansing and disinfection procedures, metals taps may also be flame gouged.

### Transportation

During transportation and storage of samples it should be ensured by preventing and regrowth of micro-organisms. The sample should be stored away from the light (both ultraviolet and visible) and from high temperatures, and appropriate conditions of hygiene applied during transportation. It's fundamental to respect brief period from the time of sampling to arrival in the lab with the optimum temperature range of 2÷8 °C being recommended.

## ANALYTICAL PROCEDURES<sup>[13]</sup>

In the Author opinion, microbiological testing procedures should not only assess the presence of environmental mesophiles and mycetes, but for detecting specific pathogens. The research and interpretation

of cultural results are showed in Table 1:

**(a) Total coliforms.** Place the membrane over the M-Endo agar LES medium and incubate at 36 ± 1°C for 18÷24 hours. Further tests should then be undertaken for identification of typical coliform colonies.

**(b) Enterococci.** Place the membrane over the Slanetz and Bartley agar medium and incubate at 36 ± 1 °C for 40÷48 hours. Tests should be undertaken to confirm enterococcus status.

**(c) Pseudomonas aeruginosa.** It is essential an aliquot of 250 ml of the sample collected. Place the membrane over the Pseudomonas agar/CN medium and incubate at 36 ± 1 °C for 40÷48 hours. After (22 ± 2) and (44 ± 4) hours assess the growth of typical colonies on isolation medium.

**(d) Clostridium perfringens.** Place the membrane over the Tryptose Sulfite Cycloserine Agar medium, and cover the membrane completely with 5-6 mL of liquid culture medium at a temperature of 50 ± 5 °C. Leave to set and incubate at a temperature of 44 ± 1°C for 21 ± 3 hours under anaerobic conditions. Tests should then be undertaken to confirm Clostridium perfringens status.

**(e) Mycetes.** Place the membrane over a Sabouraud Dextrose Agar medium + CAF and incubate at 22÷25 °C for 3 ± 5 days. View under a microscope, to identify pseudomycelium and spores.

**(f) Counting of colonies 22°C-37°C.** Analytical procedures undertaken to assess the number of micro-organisms at 37 °C and 22°C are identical for both parameters, comprising the agar inclusion technique. Seed 1 mL of the sample onto the bottom of a Petri dish and incubate one dish at 36 ± 1 °C for 40÷48 hours, and the other dish at 22 ± 1 °C for 64÷72 hours. After incubation, we proceed to count the microorganisms grown.

**(g) Counting at 22°C (Mesophiles).** An aliquot (100 ml) of the sample collected should be filtered through a 47mm cellulose ester membrane with filtration characteristics corresponding to a nominal pore size of 0.22 – 0.45 µm. Place the membrane on the agar medium and incubate at 20÷23 °C for 7 days.

**(h) Endotoxin.** Tests are carried out both on osmotic water as monitors are detached<sup>[14]</sup> and at random initial-intermediate and end points in the ring. Spectrophotometric methods are used (Endosafe®-PTS™, Charles River®) with gel-clotting at 37°C. Acceptable limits of detection on ring detachment are < 0.05, and <0.01 for online infusion liquid.

## CONCLUSIVE CONSIDERATIONS

The Author experience implicating periods of varying duration and a range of materials and procedures, demonstrated the following:

- (1) abolished PVC - mandatory<sup>[15,16]</sup>.
- (2) The overnight thermal disinfection achieved by means of TRO resulted in a dramatic decrease in microbial load<sup>[7]</sup>; this decrease appeared to be more significant following the use of PEX compared

to steel INOX under construction of the distribution ring. In the Authors opinion, this difference may be associated to a larger diameter of INOX piping, and accordingly the possibility of stagnant areas creating a suitable habitat for biofilm growth<sup>[17,18]</sup>.

(3) The application of meticulously implemented periodic thermal and chemical disinfection procedures should be further supported by additional checks and immediate correction of any “pathological” areas detected in the circuit or the central equipment<sup>[19]</sup>.

(4) The connection valves to dialysis monitors should be in stainless steel AISI 316L, in view of the potential liability of the connection and the increased risk of stagnant areas and microbial adhesions.

(5) It is important to patronize that tests should be undertaken by a certified laboratory specializing in environmental water testing all chemical, physical and bacteriological processes described, and maintain a expertise team performing sampling and lab analysis.

(6) It should be underlined how systems should be monitored continuously;

(7) Taken into account an opting for chemical disinfection, apply every 2 – 3 months solutions capable of removing both bacterial biofilms together the daily nocturnal thermal disinfection; to promote safety, an additional monthly or twice monthly disinfection of osmosis membranes<sup>[20]</sup>.

The author prefer to underline the suitability and cheap of PEX circuits and it is difficult today to establish a sure period for a scheduled replacement of them. The duration of PEX is probably much longer than we'll expect

## CONCLUSION

TRO could represent a necessary investment aimed at providing a safer microbiological profile and producing a positive impact on microinflammation in dialysis patients, particularly using high infusion volumes during on-line high flux hemodialysis<sup>[21]</sup>.

Likewise, daily overnight thermal disinfection procedures have proved at times to be more effective than frequent chemical disinfection.

Medical and Nursing staff working in dialysis units have to be motivated on procedures and cultural background in order to supply the best possible quality water to consumers. Indeed, dialysis water today should be considered a medicinal product in its own right.

## CONFLICT OF INTERESTS

The author affirm that they have no conflict of interest related to the content of this article.

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**Peer reviewers:** Thomas Otto, Professor, Chefarzt der Urologischen Klinik, Städtische Kliniken Neuss, Lukaskrankenhaus GmbH, Preussenstr, Neuss, Deutschland, Germany; Frens Steffen Krause, Professor, Department of Urology, AKH – General Hospital – Linz, Austria; Petros Sountoulides, Department of Urology, General Hospital Of Veria, Thessaloniki, Greece.