

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/11274285>

Water Treatment for Hemodialysis

Article in *Contributions to nephrology* · February 2002

DOI: 10.1159/000060253 · Source: PubMed

CITATIONS

4

READS

889

4 authors:



Gianni Cappelli

Università degli Studi di Modena e Reggio Emilia

158 PUBLICATIONS 1,149 CITATIONS

[SEE PROFILE](#)



Paola Inguaggiato

Azienda Sanitaria Ospedaliera S.Croce e Carle Cuneo

53 PUBLICATIONS 1,251 CITATIONS

[SEE PROFILE](#)



Emiliana Ferramosca

Policlinico S.Orsola-Malpighi

52 PUBLICATIONS 917 CITATIONS

[SEE PROFILE](#)



Alberto Albertazzi

Università degli Studi di Modena e Reggio Emilia

217 PUBLICATIONS 2,460 CITATIONS

[SEE PROFILE](#)

Some of the authors of this publication are also working on these related projects:



Italian survey on vascular access for hemodialysis [View project](#)

Ronco C, La Greca G (eds): Hemodialysis Technology.
Contrib Nephrol. Basel, Karger, 2002, vol 137, pp 317–324

Water Treatment for Hemodialysis

*Gianni Cappelli, Paola Inguaggiato, Emiliana Ferramosca,
Alberto Albertazzi*

Division of Nephrology, University Hospital of Modena, Italy

Water treatment represents a fundamental aspect of modern hemodialysis technology [1]. While at the beginning of chronic hemodialysis therapy, chemicals were major contaminants, over the last decade microbial contamination has become a major concern. Water supplied to hospitals is normally of a quality similar to that supplied to homes but its use in hemodialysis deserves further treatment as impurities can be responsible for many unwelcome acute side effects, including cramps, nausea, hypotension and fever. Water impurities have also resulted in epidemics of severe, occasionally fatal, disease in dialysis patients and can cause a range of clinical problems including anemia, bone disease, hyper- and hypotension, acidosis, muscle weakness, nausea, vomiting and neurological disturbance. Recently, chronic exposure to low levels of dialysate impurities has also been linked with malnutrition, heart disease and amyloidosis, which, in turn, are associated with reduced survival [2, 3].

Fatal or life-threatening mishaps still occasionally occur in the process of performing hemodialysis treatment. These events are rare, but several have been due to tragic failures in dialysis water delivery systems. Examples of actual events that serve to point out some of the avoidable causes of such disasters are reported in table 1 [4].

Standard Setting

In order to ensure that tap water is safe to drink, national agencies prescribe regulations which limit the amount of certain contaminants in water supplied to public water systems. Contaminants in drinking water sources may include microbial and inorganic contaminants, pesticides and herbicides,

Table 1. Recent failures of dialysis water delivery systems

Contaminant	Aluminum	Water	Chloramines	Fluoride	Cyanotoxin of blue algae
Date	March 1993	October 1994	September 1987	July 1993	February 1996
Place	Alentejo, Portugal	Southwestern USA	Philadelphia, Pa., USA	Chicago, Ill., USA	Caruaru, Brazil
Clinical effect	Neurological, encephalopathy	Chest pain, nausea, vomiting, cramps	Anemia, low blood pressure, acute dyspnea	Nausea, malaise, itching, severe arrhythmias	Vomiting, jaundice, ascites, high blood pressure
Prologue	Need to remove particulates from public water in a dry summer	Dialysate supplying system by two CDM working alternatively	Recent changes in water system with increased water flow rate, a single GAC filter	Unit renovations with temporary use of a water treatment system with GAC and DI tanks	Changing of water supply
Circumstances	Use of aluminum sulfate as flocculating agent, clogged RO membranes	Wrong CDM switched to rinse mode	Defect in chloramine clearance due to a too fast water flow	Leaking of fluoride from exhausted DI tank and failure to recognize the alarm light	Use of surface water supplied directly from a lake
Patients affected	71	6	44	11	108
Patients dead	25	1	0	3	60

CDM = Central dialysate machine; GAC = granular activated carbon.

organic chemical contaminants, including synthetic and volatile organic chemicals, and radioactive contaminants which can occur naturally. In contrast to a normal person who drinks around 15 liters of water per week and can inactivate toxins in the gastro-intestinal tract, a dialysis patient is exposed to 250–500 liters of water per week and contaminants are transferred directly into the blood across the dialyzer membrane. Moreover, any toxic material absorbed by normal individuals can be inactivated by first-pass metabolism in the liver or excreted by the kidney. It is, therefore, not surprising that impurities in the dialysis water as well as contamination from a failing dialysis water treatment system can cause significant problems for the dialysis patient. To assure quality, in 1970 the Association for the Advancement of Medical Instrumentation (AAMI) did the first proposal of national standards for

hemodialysis systems, subsequently issued in 1981 and approved by ANSI in 1982 [5]. For several years these standards represented the only references for the whole nephrological community and finally in the 1990s some European nations started to regulate some contaminants. Nowadays water for dialysis is subject to regulatory standards but for most of them the regulations are applied, at least in Europe, on a voluntary basis. The European Pharmacopoeia (EP) monograph on water for diluting concentrated hemodialysis solutions states, in fact, that it is given for reasons of information and guidance and it does not form a mandatory part of the Pharmacopoeia [6]. To note, a further difference in the EP compared to the AAMI standards is the lack of a definition of the people carrying the responsibility for the water system. Recently, as several reports have outlined that the dialysate purity is a main factor to prevent dialysate-related microinflammation, national legislator and professional associations have focused with more attention on dialysis fluid purity. The last European contributions are represented by the EDTNA/ERCA guidelines on quality assurance for dialysis quality water and dialysis fluid [7] and the French ministry 'circulaire' on technical specifications and medical security for the 'on-line' procedures [8]. Table 2 lists allowed limits for impurities comparing EP with the recent draft from AAMI [5, 6]. It is worth noting that European standards pay more attention to microbiological contamination, even if AAMI has modified previous values (200 CFU/ml in water for diluting concentrate solutions and 2,000 CFU/ml in dialysate) and set an action level that approximates EP standards.

Water Treatment Plant

Whichever standard should be met, the same equipment required to purify the water could be used. The size, specification and maintenance schedules for the devices will depend on the quality of tap water, the rate of use and the purity required. Water treatment technology has evolved throughout the history of hemodialysis. Clinical problems associated with chemical contamination of water used for dialysis began to emerge in the pioneering days when patients were dialyzed using a bath of dialysis fluid made with untreated tap water. From this time, particle filters (beds of sand and gravel or membranes) were required to remove suspended matter as well as softener to remove calcium and other multivalent cations in exchange for sodium. Nowadays a standard water treatment plant is made of a pretreatment section including softeners, granular activated carbon and microfilters, followed by a final treatment section. To polish the pretreated water a deionizer (DI) or a reverse osmosis (RO) may be used. Recently the new DI with electrochemical regeneration

Table 2. Allowed limits for impurities (ppm)

Contaminant	EP	New AAMI (Draft RD-62 ^a)
Aluminum	0.01	0.01
Ammonium	0.2	
Antimony		0.005
Arsenic		0.005
Barium		0.1
Beryllium		0.0004
Cadmium		0.001
Calcium	2 (0.05 mmol/l)	2
Chloramines	0.1 ^b	0.1
Total chlorine	0.1	
Free chlorine		0.5
Chlorides	50	
Chromium		0.014
Copper		0.1
Cyanide		0.002
Fluorides	0.2	0.2
Heavy metals	0.1	
Lead		0.005
Magnesium	2 (0.07 mmol/l)	4
Mercury	0.001	0.0002
Nitrates	2	2
Potassium	2 (0.1 mmol/l)	8
Sodium	50 (2.2 mmol/l)	70
Selenium		0.09
Silver		0.005
Sulfates	50	100
Thallium		0.002
Zinc	0.1	0.1
Bacteria	100 CFU/ml	200 CFU/ml (action at 100)
Endotoxin	0.25 EU/ml	2.0 EU/ml (action at 1.0)

^aRD-62 water treatment equipment for hemodialysis applications.

^bNot included in EP but introduced as suggestion by national authorities in some countries [13].

(electrodialysis) has made it possible to avoid the trouble of using chemicals for regeneration but its use, in spite of a greater chemical quality, needs a further ultrafiltration to remove potential microbial contamination. As a result usually two RO modules in series are preferred and this combination represents the optimal configuration to preserve microbiological quality of the

treated water. Finding the best assembly of the different components in terms of size (volume, fluxes, treatment capacity) and position in the chain is a major task for water engineering. To assure a consistent production of high-grade quality water, it is necessary to optimize the design of the water plant and a direct delivery to the loop is mandatory to preserve the microbiological quality of the treated water. A fundamental issue has been the discovery that microbial growth is enhanced by low flux and stagnation [9, 10]. This has changed the water distribution system from a dead-end pipeline to a distribution loop with a continuous water flow even during a period of no use; unused water enters a partial reuptake inside of the system. Material and modalities of installing a distribution loop form a critical point. For preserving water purity results depend on pipeline plumbing where high flow rate (high shear rate), avoidance of dead space and lateral arms, prevention of stagnation and possible contamination are the issues to be dealt with [1, 11]. Unprotected sampling or drain ports should be abandoned, and the pipe should be provided with adequate drainage. Medical grade polyvinyl chloride (PVC) has been the most frequently used material for piping but nowadays, based on results in pharmaceutical plants, new materials are in use. AISI 316 stainless steel, polyvinylidene fluoride (PVDF), and cross-linked polyethylene (PEX) are substituting PVC as they offer a better resistance to disinfection, the avoidance of particles or chemicals leaching, and a smooth surface able to avoid bacterial adhesion [12]. Modern technology has only a modest impact on the final cost of the hemodialytic treatment [13]. Water cost for a single dialysis treatment may vary from 1.8 to 3.1 Euro depending on the type of water treatment plant, material in use and system of disinfection. Considering a dialysis unit working on two shifts a day, table 3 reports results on costs of a single treatment comparing a standard hemodialysis (Cuprophane membrane, water treatment plant with a PVC distribution loop and chemical disinfection) with a biocompatible hemodialysis ('high-flux' membrane, ultrapure dialysate, water treatment plant with an AISI 316L stainless steel distribution loop and steam disinfection). The percentage of total costs of a water plant is minimal if considering the amount spent on a biocompatible treatment where water represents a fundamental factor.

Quality Control

Whatever the water treatment system or the disinfection protocol in use, the only way to assure a proper water quality is to have a maintenance and quality control program [7, 8, 11]. Some parameters may be checked continuously with an automatic device while for most of them there should be a periodical

Table 3. Cost analysis of a single hemodialysis treatment from different water treatment plants (see text for details)

	Standard hemodialysis	Biocompatible hemodialysis
Treatment		
Materials		
Staff	182 Euro	245 Euro
Maintenance and technical costs		
General costs		
Water treatment plant (A)		
Double RO	1.8 Euro	
PVC distribution loop		
Chemical disinfection		
Water treatment plant (B)		
Double RO		
AISI 316L stainless steel distribution loop		3.1 Euro
Steam disinfection		
Water cost as % of total treatment	0.98%	1.26%

monitoring. Frequency is regulated on manufacturer's and water engineering recommendations and on suggestions from reference standard authorities. The control program in a particular dialysis unit should be based not only on these suggestions but also on knowledge of local contaminants, specific to the area, on historical results, on clinical indications and on balance with cost [14]. Some indications may be derived from the literature and in table 4 we summarize the most recent suggestions [7, 8, 15]. For successful results water quality has to be guaranteed at the point of use and, microbiological contamination being the most important issue, the lack of real-time monitoring possibilities makes the problem worse. In some industrial fields, systems are used to rapidly detect the degree of microbial contamination: these systems are actually not sensitive enough to test real-time sterility and apirogenicity. Therefore a quality control program with periodical audit will assure the effectiveness of maintenance, cleaning and disinfection procedures. In contrast to the natural human tendency to have faith in sophisticated equipment and new technology, a quality control program should include a documented procedure for characterization of the process and involved parameters, definition of methods and tests to check the process, definition of the accepted limit values for each part of the process and for final water product results. Last but not least the quality procedure should

Table 4. Frequency of sampling for routine quality monitoring of water

	EDTNA/ERCA guidelines	Renal association	French regulations for 'on-line' treatments
Acidity or alkalinity	3-monthly	3-monthly	3-monthly
Aluminum	3-monthly	3-monthly	3-monthly
Ammonium	3-monthly	3-monthly	3-monthly
Calcium	3-monthly	3-monthly	3-monthly
Chloramines	3-monthly	3-monthly	3-monthly
Total chlorine	3-monthly	monthly	3-monthly
Chlorides	3-monthly	3-monthly	3-monthly
Conductivity	n.i.	n.i.	daily
Copper	3-monthly	3-monthly	3-monthly
Fluorides	3-monthly	3-monthly	3-monthly
Heavy metals	3-monthly	3-monthly	3-monthly
Lead	3-monthly	3-monthly	3-monthly
Magnesium	3-monthly	3-monthly	3-monthly
Mercury	3-monthly	3-monthly	3-monthly
Nitrates	3-monthly	3-monthly	3-monthly
Oxidizable substances	3-monthly	3-monthly	3-monthly
Potassium	3-monthly	3-monthly	3-monthly
Sodium	3-monthly	3-monthly	3-monthly
Silver	3-monthly	3-monthly	3-monthly
Sulfates	3-monthly	3-monthly	3-monthly
Zinc	3-monthly	3-monthly	3-monthly
Bacteria	monthly	weekly	monthly
Endotoxin	monthly	weekly	monthly

n.i. = Not indicated.

include an operational problem analysis, taking into account abnormal test results as well as clinical side effects eventually reported.

Conclusion

Modern technology allows to improve water quality and to assure a water product within the current standards. Success will depend not only on excellent technology but also on procedures and policies tailored to the individual units. This requires an absolute compliance with quality control procedures and testing and a trained and educated staff vigilant at all times.

References

- 1 Canaud BJ, Mion CM: Water treatment for contemporary hemodialysis; in Jacobs C, Kjellstrand CM, Kock KM, Winchester JF (eds): Replacement of Renal Function by Dialysis. Dordrecht, Kluwer Academic Publishers, 1996, pp 231–255.
- 2 Brunet P, Berland Y: Water quality and complications of haemodialysis. *Nephrol Dial Transplant* 2000;15:578–580.
- 3 Kaysen GA: Inflammation nutritional state and outcome in end stage renal disease. *Miner Electrolyte Metab* 1999;25:242–250.
- 4 Ward DM: Water disasters: Pitfalls and precautions. *Contemp Dial Nephrol* 1999;12:24–28.
- 5 AAMI: Standard/American National Standard: Water Treatment Equipment for Hemodialysis Applications. AAMI/DS RD62, 2000.
- 6 European Pharmacopoeia: Haemodialysis Solutions, Concentrated, Water for Diluting. Monograph 1997: 1167, ed 3. Council of Europe, Strasbourg 1996.
- 7 EDTNA/ERCA: European best practice guidelines for haemodialysis. 8. Dialysis fluid purity. *Nephrol Dial Transplant*, in press.
- 8 Ministère de l'Emploi et de la Solidarité: Circulaire relative aux spécifications techniques et à la sécurité de la pratique de l'hémodifiltration et de l'hémodiafiltration en ligne dans établissements de santé. République Française, Circulaire DGS/DH/AFSSAPS No 311, June 7, 2000.
- 9 Man NK, Degremont A, Darbord JC, Collet M, Vaillant P: Evidence of bacterial biofilm in tubing from hydraulic pathway of hemodialysis system. *Artif Organs* 1998;22:596–600.
- 10 Cappelli G, Ballestri M, Perrone S, Ciuffreda A, Inguaggiato P, Albertazzi A: Biofilms invade nephrology: Effects in hemodialysis. *Blood Purif* 2000;18:224–230.
- 11 Cappelli G, Perrone S, Ciuffreda A: Water quality for on-line hemodiafiltration. *Nephrol Dial Transplant* 1998;13(suppl 5):12–16.
- 12 Cappelli G, Ballestri M, Facchini F, Carletti P, Lusvarghi E: Leaching and corrosion of polyvinyl chloride (PVC) tubes in a dialysis water distribution system. *Int J Artif Organs* 1995;18:261–263.
- 13 Commissione dialisi SIN: Rapporto della commissione dialisi sui costi della terapia dialitica. *G Ital Nefrol* 1997;14:321–338.
- 14 Cappelli G, Lusvarghi E: La qualità delle acque per dialisi: normativa italiana e proposta operativa di controllo periodico. *G Ital Nefrol* 1990;7:165–170.
- 15 The Renal Association: Treatment of Adult Patients with Renal Failure: Recommended Standards and Audit Measure, ed 2. London, Royal College of Physicians, 1997.

Prof. Gianni Cappelli, Division of Nephrology, Dialysis and Transplantation,
University Hospital of Modena, Via Del Pozzo, 71, I–41100 Modena (Italy)
Tel. +39 059 4222481, Fax +39 059 4222167, E-Mail cappelli@unimo.it