Efficacy of Heat Disinfection With the Aksys Personal Hemodialysis System

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The first objective of this study was to validate the use of water at 85°C ± 5°C to achieve high-level disinfection of a clean-in-place extracorporeal dialysis circuit. The second objective was to demonstrate that applying this hot water method to the entire fluid pathways of a newly designed dialysis instrument, including an integral reverse-osmosis membrane, routinely allowed the production of back-filtered dialysate meeting the U.S. Pharmacopeia (USP) standard for the water for injection (WFI). In a first study, six dialyzers were inoculated with P. aeruginosa*, incubated, and subjected to 75°C water for 30 minutes. No organisms could be recovered from the experimental dialyzers nor from three negative controls, but they were recovered from three positive controls. In a second study, the carbon tanks in the water inlet line and the dialysate tank were both inoculated with massive amounts of dialysis water-adapted Gram-negative organisms, followed by seven dialysis treatments using bovine blood, where the fifth and sixth procedures were separated by 2 idle days and the sixth and seventh procedures were separated by 3 idle days. In addition, the bovine blood used in each treatment was highly contaminated. In every case, the back-filtered dialysate met the WFI standard.*

From the above results we conclude that a hot water disinfection process is efficacious in reducing even grossly exaggerated contamination in the Aksys personal hemodialysis system to the point where it can produce water and dialysate that greatly exceed the Association for the Advancement of Medical Instrumentation (AAMI) standards and priming and rinse-back solution (back-filtered dialysate) that meets the USP standard for WFI.

(Home Hemodial Int., Vol. 1, 36 – 40, 1997)

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Key words

Hemodialysis machine, personal hemodialysis system, dialyzer reuse, disinfection of extracorporeal circuit, hot water disinfection

Introduction

There are many locations where dialysis can be advantageously performed outside of a traditional outpatient dialysis clinic. These venues include nursing homes, hospitals, self/limited-care clinics, and patients' homes. However, the design of contemporary hemodialysis machines is universally optimized for use in outpatient clinics and, therefore, not suitable for use for alternative sites. In addition, a growing body of evidence has substantiated the advantages of performing hemodialysis at frequencies greater than three times per week (1–7). It is for these reasons that a newly designed "personal" hemodialysis system is being developed by Aksys Ltd.

The goal of this product is to reduce to a minimum the impediments to performing hemodialysis at frequencies greater than three times per week at locations other than traditional dialysis clinics. Meeting this goal can largely be achieved by reducing the skill necessary to operate the system, minimizing the time and effort required to perform the treatment, and by minimizing the disposable items consumed with each treatment. In turn, these specific design objectives can be accomplished by cleaning and disinfecting the extracorporeal circuit in-place on the instrument between treatments and automatically priming and rinsing the extracorporeal circuit with injectable quality, back-filtered dialysate. Effecting these design features then becomes dependent on implementing an automatic, safe, and efficacious method of system-wide disinfection.

In considering the various options available for disinfection, the commonly used chemical disinfectants such as formaldehyde, peracetic acid, and

glutaraldehydes were first considered and the conclusion reached that they all suffered from the following drawbacks:

- manufacturing and shipping costs;
- special handling and storage requirements not easily fulfilled by the patient;
- hazardous exposure to noxious fumes;
- safety systems required to ensure that an adequate concentration of disinfectant has been infused and completely rinsed out prior to treatment;
- sequestration of disinfectants in the potting compounds of dialyzers from which they can leach out during treatment;
- environmental concerns;
- potential degradation of the dialyzer membrane (8–10).

For these reasons, a decision was made to avoid using chemicals and instead use a substantially equivalent, nonchemical disinfectant that is already present in every household: hot water. Once this decision was made, the following design requirements were applied:

- the process must achieve high-level disinfection, the long-standing industry requirement for reuse of dialyzers (11);
- the water used to prepare the dialysate must meet the Association for the Advancement of Medical Instrumentation (AAMI) standard, which requires <200 colony-forming units (cfu) per milliliter (11);
- the dialysate must also meet the AAMI standard, which is <2000 cfu/mL, and the back-filtered dialysate must meet the U.S. Pharmacopoeia (USP) requirement for water for injection (WFI), which is <0.1 cfu/mL and <0.25 endotoxin units (eu) per milliliter (12).

Material and methods

In order to meet these requirements, the system was designed as illustrated schematically in Figure 1. The dialyzer used is one known to be unaffected by repeated exposure to hot water, that is, polysulfone membrane encased in polycarbonate. The arterial and venous blood tubing sets are constructed of materials able to withstand high temperatures throughout, and two ports are provided on the face of the instrument into which the arterial and venous cannula connectors are inserted at the end of a treatment. By so doing, a continuous fluid pathway is created between the extracorporeal circuit and the dialysate circuit. The dialysate is constituted in a 52-L tank into which the dialysate chemicals and ultrapure water are automatically dispensed. The dialysate is then perfused through a depyrogenation filter prior to entering the dialyzer after which it is returned to the same tank but kept from mixing with the virgin dialysate by means of a thermocline.

A reverse-osmosis (RO) membrane is integrated into the instrument for production of ultrapure water. During the high-temperature disinfection cycle, water at 85°C ± 5°C is circulated for >1 hour through all internal fluid pathways, including both the feed and product sides of the RO membrane as well as the entire extracorporeal circuit. This is assured by monitoring 12 different temperature sensors placed throughout the fluid pathways. The location of five of these sensors is shown in Figure 1. Sterile and depyrogenated stainless steel sampling ports (ESP sampling valve #CP6AM3907, Millipore Corp., Bedford, MA, USA) were installed at six different locations in the system fluid path (Figure 1) in order to draw samples for microbiological assays.

To confirm that this design met its requirements, two different studies were performed: one focusing on the dialyzers alone and another examining the entire system. For the dialyzer study, six dialyzers (F80, Fresenius USA, Lexington MA, USA) were contaminated with 10^6 *P. aeruginosa* (ATCC 9027). Three positive controls were included, where the inoculum was only 100 cfu in order to demonstrate that the test procedure was capable of detecting low levels of survivors. Three negative controls were also included. Water at 75°C was recirculated through the dialyzers for 30 minutes, purposely representing both a lower time and temperature than actually implemented in the system. The dialyzers were then filled with media (soybean casein digest broth) and incubated for 14 days. The media were then drained and growth recorded and verified by Gram stain, growth on Cetrimide or Pseudosel agar, oxidase test and growth at 41°C.

On day 1 of the system-wide study, the carbon beds and dialysate vessel were inoculated with 10 mL of a suspension containing 2.3×10^8 organisms composed of the following:

- *Pseudomonas aeruginosa* (ATCC 15422);
- *Burkholderia cepatia* (ATCC 25416);
- *Brevundimonas diminuta* (ATCC 19146).

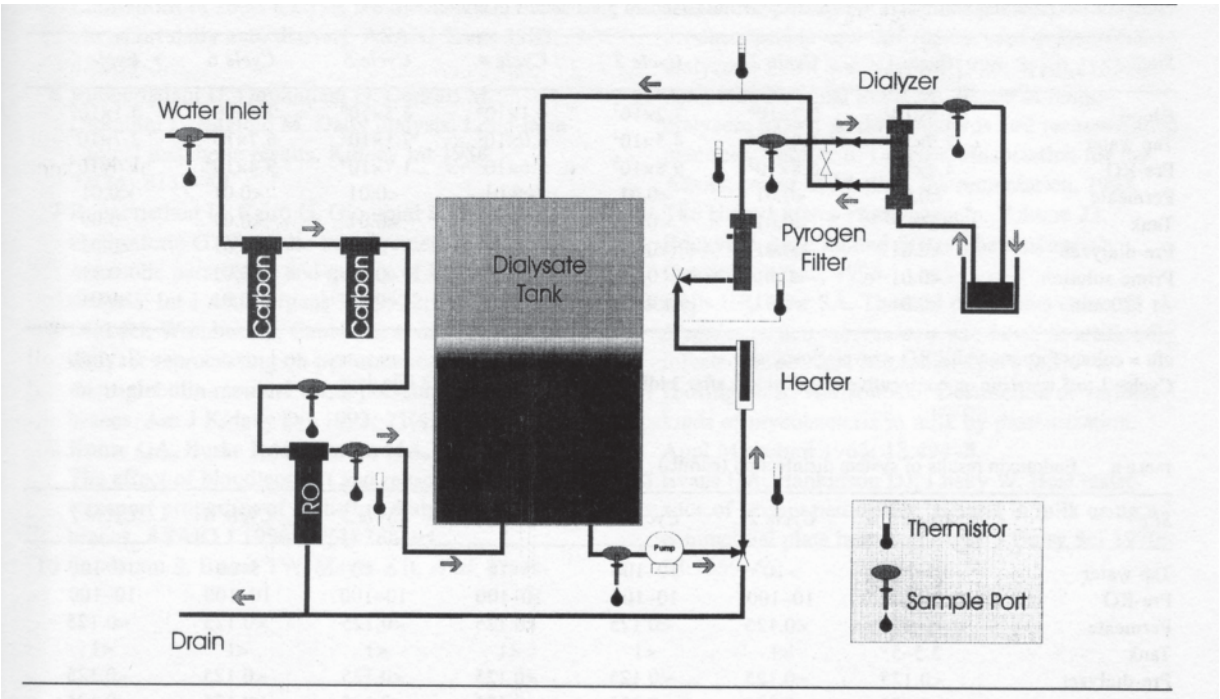

FIGURE 1 Schematic representation of the Aksys personal hemodialysis system with locations of thermistors and sample ports.

Two hours of dialysis followed by disinfection was then performed on 5 consecutive days. During each dialysis session, the extracorporeal circuit was perfused with slaughterhouse bovine blood, which was collected taking no particular care in its handling, resulting in high levels of nonspecific bacterial contamination. After the fifth procedure, the system was left idle for 2 days followed by a sixth dialysis treatment/disinfection. Finally, the system was left idle for 3 days followed by a seventh treatment. Samples for viable organisms and endotoxin were taken at the following locations (Figure 1):

- tap water;
- feed water (pre-RO);
- RO permeate (water for dialysis);
- dialysate in the tank (post-chemical addition);
- dialysate delivered to the dialyzer (post-ultrafilter);
- priming solution in the extracorporeal circuit (immediately prior to dialysis);
- post-pyrogen filter dialysate after 120 minutes of dialysis.

Results

The results of the dialyzer study were that no organisms could be cultured from any of the inoculated/disinfected dialyzers or negative controls, but inoculated organisms were recovered from all positive control dialyzers. The results of the system-wide study are shown in Tables I and II illustrating the levels of viable organisms and endotoxin respectively recovered at each of the sampling sites for each of the simulated dialysis procedures.

Discussion

Based on the results of the dialyzer study, even water at 75°C for only 30 minutes achieves high-level disinfection by eradicating the most commonly occurring bacteria found in dialysis water systems. There is always concern regarding dialysis water systems being colonized by mycobacteria, since these tend to be much more resistant to chemical disinfectants. This same concern does not apply to hot water disinfection, however, since these organisms are known to be eliminated by temperature/time combinations that are

TABLE I Microbiology results of system disinfection (standard plate counts in cfu/mL)

Site	*Cycle 1*	*Cycle 2*	*Cycle 3*	*Cycle 4*	*Cycle 5*	*Cycle 6*	*Cycle 7*
Blood	1.4×10^5	2.7×10^6	3.2×10^7	4.1×10^6	4.5×10^6	2.0×10^3	3.1×10^6
Tap water	2.9×10^1	4.9×10^1	4.5×10^1	6.0×10^2	2.1×10^2	6.7×10^2	2.7×10^2
Pre-RO	4.4×10^3	6.8×10^3	9.8×10^3	5.6×10^3	1.7×10^4	9.4×10^4	1.6×10^4
Permeate	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Tank	2.2×10^3	<0.01	<0.01	<0.01	<0.01	<0.01	0.09
Pre-dialyzer	<0.01	<0.01	<0.01	<0.01	0.01	<0.01	<0.01
Prime solution	<0.01	<0.01	0.01	<0.01	<0.01	<0.01	0.11
At 120 min	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

cfu = colony-forming units; RO = reverse osmosis.
Cycles 1 to 5 were run on consecutive days, cycle 6 after 2 idle days, and cycle 7 after 3 idle days.

TABLE II Endotoxin results of system disinfection (eu/mL)

Site	*Cycle 1*	*Cycle 2*	*Cycle 3*	*Cycle 4*	*Cycle 5*	*Cycle 6*	*Cycle 7*
Tap water	10–100	>10	10–100	5–10	5–10	5–10	10–100
Pre-RO	5–10	10–100	10–100	10–100	10–100	10–100	10–100
Permeate	<0.125	<0.125	<0.125	<0.125	<0.125	<0.125	<0.125
Tank	2.5–5	<1	<1	<1	<1	<1	<1
Pre-dialyzer	<0.125	<0.125	<0.125	<0.125	<0.125	<0.125	<0.125
Prime solution	<0.125	<0.125	<0.125	<0.125	<0.125	<0.125	<0.125
At 120 min	<0.25	<0.25	<0.125	<0.125	<0.125	<0.125	<0.125

eu = endotoxin units; RO = reverse osmosis.

considerably lower than those used in the Aksys personal hemodialysis system (PHD) system (13–15).

Based on the system-wide study, it can first be concluded that the PHD system produces water for dialysis that meets the AAMI microbiology standard, provided that the feed water meets the EPA microbiology standard for drinking water (<500 cfu/mL), and the RO filter is within its specified operating limits. Second, once passed through the depyrogenation filter, the dialysate not only exceeds the AAMI standard for dialysate but meets the USP standard for WFI. While not specifically demonstrated in this report, the dialyzer (also a depyrogenation filter) provides a redundancy to ensure injection quality dialysate even in the event of an intratreatment pyrogen filter failure. Third, dialysate back-filtered into the extracorporeal circuit meets the USP standard for WFI. Finally, all fluid purity requirements that were set forth for the system continue to be met even after 3 days of idle time.

From the above results it can be concluded that a hot water disinfection process, where the water is kept at 85° ± 5°C for one hour, is not only efficacious in reducing even grossly exaggerated contamination in the Aksys PHD, but also enables the production of water and dialysate that greatly exceeds the AAMI standards and priming and rinseback solution (back-filtered dialysate) that meet the USP standard for WFI.

References

1 Kjellstrand CM, Evans RL, Petersen RJ, *et al*. The "unphysiology" of dialysis: A major cause of dialysis side effects? Kidney Int 1975; 7(Suppl 2):S30–4.
2 Chapman GV, Mahoney JF, Farrell PC. A crossover study of short time dialysis. Clin Nephrol 1980; 13:78.
3 Uldall R, Francoeur R, Ouwendyk M, *et al*. Simplified nocturnal home hemodialysis (SNHHD). A new approach to renal replacement therapy (Abstract). J Am Soc Nephrol 1994; 5(3):428.
4 Depner TA. Daily hemodialysis: A quantitative perspective. Semin Dial 1995; 8(5):266–8.
5 Hombrouckx R, Bogaert AM, Leroy F, *et al*.

Limitations of short dialysis are the indications for ultrashort daily auto dialysis. ASAIO Trans 1989; 35:503–5.

6 Buoncristiani U, Quintaliani G, Cozzari M, Giombini L, Ragiolo M. Daily dialysis: Long-term clinical metabolic results. Kidney Int 1988; 33(24):S137–40.

7 Buoncristiani U, Cairo G, Giombini L, Quintaliani G, Bonforte G. Dramatic improvement of clinical-metabolic parameters and quality of life with daily dialysis. Int J Artif Organs 1989; 12:133–6.

8 Diaz RJ, Washburn S, Cauble L, *et al*. The effect of dialyzer reprocessing on performance and beta 2-microglobulin removal using polysulfone membranes. Am J Kidney Dis 1993; 21(4):405–10.

9 Kunas GA, Burke RA, Brierton MA, Ofsthun NJ. The effect of blood contact and reuse on the transport properties of high-flux dialysis membranes. ASAIO J 1996; 42(4):288–94.

10 Sundaram S, Barret TW, Meyer KB, *et al*. Trans-membrane passage of cytokine-inducing bacterial products across new and reprocessed polysulfone dialyzers. J Am Soc Nephrol 1996; 7(10):2183–91.

11 American National Standard. Reuse of hemodialyzers RD47. AAMI standards and recommended practices. Volume 3: Dialysis. Association for the Advancement of Medical Instrumentation, 1993.

12 The United States Pharmacopeia. Volume 23. Rockville, MD: United States Pharmacopeial Convention, Inc, 1995.

13 Kells HR, Lear SA. Thermal death time curve of *Mycobacterium tuberculosis var. bovis* in artificially infected milk. Appl Microbiol 1960; 8:234–6.

14 Harrington R, Karlson AG. Destruction of various kinds of mycobacteria in milk by pasteurization. Appl Microbiol 1965; 13:494–5.

15 Evans DA, Hankinson DJ, Litsky W. Heat resistance of certain pathogenic bacteria in milk using a commercial plate heat exchanger. J Dairy Sci 1970; 53:1659–65.