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REVIEW ARTICLE

Water treatment for hemodialysis

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Abstract

Water treatment plays a vital role in the delivery of safe and effective hemodialysis (HD). Ensuring that water quality meets the American Association for the Advancement of Medical Instrumentation standards and recommendations (or equivalent) is necessary to reduce the incidence of chemical hazards and endotoxemia associated with the use of water for HD. This review will discuss the principles of water treatment for HD, the essential components of water purification, the recommended system monitoring and maintenance procedures, and some of the historical incidents of adverse reactions that resulted from the use of contaminated dialysis water.

Key words: Dialysis solutions, Hemodialysis (HD), Pyrogenic reactions, Reverse osmosis (RO), Water purification

中文摘要

水處理對安全有效的血液透析(HD)非常重要。確保水質量符合美國醫學藥器具標準和建議是減少與水相關的HD化學物污染危險和內毒血症的發生率的重要因素。本文獻回顧討論HD中水處理原則，水純化的必要儀器，監控系和措拖，以及既往的一些由污染的透析水導致不良反應的病例。

INTRODUCTION

Since the early 1960s, hemodialysis (HD) has been increasingly used for the treatment of acute renal failure and end-stage renal failure. Technologic advances in dialyzer membranes, dialysis machines and vascular access have made HD a routine procedure today. Nonetheless, it remains potentially hazardous, both as a result of mechanical malfunctions and human error (1). HD replaces kidney function by using a semi-permeable membrane inside a dialyzer to filter wastes and water from the blood into the dialysate fluid. Water is used in HD to prepare dialysate. If dialysis water contains impurities such as bacteria, endotoxins, metals, mud, sediment or chemicals, these impurities may enter the patient's bloodstream through the dialyzer membrane and cause disease or injury. Because dialysis uses large amount of water, even tiny amount of contaminants can be dangerous. Some substances can cause conditions such as anemia or pyrogenic reactions, while some substances can build up to toxic levels, causing long-term physical harm, and other substances are immediately toxic and can cause death. A normal person also encounter these contaminants through drinking water, but the healthy kidney is able to remove these substances. Renal failure patients do not have this capability. It is ironic that the same dialysis treatment that save lives can also expose patients to substances that could injure them. In order to be safe for patients, dialysis water must be carefully treated with a water treatment system, consisting of a series of devices, each of which removes certain contaminants. Concerns over the safety of dialysis water have also been revived recently with the developments of highly permeable dialysis membranes in high-flux and high-efficiency dialysis, dialyzer reuse and reprocessing, and bicarbonate dialysate. Fortunately, these advances in dialysis practices have been paralleled by continuous improvements in water treatment technology. This review discusses why and how water is treated before being used

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Table 1. Effects of chemical contaminants in the HD patient.

Signs and Symptoms	Possible Water Contaminant
Anemia	Aluminum, Chloramines, Copper, Zinc, Formaldehyde, Nitrates
Bone disease	Aluminum, Fluoride
Hypertension	Calcium, Sodium
Hypotension	Bacteria, Endotoxins, Nitrates
Metabolic acidosis	Low pH, Sulphates
Muscle weakness	Calcium, Magnesium
Nausea and vomiting	Bacteria, Calcium, Copper, Endotoxins, Low pH, Magnesium, Nitrates, Sulphates, Zinc
Neurological deterioration and encephalopathy	Aluminum
Hemolysis	Chloramines, Copper, Nitrates, Formaldehyde

for dialysis, monitoring and maintenance of the water treatment system and some historical incidents of things gone wrong.

PRINCIPLES OF WATER TREATMENT

In the early days of HD, potable city water was routinely used to prepare dialysate. The assumption made at that time was that if potable water from a community water treatment system was safe to drink it was also safe to use for HD (2). As chronic HD treatment became more popular and widespread, evidence began to accumulate linking chemical and microbiological water-borne contaminants to adverse reactions in patients. Specifically, it was found that organic and inorganic chemicals in the water used to prepare dialysate could diffuse through the dialyzer membrane and enter the patient's blood (2). We now realize that the quality of the water used to prepare dialysate is an extremely important aspect of HD. Some of the most serious dialysis patient injuries reported in the medical literature are related to inadequate or improper water treatment. The drinking water standards that water authorities have to meet are based on a drinking water exposure of 2 L per day (14 L/week). In contrast, a patient on HD is exposed to over 300 L of dialysis water weekly. The pores of the semi-permeable dialysis membrane are sized to allow solutes up to a certain size to pass through; the non-selective diffusion of chemicals and toxins across dialysis membranes exposes these patients to the hazards of water contamination in the inadequately treated dialysate. In addition, municipal water that is suitable for drinking is rendered so by the addition of substances that are toxic in the HD setting. Examples of these additives include aluminum sulfate alum to flocculate organic contaminants in the water supply, chlorine gas used as bactericidal agent, and fluoride added to prevent dental caries. There may also be seasonal changes in source water contaminants and water hardness. Hence, all municipal water supplies must undergo additional purification treatment before being used for HD. The same level of care must be given to the final preparation of the dialysate. Dialysate quality must be checked regularly and defined in terms of chemical, physical and microbiologic characteristics. The disinfection of the dialysis machine is also crucial in the achievement of a safe dialysate.

Table 2. The Association for the Advancement of Medical Instrumentation: HD water quality standards: maximum chemical contaminant levels (3).

Contaminant	Suggested maximum level (mg/L)
Calcium	2 (0.1 mEq/L)
Magnesium	4 (0.3 mEq/L)
Sodium	70 (3 mEq/L)
Potassium	8 (0.2 mEq/L)
Fluoride	0.2
Chlorine	0.5
Chloramines	0.1
Nitrate	2
Sulphate	100
Copper, Barium, Zinc	0.1
Aluminum	0.01
Arsenic, Lead, Silver	0.005
Cadmium	0.001
Chromium	0.014
Selenium	0.09
Mercury	0.0002

The symptoms and signs of possible water-related chemical toxicity identified in the HD setting are listed in table 1.

WATER TREATMENT MODALITIES

A water treatment system provides water in which levels of contaminants known to be toxic to dialysis patients are consistently kept below recommended limits (Table 2). In practice, a water treatment system utilizes several devices and processes for adequate water treatment because different substances are removed with various modalities applied in series. The quality of the water supply, the amount of water required and economic considerations all play a role in the choice of these devices and their combination. In general, no schema

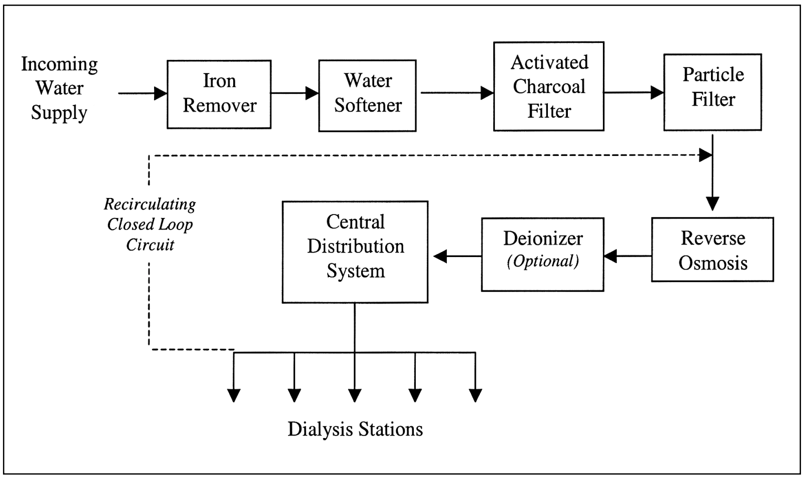

Figure 1. Simplified schematic diagram of a water treatment system. Deionizer is optional if RO produces water of adequate quality. Some would advocate particulate filters both before and after the activated charcoal filter.

exists which defines a water product standard for all HD units; the number and order of devices in the system must be arranged to best suit the needs of any given unit. Figure 1 is a schematic representation of a typical water treatment system.

Iron removal filter

The exact combination and configuration of components of a water treatment system will, amongst various factors, depend on the quality of the feed water. In Hong Kong where the feed water has a high content of iron, an iron removal filter is necessary. Suspended and dissolved iron is removed in the iron removal filter by green sand and alkaline dolomitic rocks. Green sand facilitates the oxidation of ferrous salts to the insoluble ferric hydroxide. The alkaline reaction on the surface of the alkaline rocks then enable the direct removal of iron by trapping it in the hydroxide form. The hydroxides retained can be easily removed by back-washing regularly.

Water softeners and deionizers

Calcium and magnesium, the hardness-forming ions in water, can cause precipitate to form and clog equipment as well as damage the reverse osmosis (RO) membrane. To eliminate these problems, feed water must be softened. This is carried out by means of an ion exchange process, which removes from feed water inorganic ionic contaminants. Water softeners and deionizers are both ion exchangers. In this process, water is rinsed through a column containing synthetic spheres, called "resins". Certain ions present in water are exchanged for other ions fixed to the resins. Water softeners contain sodium-coated resins and these are exchanged mainly for calcium and magnesium ions. Water softeners have a more limited binding capacity for other polyvalent cations like iron, manganese and aluminium. On the other hand, deionizers differ from water softeners in that they contain both cation and anion exchange resins. Cations are exchanged for hydrogen (H^+) ions and anions are exchanged for hydroxide (OH^-) ions. The H^+ and OH^- then combine to form H_2O. Hence, it removes all types of cations and anions for pure water. Deionizers produce the purest water in terms of ionic contaminants. But at the same time, they harbor bacteria and produce significant colloidal material. Deionizer tanks should be monitored with resistivity meters, and produce water that always exceeds 1 MΩ/cm in resistance. When the exchange sites on a resin bed are depleted, the bed is said to be exhausted and needs to be regenerated. Water softeners are regenerated by flushing the resin bed with water and then with a brine of sodium chloride (a concentrated salt solution). If regeneration is not performed at the appropriate intervals before exhaustion, previously adsorbed ions may elute into the effluent, causing ion-related toxicities. Reports of fluoride and copper intoxications have appeared as a consequence of unrecognized deionizer exhaustion (4,5).

Granular activated carbon filters

Granular carbon (charcoal) activated by heat treatment will adsorb chlorine, chloramines and other organic substances from water. Activated charcoal also removes chlorine by a catalytic action, resulting in the conversion of chlorine into hydrochloric acid that is neutralized by the bicarbonates in the water. Chlorine hurts membranes and chloramines hurt patients (chloramines are oxidants and react with oxygen to destroy cell walls, including red blood cells causing hemolytic anemia). Feed water must remain in contact (empty bed contact time) with the carbon long enough to allow adequate removal of chloramines. The U.S. Food and Drug Administration (FDA) recommends a minimum of 10 minutes of empty bed contact time. The FDA also recommends that two tanks filled with activated carbon be used in series. When the first filter has a chloramine concentration in the effluent > 0.1 mg/L, it should be replaced and if the chloramines level in the effluent of the second tank exceeds 0.1 mg/L, the water must not be used for dialysis. Since carbon filters are highly porous with a high affinity for organic materials, they can be contaminated with bacteria if they are not serviced properly or replaced frequently.

Particle filters

All feed water contains particles. These particles can cause downstream dialysis equipment malfunction by clogging orifices and valves. Filters remove particles, solutes and other substances above a given size by mechanical filtration. There are different types of filters available and these are rated by the filter pore size, which is measured in microns. Five-µm filters are generally accepted as the size necessary to provide adequate water treatment and protection for equipment.

Reverse osmosis

The primary water purification process of choice in most applications is RO. It applies the rejection characteristics of ion exclusion semi-permeable membranes. In normal osmosis, water molecules will flow from areas of lesser solute concentration to that of greater concentration until the fluid concentration on both sides of the membrane is equal. Essentially, natural osmosis tries to dilute the side with the higher salt concentration to a point where both sides of the semi-permeable membrane have equal osmotic pressure. RO overcomes osmosis and concentrates salts on the reject side of the membrane, while collecting pure water on the product side. This is accomplished by applying high hydrostatic pressure to the feed water and driving water across the membrane. The end result is the production of purified water. This process can reject 90% to 99% of ionic as well as microbiologic contaminants, including bacteria, endotoxins, viruses, salts, particles and dissolved organic substrates. Depending on the quality of the source water, RO generally produces water that is safe for dialysis; otherwise, it may be necessary to polish the RO product water with a deionizer. Measuring the conductivity of the feed and product water and calculating the percentage of rejection from these measurements monitors the performance of RO devices. When the percentage of rejection falls below acceptable levels, the RO membrane has to be cleaned to restore its efficacy. Calcium, magnesium and iron can form scales on the RO membranes. Also, membranes are susceptible to damage by chlorine and chloramines, extreme pH and bacterial degradation. Hence, appropriate pre-treatment of feed water is necessary to protect the RO membrane and can prolong its life by several years.

MICROBIOLOGIC CONTAMINATION

Microorganism levels in dialysis water must be kept substantially lower than the levels tolerated in drinking water. In addition to source water, all the components of the water treatment and delivery system itself can harbor bacteria and endotoxins. The primary waterborne microbial contaminants of dialysis fluids are the gram-negative bacteria and non-tuberculous mycobacteria, microorganisms that are capable of surviving even in water containing minimal amounts of organic elements (6). These bacteria can form a biofilm that allows them to cling to surfaces, such as dialysate containers or feed hoses. The biofilm protects the bacteria from disinfectants, making them difficult to remove. Bacteria can grow rapidly in dialysis fluid, which consists of treated water mixed with a salt solution.

System disinfection

It is extremely important for the entire dialysate flow path within the delivery system to be cleaned and disinfected regularly to prevent the formation of biofilm. Disinfection may be achieved by heat or by chemical sterilants (aqueous formaldehyde, peracetic acid or sodium hypochlorite). Formaldehyde is a chemical disinfectant that has been widely used for disinfecting delivery systems. It is a very effective disinfectant against most bacterial species except mycobacterium species. Formaldehyde is a toxic substance and an irritating fume may be observed. Staff members may be exposed to health hazards if the concentration of formaldehyde in the air exceeds the safety standards. If the delivery system is not adequately rinsed before the dialysis mode is initiated, the potential for formaldehyde crossing the dialyzer membrane into blood exists.

Nowadays, sterilization using peracetic acid is gaining popularity because it lacks most of the toxic effects of formaldehyde and at the same time is more environmentally friendly in that it will eventually break down to acetic acid and water.

Heat disinfection of the water flow path using hot water > 85 ^{o}C to 90 ^{o}C is an attractive but more expensive alternative and avoids the hazards associated with chemical disinfectants.

Pyrogenic reactions during hemodialysis

Pyrogenic reactions developing during or after dialysis treatment are well recognized. Contaminated dialysate activates monocytes in the patient's blood stream due to the transit of bacterial products including endotoxins (lipopolysaccharides from bacterial cell walls) peptidoglycans or its fragments across dialysis membranes; eliciting mononuclear cell release of pro-inflammatory cytokines, e.g. interleukin-1 (IL-1) and tumor necrosis factor (TNF-α). These cytokines may express multiple biological activities including the induction of fever, cardiovascular instability, release of acute phase proteins and possibly the mediation of chronic inflammatory processes such as fibrosis, protein catabolism, ß2-microglobulin amyloidosis or cardiovascular diseases. Recent *in vivo* data have confirmed that even dialysate within recommended standards (< 200 CFU/mL) is associated with increased cytokine production in HD patients (7). Symptoms of pyrogenic reaction include fever, chills or rigor, hypotension, nausea and vomiting. The reaction usually begins shortly after the initiation of dialysis and may resolve spontaneously over the course of the treatment or shortly afterwards. Reported incidence of pyrogenic reactions ranged from 0.5 to 1.2/1000 treatments in one study (8). In addition, numerous outbreaks of bacteremia and endotoxemia have been reported in the medical literature (9-13). One or more pyrogenic reactions per year in the absence of septicemia were reported by 20% of chronic HD centres in United States, and a higher risk of pyrogenic reactions was found with dialyzer reuse, the use of high flux dialyzers and bicarbonate dialysate (14).

QUALITY CONTROL FOR THE WATER TREATMENT SYSTEM

The Association for the Advancement of Medical Instrumentation (AAMI) of the U.S. has set water quality standards that have become widely accepted (Table 2,3). These standards were based on the findings of a FDA-sponsored study on the risks and hazards of HD systems (15) as well as research performed by the Centers for Disease Control.

If left alone, any water treatment system will deteriorate in performance with time. Source water quality may change, components with finite capacity will exhaust and bacteria will contaminate delivery systems. As an example, a multi-centre study of quality of HD water in Canada demonstrated that 30%, 44%, and 14% of fully treated water samples did not meet the Canadian Standards Association standards for bacteria, pyrogens and chemical contaminants respectively (16). These changes can result in catastrophic failure of the system, resulting in patient injury or expensive repairs. Hence, written quality control protocols must be developed and enforced to safeguard against such failures. Results of all monitoring and maintenance procedures must be recorded in logbooks and these should be independently reviewed on a regular basis.

Monitoring

Monitoring provides information on product and source water quality and on the performance of individual system components. Product water quality must be regularly monitored to ensure it continues to meet the required standards. Source water quality is monitored to ensure that it does not deteriorate beyond that assumed in the system design. A dialysis unit should maintain ongoing communications with its local water treatment plant. Whenever there is a change in water treatment,

Table 3. AAMI HD water quality standards: microbiologic and endotoxin standards for dialysis fluids (3).

Type of fluid	Microbial count CFU/mL	Endotoxin EU/mL
Water to prepare dialysate	≤ 200 (< 100*	No standard < 0.25*)
Dialysate	≤ 2000	No standard
Water to rinse and reprocess dialyzers	≤ 200	≤ 5
Water to prepare dialyzer disinfectant	≤ 200	≤ 5

*European Pharmacopoeia (17)

Table 4. Recommended parameters used to monitor the performance of water treatment system components.

Purification Process	Monitored Parameter	Frequency of Monitoring
Filtration	Inlet & outlet pressure	Daily
	Product water flow rate	Daily
Softener	Product water hardness	Daily
Granular Activated Carbon filter adsorption	Inlet & outlet pressure	Daily
	Product water chloramine concentration	Prior to each patient*
Reverse Osmosis	Feed & product water conductivity (% Rejection)	Daily
	Feed & product water flow rate (% Recovery)	Daily
	Inlet & outlet pressure	Daily
	Feed water temperature	Daily
Deionization	Product water specific resistance	Continuous

*U.S. FDA recommendation

excessive amounts of a substance or other extreme fluctuations in the water supply, the dialysis unit should be notified by the water authority. An AAMI chemical contaminants analysis should be performed at least half-yearly or yearly and bacterial monitoring done at least monthly. Monitoring of the bacteriological quality of water and dialysate currently involves both culture of water and dialysate samples, as well as the measurement of endotoxins (lipo-polysaccharide) by the Limulus amoebocyte lysate (LAL) assay. The European Pharmacopoeia (17) recommends more stringent standards for bacterial contamination and endotoxin than the AAMI (Table 3). Additional testing should be performed when incoming city water quality varies or when changes occur in functioning system components (e.g. new system, modification of previous system, or whenever bacteremias or pyrogenic reactions are observed in patients).

Equipment performance is monitored to determine when replacement of exhausted components is required or when maintenance of permanent equipment is needed. Also, many important water treatment parameters can be measured continuously using gauges and monitors placed in the water stream. Daily inspection of these performances of individual system components, including water pressures, flow rates, temperatures and conductivity, provide ongoing assurance that product water quality is being maintained (Table 4).

Patient symptoms should also be monitored; if several patients have similar symptoms at the same time, certainly a problem with the water treatment or delivery system should be looked for .

Maintenance

System maintenance includes replacement of exhausted components and preventive measures designed to sustain system performance. Ion exchange beds of softeners and deionizers, filters and carbon-adsorption beds have a finite capacity and must be regenerated or replaced. Reverse osmosis units also require regular cleansing and disinfection to remove organic materials, scale and bacteria. Over time, bacteria can grow through the RO membrane into the product side, resulting in pyrogenic reactions.

HISTORICAL INCIDENTS

The number of clinically significant adverse dialysis reactions reported has been small, considering the volume of dialysis treatment that is being delivered. Yet, dialysis accidents have occurred as a result of machine failure as well as personnel error. Adverse reactions have been reported due to elevated dialysis water concentrations of aluminum (18), chloramines (19), sodium azide (20), fluoride (4), calcium/magnesium (21), nitrates (22), copper (23), zinc (24), formaldehyde (25), sulphate (26), sodium (27), and hydrogen peroxide (28). A recent report of three clusters of gram-negative bloodstream infections at HD centers in Canada, the United States and Israel found that all three outbreaks probably resulted from contamination of the waste drain ports in the same model of HD machine (29). Within the past 5 years, two notable outbreaks of patient intoxication have been reported in Brazil (30,31) and in Chicago (4).

On 16 July 1993, 12 patients treated at a long-term HD unit in Chicago became ill during or soon after HD (4). The patients experienced symptoms of severe pruritus, headache, nausea, and chest or back pain. Three patients developed fatal cardiac arrest due to ventricular fibrillation after completion of dialysis that day. Subsequent investigations found that fluoride was released from the deionization system after the ion exchange resin inside was exhausted. As exchange sites on the resin become depleted, fewer ions are removed. Continued use of the resin causes low affinity ions, such as fluoride, to be displaced from the resin into the effluent by ions with higher affinity. The investigator concluded that the incident was caused by errors in maintenance of the deionization system. The outbreak occurred during use of a temporary water treatment system when the central treatment area of the dialysis unit had been closed for three months prior to the incident for renovation. During this period, temporary water purification systems and dialysis stations were installed. The system was equipped with resistivity monitors, and the monitors were set to change illumination from a green to a red light when the quality of the treated water decreased to less than the standard of 1 MΩ/cm. In contrast, the monitoring apparatus previously used in the dialysis unit had only a red light that remained lit as long as resistivity remained above 1 MΩ/cm. Indeed, when the dialysis unit was surveyed after the incident, the green light was out and the red light lit on the resistivity monitors. Lessons that can be learnt from the incident include, firstly, that adherence to guidelines for calculating exchange resin capacity and for the monitoring of components of water treatment system are essential to prevent inadvertent use of these systems beyond exhaustion. In particular, unambiguous audible and visual alarms are essential. Secondly, whenever a change is made to the system, it is important to ensure that personnel are appropriately trained and that adequate attention is devoted to monitoring critical equipment and procedures. And lastly, an increase in the frequency or severity of common symptoms should raise our suspicion of a new and potentially serious problem.

Table 5. AAMI recommended monitoring and maintenance procedures for water treatment system.

Microbiologic monitoring

All dialysis delivery systems must contain acceptable levels of bacteria as recommended by AAMI, as listed in table 3

Bacterial cultures of the dialysis machines and the RO system are performed at least monthly

All results of culture counts are recorded on documentation sheets for each dialysis machine and water delivery system

Additional assays to be done if clinical indications suggest a pyrogenic reaction has occurred, after modification of the water treatment or distribution system, or for any new systems

Chemical contaminants monitoring

At facility start-up and on a 6 to12 monthly basis, the RO product water is analyzed for AAMI listed chemical contaminants (Table 2)

Chlorine/chloramine levels are tested daily on-site prior to each patient*

Analysis results should be documented in log-books

Start-up and testing of RO system

The RO unit must be tested with each start-up to assure safe water is available

All test results should be recorded in daily documentation sheets

Procedure:

1. Check and maintain salt level in the salt storage tank
2. Test the hardness of post-softened water
3. Test the chlorine/chloramine of the product water, water that exceeds the AAMI standard should not be used for dialysis
4. Check and record pressure, temperature, flow and conductivity of all meters

Maintenance

All equipment should be maintained following the manufacturer's recommendations.

Quality control checks should be done following the procedure and schedule recommended by the manufacturer

Electrical current leakage checks should be done regularly

All equipment, including water treatment and HD machines, should have an individual checklist and record of repairs and maintenance.

Entries are made when preventive maintenance or repairs are performed

The person performing the maintenance or repair should sign and date the maintenance checklist and log

*U.S. FDA recommendation

A more recent and serious incident occurred during February 1996 in a HD centre in Brazil (30,31). All 126 patients who underwent dialysis there at that time developed symptoms and signs of neurotoxic and hepatotoxic illness of varying severity, leading to the death of 60 patients. Investigations conducted subsequently found that the incoming municipal water and the water treatment system in the dialysis centre were contaminated with the toxin microcystin, produced by Cyanobacteria (blue-green alga). The outbreak was facilitated by inadequate water treatment at both the municipal water plant and the dialysis center. For about a year before the incident, the water used for dialysis at the center had been delivered by water-delivery trucks from a local reservoir without being adequately treated. The water from the municipal plant contained micorcystins, and these were not removed by the inadequately maintained treatment system at the dialysis center. Also, the quality of the water was not regularly tested at the dialysis center.

COSTS OF WATER TREATMENT

The costs involved in running a water treatment system for HD include capital and maintenance costs. The price for a new water treatment system unit may vary from HK$500,000 to over HK$1 million, depending on specific requirements and design, for example the length and type of the water piping required (heat resistant piping is necessary if heat disinfection is used). For system utilizing heat disinfection, the hot water generator itself may cost up to HK$1 million.

Maintenance of the system involves expenses in the supply of water and electricity, and expenditures for quality control measures like regular water cultures, laboratory analysis for water chemical contaminants, and endotoxin assays. In addition, recurrent costs include the purchase of consumables including particle filters (~ HK$150/month), salt tablets for the water softener (~ HK$800/month), chemical sterilants and test-strips (~ HK$10000/year), as well as the renewal of the RO membrane (~ HK$50000) which needs to be replaced every 5 years or so.

CONCLUSIONS

In Hong Kong, approximately 600 patients are receiving long-term HD for the treatment of end-stage renal disease. Water treatment is a vital aspect of the practice of safe and effective HD for these patients. No matter how carefully a dialysis treatment is prescribed and delivered, it cannot benefit the patient unless the water used has been adequately treated. Dialysate contam-ination and its implications for HD continue to be an important topic for HD personnel. AAMI (or equivalent) standards and recommended practices for HD must be strictly followed at all times, and continuous quality control must be provided. This review demonstrates that proper treatment of city water and appropriate design, installation, monitoring, and maintenance of water treatment systems in HD centers are all crucial in preventing patients from potential exposure to harmful chemicals and toxins.

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