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Reducing endotoxin from dialysis water by using different disinfection processes

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ABSTRACT

Hemodialysis centers in Baghdad show elevated concentrations of endotoxin. This reflects the inefficient treatment process used to purify dialysis water. The objective of this research is to evaluate several treatment processes to inactivate endotoxin concentration in dialysis water. The studied treatment options include utilizing ultrafiltration membrane (UF), disinfection with ozone (O_3), and disinfection with hydrogen peroxide (H_2O_2). Hybrid treatment was also considered by joining two or more of the above treatment methods. A lab-scale unit was built to implement the experiments and synthetic water (feed solution) was prepared with a known value of endotoxin concentration (0.48 EU/ml). Limulus amebocyte lysate test was used to determine endotoxin concentrations in the treated water. The results showed that all the tested treatment methods resulted in reducing the levels of endotoxins and providing high purity dialysis water. However, the best treatment was achieved when using triple treatment (i.e. UF, O_3, and H_2O_2). This combination reduced endotoxin concentration using the minimum feed of H_2O_2 at a significantly short contact time for oxidation agents (i.e., O_3 and H_2O_2). Accordingly, it is important to change the design of the currently used water treatment units in Baghdad to produce dialysis water in compliance with the international dialysis water quality standards and save patients' lives.

Keywords: Dialysis water; Bacterial endotoxin; Physical/chemical water treatment; Treatment systems; Water disinfectants; Water quality

1. Introduction

The source of hemodialysis (HD) water is mainly the municipal drinking water [1]. In general, this water passes through different levels of pretreatment including sediment filters, softeners, activated carbon filters, microfiltration, ultrafiltration (UF), reverse osmosis (RO) units, and ultraviolet disinfection. Finally, the product water is distributed through a hydraulic circuit in either direct method (directly to HD machines) or indirect method (stored in tanks to be used when needed [2].

The qualities of the dialysis water and the dialysate fluid depend mainly on the quality of the feed water (drinking water) and the design of the treatment units [3]; without a proper treatment system for the feed water, a low-quality water will be produced which cannot be considered safe to use in the HD systems [4].

HD patients are normally exposing to extremely large amounts of water more than 90 to 192 liters of water per session, two or three times a week [5], for that, the quality of the water utilized for dialysis is very important to prevent the chemical and the bacteriological contaminations transferring from the dialysate into the patients' bloodstream [3]. Therefore, the use of insufficiently treated water as dialysis water could be a probable cause of a high mortality rate for HD patients [6].

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Gram-negative bacteria are considered the most difficult contaminants to be removed in dialysis water especially after the formation of biofilm in the HD piping system which participates in the release of bacteria and bacterial fragments (endotoxins, muramyl peptides, and polysaccharides) [7]. These endotoxins are very difficult to remove from water because they are stable in different levels of heat and pH values [8], and also they have a high molecular weight that usually exceeds 10 kD.

The guidelines of the American National Standards Institute (ANSI/AAMI) for the total bacteria count (TBC) is <100 CFU/ml and for the endotoxin concentration is <0.25 endotoxin units per milliliter (EU/ml), while the standard limits for the ultrapure dialysate are TBC <0.1 CFU/ml and for the endotoxin concentration is <0.03 EU/ml for dialysis water [9].

These values will be considered to compare the results of this research to evaluate the quality of the produced dialysis water and to suggest the best strategy that will make the water in compliance with the international standard limits.

In this study; the efficiency of three treatment methods was investigated y to reduce endotoxins from dialysis water. The first one is the UF process that uses porous membranes to separate particles with a specific size [10]; the second and the third methods are advanced oxidation process using ozone and hydrogen peroxide to destroy bacteria and protoplasmic oxidation that leads to cell wall lysis [11].

2. Materials and method

2.1. Work strategy

Reagents from Wako Chemicals Inc., USA were used to prepare standard endotoxin control (CSE) *E. coli* (500 ng/vial) at a concentration of (1,000 EU/ml) to be used with the Gel clot endpoint method by Limulus amebocyte lysate test [12]. After that, this solution was mixed with double-pass RO water with electric conductivity of (0.5 μS/cm) at room temperature to get synthetic water (feed solution) that will be used in all experiments with endotoxin concentration of (≥0.48 ± 0.06 EU/ml). This endotoxin concentration is higher than that of the ANSI/AAMI guidelines for dialysis water and it is close to the range of endotoxin concentration values that have been previously found in dialysis water analyzed from several dialysis centers in Iraq [6]. All these solutions were prepared in the dialysis lab in the environment and water directorate at the Iraqi Ministry of Science and Technology, Baghdad.

2.2. UF membrane treatment method

A bench-scale system (Fig. 1) from Sterlitech Corporation, USA with a cross-flow UF membrane, with (60 kDa) molecular weight cut-off, and an effective filtration area of (266 cm^2) was used to investigate the effect of pressure on endotoxin removal. The trans-membrane pressure was set in the range of 0.5–3.5 bar using a digital controller. The tests begin with washing the system with pure multi-pass RO water that has endotoxin concentration of (<0.06 EU/ml) with almost zero pressure [13].

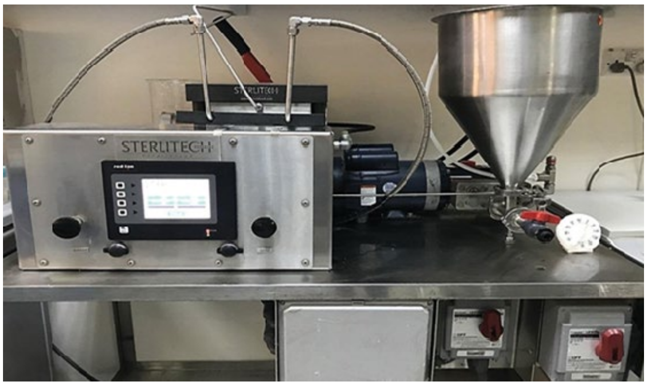

Fig. 1. Lab-scale membrane testing skid (Sterlitech Corporation, USA).

2.3. Hydrogen peroxide (H_2O_2) treatment method

Hydrogen peroxide (H_2O_2) experiment used the same system described above (Fig. 1) at a low pressure of 2 bar and room temperature. Contact time between the H_2O_2 and the feed solution in the feed tank was adjusted between 5 and 10 min, which is similar to previous work [14]. Samples were withdrawn from the reactor after completion of the reaction and analyzed for endotoxin. The test was implemented using several concentrations of H_2O_2 ranged from 0.5% to 2.5%.

2.4. Ozone (O_3) treatment method

In this experiment, the ozone generator setup consists of three primary blocks was used [15]. The ozone generator is a lab-scale device manufactured by Ozotech Inc., USA. Fig. 2 shows its main component: an air-drying unit, a high voltage transformer and a tube for the ozone generator. The ozonated air with an ozone concentration of about (4.7 g/m^3) was pumped to the feed solution with a flow rate of (15–18 L/min). It is assumed that this concentration will be consumed by the tested 3 L sample. For this flow rate, the contact time was adjusted from 0 to 25 min.

2.5. Hybrid treatment

These experiments were designed to identify the effect of the hybrid treatment process: (UF, O_3), (UF, H_2O_2), (O_3, H_2O_2), and (UF, O_3, and H_2O_2) at a feed pressure of 2 bar and at a different contact time between oxidant reagents and water to reduce endotoxin concentration.

In the triple hybrid experiment (UF, O_3, and H_2O_2), two different concentrations for H_2O_2 (i.e. 0.5% and 0.75%) were used with a contact time of 3 and 8 min respectively, after that, 2 min of O_3 treatment was applied.

2.6. Statistical analysis

Data were analyzed using Excel (Version 2010, Microsoft) with a *t*-test hypothesis of equal variance, double-tailed) for the comparison of two sets of results, and analysis of variance for the comparison of more than two sets of results. The marginal significant value (*P*-value) for both methods was set to ($P < 0.05$).

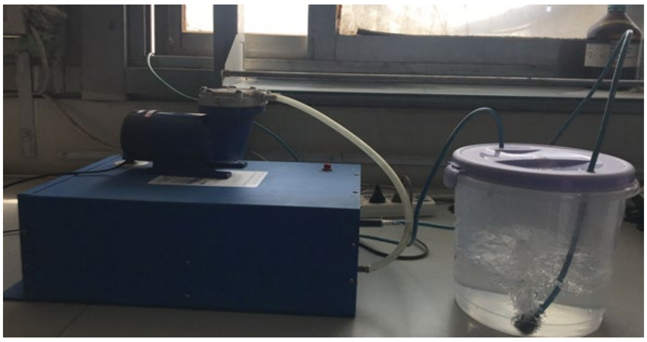

Fig. 2. Photograph of the lab-scale ozone treatment system.

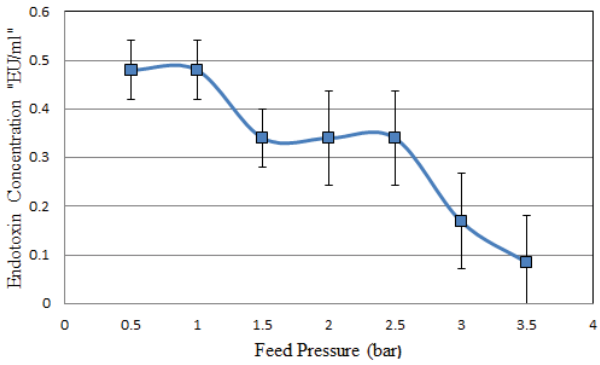

Fig. 3. Ultrafiltration treatment for feed water.

3. Results

3.1. UF treatment

The results of using UF treatment to remove endotoxin at several feed water pressures are shown in Fig. 3.

The best result of product water was obtained at 3 bar where the main endotoxin concentration was decreased to (0.17 ± 0.09 EU/ml), which is well below the permissible standard value of (0.25 EU/ml) [9].

3.2. Hydrogen peroxide treatment

Fig. 4 shows the results when using H_2O_2 as the treatment method. It has been found that endotoxin concentration decreases as hydrogen peroxide dosage increase until (1.5%) concentration. After that, there was no significant effect for hydrogen peroxide dosage or contact times on endotoxin concentration, Fig. 4.

In general, the endotoxin concentration declined from (0.48 ± 0.06 to 0.24 ± 0.06 EU/ml) when H_2O_2 was used with a concentration of more than 1.5% at contact time (5 and 10 min). The results came in compliance with the international standard endotoxin concentration value (0.25 EU/ml) ANSI/AAMI.

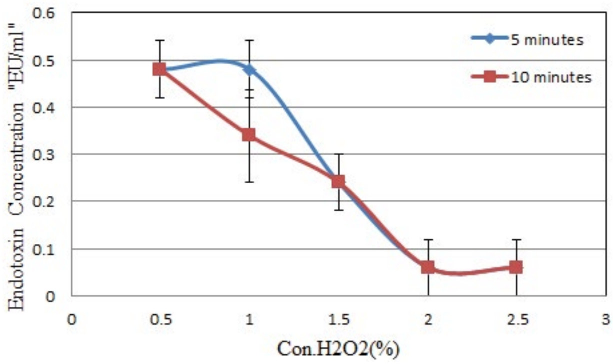

Fig. 4. Hydrogen peroxide treatment of the feedwater at several concentrations.

3.3. Ozone treatment

The results of using ozone to reduce endotoxin concentration at different contact times (2, 5, 8, 10, 15, 20, and 25 min) are shown in Fig. 5.

At the beginning of this experiment, endotoxin concentration was (0.48 ± 0.06 EU/ml), the best contact time to decrease endotoxin concentration to 0.06 ± 0.06 EU/ml was obtained at 20 min while the guideline endotoxin value was achieved at a time of 10 min.

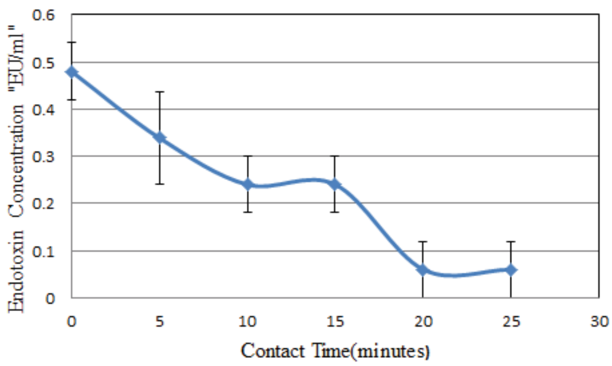

Fig. 5. Ozone treatment of feed water at several contact time.

3.4. Hybrid treatment

Double treatment using UF and ozone (O_3) as a hybrid treatment was tested and compared to those obtained when using ozone alone as can be seen in Fig. 6.

This treatment is more efficient to reduce endotoxin concentration compared to ozone treatment alone. The results showed that the guideline value of endotoxin concentration was achieved at a contact time of (8 min) (0.24 ± 0.06 EU/ml) when using (UF and O_3) in comparison to more than (10 min) when using ozone separately. Statistically, there was a significant difference between the treatment with (UF and O_3) and treatment with ozone alone at ($P < 0.05$), where P value = 4.35%.

The next implemented double treatment is using UF and hydrogen peroxide (H_2O_2) as a hybrid treatment. The test was conducted and the results were compared to those obtained when using H_2O_2 alone at dosages of 0%, 0.25%, 0.5%, 0.75%, and 1.0% at a contact time of 10 min, the comparison is shown in Fig. 7. Statistical analysis showed a significant difference between treatment with (UF and H_2O_2) and treatment with H_2O_2 alone at ($P < 0.05$), where P value = 3.94%.

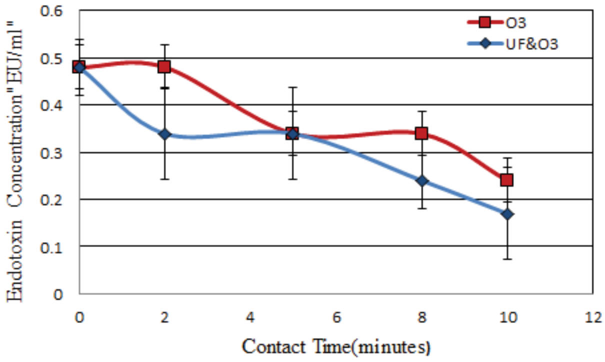

Fig. 6. Hybrid treatment of feed water using UF at 2 bar and ozone.

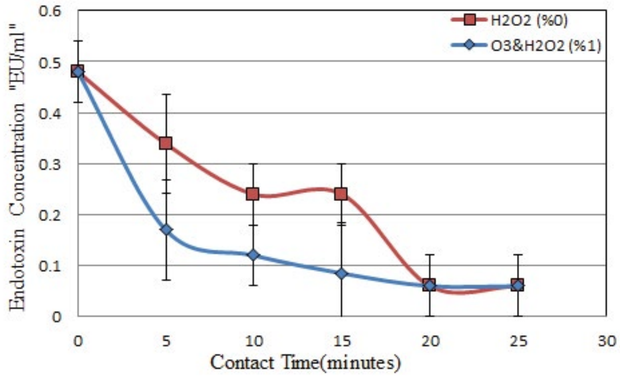

Fig. 8. Hybrid treatment of feed water O_3 and H_2O_2.

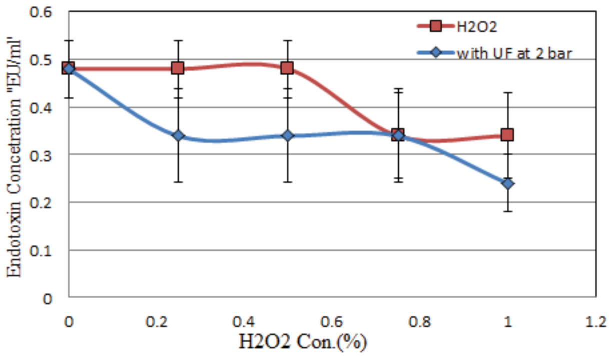

Fig. 7. Hybrid treatment of feed water using UF at 2 bar and H_2O_2.

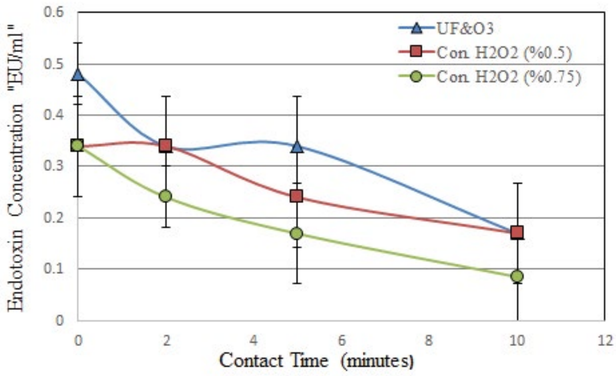

Fig. 9. Triple treatment for feed water using UF at 2 bar, H_2O_2, and O_3.

The figure shows that the best result of endotoxin concentration was (0.24 ± 0.06 EU/ml) when using hybrid treatment at H_2O_2 concentration of (1.0%), which merely achieved the acceptable endotoxin concentration limit.

The last double treatment was employed by using both oxidizing reagents (O_3 and H_2O_2) to reduce endotoxin concentration. The H_2O_2 concentration in this case was 1%, which is the same concentration obtained in the previous test. The results were compared with those obtained when using O_3 alone, at contact times of (0, 5, 10, 15, 20, and 25 min). The results of the comparison are shown in Fig. 8. Also, statistical analysis showed a significant difference between treatment with (O_3 and H_2O_2) and treatment with ozone alone at ($P < 0.05$), where P value = 3.99%.

The figure shows a significant reduction of endotoxin concentration when using this method in comparison to using O_3 alone. A concentration of (0.169 ± 0.09 EU/ml) was achieved at only 5 min contact time in comparison to 10 min when using ozone alone.

Fig. 9 illustrates the dialysis water quality after triple treatment of feed water solution, (i.e. UF, O_3, and H_2O_2) at two concentrations of H_2O_2 (0.5% and 0.75%) and at a contact time of 0–10 min. The figure also shows a comparison to those obtained when using the double treatment of (UF and O_3). Statistical analysis showed significant differences among triple treatment with both H_2O_2 concentrations and treatment with (UF and O_3) at ($P < 0.05$), where P values = 3.13% and 4.31% for H_2O_2 concentration of 0.5% and 0.75% respectively.

In general, the triple treatment is more efficient than dual treatment with (UF and O_3) with the exception of a few points when using 0.5% H_2O_2 concentration. The trend of endotoxin concentration in the product water was lower than that of the dual treatment at all times and for both H_2O_2 concentrations. Triple treatment, using 0.75% H_2O_2 concentration, reduced the concentration of endotoxin by 82.3% compared to the 0.5% H_2O_2 concentration which was 64.8%.

4. Discussion

The results obtained in the UF experiment shown in Fig. 3 came in agreement with other studies. According to a previous study [16], endotoxin concentration in dialysis water samples after UF was reduced from a mean value of 0.44 to 0.013 EU/ml. Another study implements a conventional water treatment to produce dialysis water with an endotoxin concentration of (0.125 EU/ml) and obtained an endotoxin concentration of zero EU/ml after UF [17]. In general, as many previous studies confirmed, using UF treatment to remove endotoxin from dialysis water samples succeed in lowering concentration to the international guideline values [18].

In another experiment, (Fig. 4) hydrogen peroxide activity depends on the type of the pollutant (where some types of bacteria may be able to resist H_2O_2 even at varying concentrations), and the water temperature (where the H_2O_2 decomposes into water and oxygen at elevated temperatures) [19]. For this reason, it is important to use a new method that can give the best results at a low dosage and a short contact time.

The results of the ozone experiment came in agreement with other studies [20] which found the efficiency of ozone in reducing endotoxin increased with increasing contact time, also another study shows that endotoxin reduction was approximately (10%) at 10 min [21]. This result agrees with Ren et al. [22], who showed that when increasing the contact time, ozone treatment reduces endotoxin concentration, in spite of the immediate action of ozone in increasing the release of the cell-bound endotoxin.

However, a large storage tank will be needed to reach such contact times. Storage tanks are a shortcoming in the treatment unit as they will always be a threat to water contamination and a source of biofilm bacteria. Therefore, shortening the contact time will be an advantage in the HD water treatment unit.

Comparing the hybrid treatment results with the single treatment (as shown in Fig. 6) revealed that using ozone in front of the membrane filters has another advantage because it would prevent permanent biofouling. However, the use of high ozone concentrations will require an activated carbon filter stage upstream of the membrane to completely reduce the residual ozone in order to avoid damaging the membrane materials [23].

Also, Fig. 7 in the double treatment showed that UF and H_2O_2 process is more effective than H_2O_2 alone to reduce the endotoxin concentration. In addition, in order to increase the lifetime of the membrane, it is highly recommended to reduce the membrane exposure to oxidizing agents to the minimum [24].

The addition of H_2O_2 in conjunction with ozone produces powerful hydroxyl radicals (Fig. 8) which are more effective than ozone or H_2O_2 alone [25]. A previous study showed that adding H_2O_2 during ozone treatment has enormously improved the removal of endotoxin by 80%, whereas approximately 10% of endotoxin was removed during ozone alone at 10 min [21].

The dosages of ozone and H_2O_2 will affect the operating costs and chemical consumption [15] and will have a significant effect on reducing both capital and operating costs [26].

In the triple treatment experiment, the target endotoxin concentration (0.25 EU/ml) was reached at only (2 min) of treatment, which is an advantage that can reflect a smaller size for contact tanks in the field.

The triple treatment process is well suited for water treatment and offers several advantages over conventional treatment processes. The most important advantage is that it is a reliable water treatment with a minimum of H_2O_2 concentration and a significant reduction in contact time for oxidizing agents. However, the triple treatment method is more expensive than other available methods.

5. Conclusions

All kinds of treatment processes applied in this study have improved dialysis water purity and reduced levels of endotoxin. Hybrid treatment using ultrafilter, ozone and hydrogen peroxide for disinfection was the most efficient treatment in reducing endotoxin concentration of dialysis water.

Accordingly, adopting a new design to modify the currently working dialysis water treatment units in Baghdad is vital to produce ultrapure water for HD application that is in compliance with the international dialysis water quality standards and save patients' life.

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