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การกำจัดอนุมูลอิสระจากกรดเปอร์อะซิติกในตัวกรองเลือดที่ใช้ซ้ำด้วยกรดแอสคอร์บิก

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บทคัดย่อ

กรดเปอร์อะซิติกนิยมนำมาใช้กำจัดจุลชีพในตัวกรองเลือดที่ใช้ซ้ำสำหรับผู้ป่วยที่เข้ารับการฟอกเลือด ซึ่งอาจมีการตกค้างของสารดังกล่าวในเยื่อกรองฟอกเลือดได้แม้จะผ่านการกำจัดออกตามมาตรฐาน ทำให้เกิดอนุมูลอิสระที่มีผลต่อพยาธิสภาพของโรค ผู้วิจัยจึงทำการทดสอบว่ามีการตกค้างของกรดเปอร์อะซิติกและไฮโดรเจนเปอร์ออกไซด์ที่ได้จากการสลายตัวจากกรดเปอร์อะซิติกในเยื่อกรองฟอกเลือดภายหลังจากการกำจัดด้วยวิธีมาตรฐานแล้วและหาปริมาณของกรดแอสคอร์บิกที่เหมาะสมต่อการกำจัดสารอนุมูลอิสระ โดยนำตัวกรองเลือดที่ผ่านการใช้ซ้ำด้วยจำนวนครั้งที่มากที่สุด (N=40) แบ่งออกเป็นกลุ่มควบคุม (N=15) และ กลุ่มทดลองที่ฉีดกรดแอสคอร์บิกความเข้มข้น 3.9 - 500 มิลลิกรัม (N=25) จำนวน 5 กลุ่มย่อย ตัวกรองเลือดที่ผ่านการกำจัดเชื้อโรคด้วยกรดเปอร์อะซิติกจะถูกชะล้างด้วยน้ำเกลือนอร์มัลโดยวิธี ultrafiltration ของเครื่องไตเทียม จากนั้นปิดการไหลของน้ำเกลือนอร์มัลและน้ำยาฟอกเลือด เมื่อทำการวัดปริมาณสารตกค้างโดยแผ่นทดสอบกรดเปอร์อะซิติกและไฮโดรเจนเปอร์ออกไซด์ที่เวลา 2 - 180 นาที ผลการทดลองพบว่า ในกลุ่มควบคุมมีกรดเปอร์อะซิติกและไฮโดรเจนเปอร์ออกไซด์ทั้งในส่วนของ blood และ dialysate compartments และมีการเพิ่มขึ้นของไฮโดรเจนเปอร์ออกไซด์ตามระยะเวลาอย่างมีนัยสำคัญ ในขณะที่กลุ่มทดลองที่ให้กรดแอสคอร์บิกเมื่อเพิ่มความเข้มข้นที่สูงขึ้นพบว่าสามารถกำจัดไฮโดรเจนเปอร์ออกไซด์ได้มากขึ้น ตามลำดับ โดยเฉพาะกรดแอสคอร์บิก 125 มิลลิกรัม สามารถกำจัดอนุมูลอิสระทั้งสองชนิดได้จนหมดทั้งในส่วนของ blood และ dialysate compartments อย่างมีนัยสำคัญที่ $P < 0.001$ ดังนั้นแนวปฏิบัติในการนำตัวกรองเลือดกลับมาใช้ซ้ำจึงมีข้อเสนอแนะ คือ การเติมกรดแอสคอร์บิก 125 มิลลิกรัมเข้าสู่ตัวกรองเลือดขณะทำการล้างตัวกรองเลือด ซึ่งสามารถช่วยเพิ่มคุณภาพการดูแลรักษาให้กับชีวิตของผู้ป่วยได้

คำสำคัญ: *กรดเปอร์อะซิติก, ตัวกรองเลือดที่ใช้ซ้ำ, อนุมูลอิสระ, กรดแอสคอร์บิก, เยื่อกรองฟอกเลือด*

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The Free Radical Elimination From Peracetic Acid in Reused Dialyzer By Ascorbic Acid

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ABSTRACT

Peracetic acid sterilant for dialyzer reprocessing is a practical approach in patient receiving Hemodialysis. However, the substances may persist in the dialysis membrane despite the reused dialyzer undergoing a standard rinse procedure. The free radical-related diseases may occur for patients. Our objectives were to determine the in vitro residual levels of peracetic acid and their by-products hydrogen peroxide liberated from dialysis membranes after reprocessing process and explore the optimal dose of ascorbic acid in role of free-radical degradation. A dialyzer reuses (N=40) under the criteria in a maximum number of reuses were divided in control group (N=15) and five subgroups of sample with ascorbic acid injection in ranging from 3.9 - 500 mg (N=25). The complete dialyzer reprocessing with peracetic acid was rinsed by normal saline solution coupled with ultrafiltration on the hemodialysis machine to remove all traces of disinfectant. After termination of saline and dialysis fluid flows, amount of disinfectant was quantified by inspecting with peracetic acid and hydrogen peroxide test strip at selected time points (2 - 180 min). The control group found amounts of peracetic acid and hydrogen peroxide both in blood and dialysate compartments, which had significantly increased hydrogen peroxide values in a time dependent manner. In contrast, increased levels of ascorbic acid in sample group produced a concentration-dependent decrease in hydrogen peroxide production. Specifically, ascorbic acid 125 mg dramatically destroyed both residues until the residuals residing in both compartments has been cleared ($P < 0.001$). The clinical practice guideline of reused dialyzer by 125 mg ascorbic acid upon dialyzer rinsing procedure may give rise to improve the quality of medical expertise for saving patient's life.

Key words: *Peracetic acid, Dialyzer Reuse, Free Radical, Ascorbic Acid, Dialyzer Membrane*

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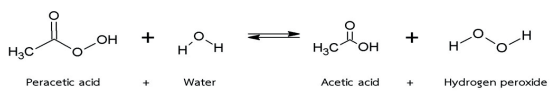
Background

The reusable dialyzer has been widely utilized for the patients undergoing hemodialysis (HD). The dialyzer reused is necessary for sustainable advantage by reducing non-biodegradable medical waste and first use syndrome from new dialyzer[1]. However, the dialyzer reprocessing should comply with regulatory standard medical devices guidelines of The American Association for the Advancement of Medical Instrumentation (AAMI) 2. Peracetic acid (PAA), a strong sterilizing chemical agent is currently recommended to facilitate the dialyzer reprocessing for successful elimination broad spectrum of pathogenic microorganisms. It is properly manufactured in form of peracetic acid mixture (PAM) solution, in which 4% PAA, 21% hydrogen hydroxide (H_2O_2), and 75% inert ingredients. In order to perform active disinfecting agent, PAM was dissolved in reverse osmosis (RO) water upon an amount of 0.16% PAA for incubated time limit at 11 hours. The capacity of an agent can spontaneously decomposes into acetic acid and H_2O_2 formation under equilibrium solution.[3, 4.]



Generation of H_2O_2 free radicals can also certainly inactivated microorganisms by harmful effect of oxygen toxicity. They are a highly unstable atoms or molecules with unpaired electrons in its outer valence orbital. These unstable molecules can steal an electron from neighboring molecules and occur new free radicals that affects with most macromolecules of the cell. The H_2O_2 will disassociate into dangerous hydroxyl ($OH^{\bullet}$) radical upon transition metals ion catalysis. It has a long half-life and high diffusion capacity similar to water so it can diffuse freely across plasma membrane which resulted in the cell damage and eventually lead to the human pathology.[5, 6] As described above, decontaminating dialyzers have been accomplished by PAA solutions with H_2O_2 efficacy. Even if the dialyzer reprocessing was rinsed with normal saline solution (NSS), the substances that are PAA and their metabolite H_2O_2 residues can be found in dialyzer membrane. In this preliminary study, after ultrafiltration with 500 mL of 0.9 % NSS passed from the blood compartment into dialysate compartment during the recirculation process, if by pass procedure generated (dialysis fluid closing), retained PAA and H_2O_2 radicals could be detected. Therefore, the patients received hemodialysis three times a week can be obtained these radicals deposited in dialyzer reuse. These can cause oxidative stress-related diseases. However, there is no evidence base document for reused dialyzer safety after reprocessing with PAA in term of residual concentrations distribution in the dialyzer.

Ascorbic acid (AA) is an excellent antioxidant to protect oxidative damage from reactive free radical and nonradical reactive species.[7-9] Humans must receive AA from the diet such as in many fruits and vegetables, or synthetic AA. The free radical scavenging mechanism of AA is involved in a strong potent reducing agent caused by the addition of an electron to oxyradicals, and then still much more stable in form of ascorbyl free radical with a long half-life.[9-10] The AA supplementation may enhance the biological functions in human such as preventing damage of DNA and protect tissue damage.[9] The most common AA deficiency noticed in HD patients which further contribute to oxidative stress, atherosclerosis, and anemia. Especially, the severe anemia is a critical complication under a reduced kidney erythropoietin synthesis of patients with chronic kidney disease.[11] Thus, the clinical administration of

AA for the patients markedly improves dysfunction of the HD treatment in order to eliminate excessive free radicals coupled with protective red blood cells. It is also less expensive and safe medication for patients.[12] Administration of AA at doses of 500 mg with each HD session (for a total of 1500 mg /week) is preserved for patients on thrice a week dialysis that can cause an increase in RBCs though increased the hormone erythropoietin release in response to anemia. [13] Although AA has a potential treatment on kidney-related anemia, long-term intakes of it could form side effect of secondary oxalosis in blood vessel, bone, and all organs that can elucidate pathogenesis.[14] Patient should be considered to avoid the possibility of excessive AA doses on long-term usage. Normally, dialyzers after PAA based sterilant were completely assessed for the reduction of residual PAA efficacy. However, guideline on a certain amount of AA in role of PAA-H_2O_2 degradation after dialyzer reprocessing of previous research has not been fully reported. In this study, we proposed a new practice of exploration for increase the safety of dialyzer reuse in achieving residual PAA clearance after reprocessing before patients started HD treatment.

Objectives

The first objective is to define the potency levels of residual PAA and its degradation product in form of H_2O_2 on dialysis membranes. The second objective is to recommend adequate levels of AA that would destroy the disinfectant residual in dialyzer reuse.

Materials and methods

1. Study Design and Participants

The dialyzer reuses were provided by the Hemodialysis Center, Nopparat Rajathani Hospital and Samutprakarn Hospital, Thailand. These dialyzers were allowed to study under the eligibility criteria in either a maximum number of reuses followed by personnel of the dialysis unit or an unreachable measurements the 80 % of total cell volumes according to the standards set by Thai Nephrology Nurse Society (TNNS). Each dialyzer was recorded in the number of reuses, types of dialyzer membranes, and fiber surface areas. The experimental study was set up along hemodialysis machine (Fresenius 4008H, Germany). A total of 40 dialyzers were randomized trials for 15 dialyzers of control group and 25 dialyzers of sample group. The sample group of dialyzer with ascorbic acid (Vesco, Thailand) was equally classified as 5 subgroups based on the radical scavenging ability as: (I) 3.9 mg; (II) 7.81 mg; (III) 31.25 mg; (IV) 125 mg; and (V) 500 mg, respectively.

2. Data Collection

A step in vitro procedure was developed in control and sample group following this protocol:
1. The control group was dedicated to define the residual disinfectant on dialyzer follow the steps below.
1.1) a rinsing procedure on dialyzer reuse was regarded as the standard of TNNS with the instruction in steps a - d^2. a) 0.16% PAA solution (Meditop, Thailand) was removed from dialysate compartment of the dialyzer and then rinsed with RO water. Both sides of dialysate compartment were closed with the sterilized caps immediately. b) The dialyzer was connected to the arterial site of the blood line followed by infused 1,000 mL of 0.9 % NSS into the inlet line of the dialysis system for eliminating PAA solution out of the blood compartment. c) One venous side of the blood lines was connected directly to the dialyzers, whereas on another side was joined into arterial blood line for recirculating saline in dialyzer with blood pump flow rates of 400 mL/min. The dialysis fluid ports from

HD machine were connected to the dialysate compartment of dialyzer. The exact amount of 500 ml flowing saline from blood to dialysate compartment was adjusted with ultrafiltration rate of 3,000 mL/h for 10 mins. After rinsing, the saline flow in dialyzer circuit was adjusted by reducing the blood pump rate to 50 mL/min and closed by clamping at the intravenous fluid line of the 0.9 % NSS. d) The dialysate fluid ports were removed and further closed both sides of dialysate compartment with sterilized caps. 1.2) Amount of PAA and H_2O_2 residues was quantified by inspecting 2 ml of saline from the venous site blood line (Fig. 1 B) with peracetic acid and hydrogen peroxide test strip (Johnson, UK) at selected time points of 2, 30, 60, 120, and 180 min, respectively. The solution of dialysate compartment also provided to detect both residues at the end point time of 180 min. 2. The five subgroups of sample were prepared with doses of AA (3.9-500 mg). 2.1) the protocol was performed by following the step 1.1 (a-d). 2.2) In group I to V was administrated ascorbic acid into the injected site of arterial blood line (Fig.1 A). 2.3) The concentrated PAA and H2O2 were then detected by the test strip following step 1.2.

3. Ethical Considerations

Each dialyzer was prescribed under the eligibility criteria in a maximum number of reuses of the dialysis units. Thus, this experiment did not involve in in vivo study.

4. Statistical Analysis

All values were presented as mean ± standard error of mean (SEM). Statistical analysis of the PAA and H_2O_2 concentrations for within-group comparison at different times was achieved by one-way ANOVA followed by Duncan's multiple range test. Data for the PAA and H_2O_2 concentrations upon with or -without AA when applying at the same exposure time were analyzed by Mann-Whitney U test. The statistical significance was considered on the p-values less than 0.05.

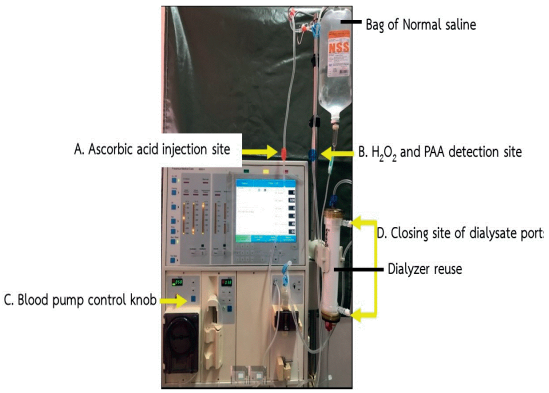


Figure 1 A module of hemodialysis machine.

Figure 1 A module of hemodialysis machine for this experimental study operating in the dialyzer reprocessing on using sterile technique. Dialyzer was placed on the machine in the vertical position, in this setting, the arterial site end down. (A) Ascorbic acid injection site (red stripe); (B) H_2O_2 and PAA detection site for blood compartment (blue stripe); (C) A circulating blood pump control knob was pressed down from 400 to 50 mL/min for slowing NSS flow; (D) A closed dialysate ports were formed on both sides of the dialyzer and then collected an aqueous dialysis solution in a container to determine the residual PAA and H_2O_2 as described in the method section. Each arrow indicates the positions. (red stripe); (B) H_2O_2 and PAA detection site for blood compartment (blue stripe); (C) A circulating blood pump control knob was pressed down from 400 to 50 mL/min for slowing NSS flow; (D) A closed dialysate ports were formed on both sides of the dialyzer and then collected an aqueous dialysis solution in a container to determine the residual PAA and H_2O_2 as described in the method section. Each arrow indicates the positions.

Results

The dialyzer reuses characteristics are listed in the Table 1. We randomized the distribution of dialyzers in control and sample groups. Both number of reuses and micro-capillary tube surface areas showed no significance difference between control and sample groups. It appeared that the dialyzer-optimized experimental condition was suitable for define the alternative ascorbic acid strategy in free radical scavenging capacity of this research.

Table 1 The characteristics of reused dialyzer were classified in control and five series of sample group.

Group[a]	Ascorbic acid Amount (mg)	Membrane Type			Surface Area (m2)	Reused Number
		PS	PEPA	CA		
Control group	0	2	4	9	2.11 ± 0.01	9.07 ± 1.75
Sample group I	3.90	-	1	4	2.10 ± 0.00	10.40 ± 3.90
Sample group II	7.81	-	2	3	2.10 ± 0.00	11.80 ± 2.80
Sample group III	31.25	2	3	-	2.13 ± 0.02	7.70 ± 2.90
Sample group IV	125	-	2	3	2.10 ± 0.00	12.20 ± 2.70
Sample group V	500	1	4	-	2.11 ± 0.02	7.70 ± 2.70

Abbreviations: PS, Polysulfone; PEPA, Polyester polymer alloy; CA, Cellulose triacetate.

[a] Data are presented as mean ± SEM

In figure 2 showed the PAA and H_2O_2 contents after dialyzer reprocessing in control group during the five time-points: 2, 30, 60, 120, and 180 min, respectively, in blood compartment together within the dialysate compartment at the time point of 180 min. The started time period at 2 min was enough duration of the flow rate of 50 mL/min for the minimum PAA and H2O2 releasing out of the dialysis membrane. Residual PAA at 2 min was 1.43 ± 0.63 ppm and significantly decreased until entirely clear at times of 30 and 60 min ($P < 0.05$) (Fig. 2). While H_2O_2 residues in blood compartment provided a time-dependent increased toxic substances levels from the lowest level of 1.57 ± 0.25 ppm at 2 min to the highest level of 8.79 ± 0.60 ppm at time 180 min (Fig. 2). These results showed that concentration of H_2O_2 after 30 min was significantly different when compared with the initial time 2 min, $P < 0.01$ and continued to rise at 60, 120, and 180 min compared to 2 min, $P < 0.001$ (Fig. 2). A significant increase of H_2O_2 concentration inside dialysate compartment during 180 min was represented as 6.50 ± 0.73 ppm compared to 2 min ($P < 0.001$) (Fig. 2). The lack of PAA production indicated that the H_2O_2 by-product has been occurred from a spontaneous decomposition of PAA within 30 min.

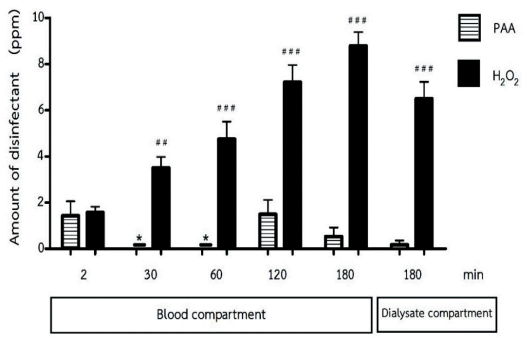


Figure 2 Amount of disinfectant in control group after dialyzer reprocessing in a closed dialysate ports for a given their concentrations in parts per million (ppm).

Figure 2 Amount of disinfectant in control group after dialyzer reprocessing in a closed dialysate ports for a given their concentrations in parts per million (ppm). (A) PAA concentration (white bar); (B) H_2O_2 concentration (black bar). Values were represented as mean ± SEM for 15 dialyzers. * *P < 0.05* the PAA concentration at different time points compared with 2 min; ## P < 0.01; ### *P < 0.001* the H_2O_2 concentration at different time points compared with 2 min.

The effect of AA administration from all sample groups successfully destroys PAA disinfectant in dialyzer until the residual eventually disappeared, which was observed after the dialyzer samples performed at 30, 60, 120, and 180 min, respectively (data not shown). In contrast, the levels of H2O2 were appeared in control and sample groups at concentration 3.90 and 7.81 mg AA (group I and II) at all time points for blood compartment and at 180 min for dialysate compartment. The sample group with 31.25 mg AA (group III) demonstrated amount of H2O2 residues appeared only at the end point time of 180 min both in the blood and dialysate compartments, while the efficient concentration of AA at doses up to 125 and 500 mg (group IV and V) entirely reduced residual H_2O_2 both in the blood and dialysate compartments of dialyzer during periods of all times (Table 2).

Table 2 Concentrations of H2O2 both in the blood and dialysate compartments of dialyzer at different time points.

The experiment was performed for at least five sampling of dialyzer with an independent experiment. [a] The values were represented as mean ± SEM. * P < 0.05; ** *P < 0.01*; *** *P < 0.001* the H_2O_2 concentration when compared to control group (without ascorbic acid) at the same time; # *P < 0.05*; ## *P < 0.01*; ### *P < 0.001*. The H_2O_2 concentration for within-group comparison at different times compared to initial time 2 min.

In order to define an adequate level of AA, the comparison of the residual H_2O_2 levels passing from dialysis membrane through the blood compartment in control and sample groups were shown in Fig. 3. A time-dependent effect of H_2O_2 production in control group can rapidly occurred which was represented by the dashed line from 1.57 ± 0.25 ppm (for 2 min) to 8.79 ± 0.60 ppm (for 180 min) (Fig. 3). However, the sample group receiving AA 3.90 mg had significantly

Table 1 The characteristics of reused dialyzer were classified in control and five series of sample group.

Group[a]	AA (mg)	BPR (mL/min)	H2O2 Concentration (ppm)					
			Blood Compartment					Dialysa Compartment
			2 min	30 min	60 min	120 min	180 min	180 min
Control	0	50	1.57 ± 0.25	3.50 ± 0.48	4.75 ± 0.75##	7.21 ± 0.75###	8.79 ± 0.60###	6.50 ± 0.73###
Sample I	3.90	50	1.40 ± 0.20	2.00 ± 0.30*	3.40 ± 0.50	4.50 ± 0.90*, ##	4.60±0.20***, ##	6.00 ± 1.00###
Sample II	7.81	50	1.40 ± 0.40	0.04±0.20***,##	0.80 ± 0.60***	1.0 ± 0.30***	2.10 ± 0.60***	1.00 ± 0.30***
Sample III	31.25	50	0.90 ± 0.50	NF	NF	NF	0.10 ± 0.10***	0.10 ± 0.10***
Sample IV	125	50	2.00 ± 0.01	NF	NF	NF	NF	NF
Sample V	500	50	1.60 ± 0.50	NF	NF	NF	NF	NF
Recommended	125	400	NF	NF	NF	NF	NF	NF

Abbreviations: AA (Ascorbic acid); BPR (Blood pump rate); NF, Not Found.

lower H_2O^2 residues than the control group with $P < 0.05$ at 30 and 120 min, and $P < 0.001$ at 180 min, respectively (Fig. 3). Similarly, the H_2O_2 residues were significantly reduced by 7.81 mg AA at 30, 60, 120, and 180 min compared to the control group ($P < 0.001$) (Fig. 3).

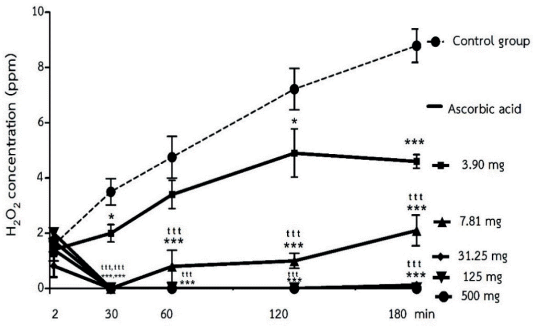


Figure 3 H_2O_2 concentration in ppm suspended in blood compartment at various time points in the presence or absence of ascorbic acid.

We did not find any H_2O_2 products after injected AA up to 31.25 mg along with three time points at 30, 60, and 120 min, thereby accumulation of H2O2 was apparent by the end of examining free radical scavenging activity at 180 min ($P < 0.001$) (Fig. 3). Particles of H_2O_2 entirely disappeared after exposure high doses of AA at both 125 and 500 mg at all durations in comparison with control group ($P < 0.001$) (Fig. 3). These finding indicated that the decreasing amount of oxidation agent H_2O_2 had occurred by AA in a concentration-dependent manner. The present investigation also explored the antioxidant activity of AA in the sample group (group I to V) by compared with low dose as 3.90 mg (group I). We founded that AA at doses of 7.81 to 500 mg were able to be suppress the H_2O_2 deposited on reused dialysis membranes with strong significant inhibition all their periods at the same time, compared to 3.90 mg AA ($P < 0.001$) (Fig. 3).

Figure 3 H_2O_2 concentration in ppm suspended in blood compartment at various time points in the presence or absence of ascorbic acid. Ascorbic acid levels ranged from 3.90-500 mg can be diminished H_2O_2 residues by dose-dependent manner that were not detected any residues in sample groups at doses of 31.25-500 mg ascorbic acid within 30 min after this administration procedure. Black dashed line with circles represented the control group. Solid line represented the sample group as 3.90 mg (squares), 7.81 mg (triangles), 31.25 mg (diamonds), 125 mg (inverted triangles), and 500 mg (circles). The data are expressed as mean ± SEM. * $P < 0.05$; *** $P < 0.001$ versus control group at the same time; ttt $P < 0.001$ versus 3.90 mg ascorbic acid at the same time.

Finally, we accompanied an evidence-based in the recommendation for 125 mg AA because the dosage utilized in this trial has been achieved (Table 2). It was demonstrated the effect of the support dose selection at which the recirculation session with NSS pumping rate of 400 mL/min. The dialyzer-access recirculation in flow rate of 400 mL/min allowed AA rapidly incorporated into the circulation for scavenging undesirable toxic species within 2 min throughout the exposure period. Subsequently, all the residues of H_2O_2 did not appear to interfere with reused dialyzer.

Discussion

The disinfectant residual measurement after dialyzer reprocessing is an important step in standardized testing of HD nursing care practice guideline due to the patients will obtain toxic residues releasing from the membrane pore structure of reused dialyzer. In this study, we proposed a novel guideline for HD unit with a special feature. The PAA sterilant disintegration and achieving the affinity of AA scavenger undergo

reprocessing had been evaluated. The limitation of this study is all dialyzers used during the procedure have three different types of membrane composition (as PS, PEPA, and CA) and a number of usages per dialyzer in each subgroup were unequal sample sizes. Thus, we verified variance between the groups in term of number of reuses and micro-capillary tube surface areas. It can unaffected in the baseline characteristics of dialyzers in each group because there were no significant differences. In addition, these membrane types have been popularly utilized by HD patients in Thailand, thus, these can sufficiently be the representative of HD membranes. For an unequal sample size, each dialyzer was difficult to obtained due to a number of dialyzers were highly reused as 15 – 20 times depending on HD unit policy. Then, the control group was firstly performed following the standard dialyzer reprocessing guideline to check baseline condition. The results showed that PAA and H_2O_2 residues in control group did not present in both blood and dialysate compartments when the dialysis fluid was continuously flowed through dialysate compartment. However, there were expressed both H_2O_2 and free PAA formulations when the flow of dialysate compartment was terminated by closing the dialysate ports. Especially, H_2O_2 levels had elevated depend on the time; thus, PAA and H_2O_2 accumulation must potentially be within the membrane even though the dialyzer with sterilant has been washed by NSS. However, the levels of PAA were less than H_2O_2 in blood compartment due to the PAA dissolved in water can be rapidly degraded into H_2O_2 formation by the spontaneous decomposition, transition metal- catalyzed decomposition and hydrolysis.[3,15-17] The H_2O_2 has the oxidation potential lower than the PAA at 1.78 versus 1.96 eV.[17] Additionally, the H_2O_2 levels were relatively low it should be emphasized even though when the patients receiving long-term of replacement therapy, the result of free radical-related disease including cancer can be induced.[11]

Next, the AA injection via the arterial blood line under the same procedure as the control group was applied to assess the PAA and H_2O_2 elimination in these studies. PAA and H_2O_2 during closed dialysate compartment ports were found for all groups at 2 min indicating that the 2 min of the blood pump rate (50 mL/min) is an enough duration for the minimum release of PAA and H_2O_2 from dialysis membrane into the blood compartment. In particular to the sample groups, this 2 min is the suitable duration for the measurement of both toxic residues. Because the AA can neither fully distribute nor reach to the detection site. For all sample groups, the AA can eliminate the propagation of H_2O_2 free radicals within dialyzer both in blood and dialysate compartments at these time points (30, 60, 120, and 180 min). Interestingly, total H_2O_2 composition in dialyzers were gradually decreased until did not detect a residual inclusion affected by AA treatment in a dosage dependent manner. The overall data demonstrated that 125 mg of AA was found to be the optimum dosage for get rid of these oxidants in dialyzers (Fig. 4). If HD patients have been continuously received this rinsing procedure in thrice-weekly, the usual doses up to 375 mg/week will be safe. Because AA safety recommendation for humans is considered range as 420-700 mg/week.[18] Actually, AA catabolism gives diketogulonic acid and then it decays into oxalic acid, L – threonic acid, and xylose for further excretion via the urine. For instance, oxalic acid typically occurs a toxicological effect in patient underwent HD because it cannot completely eliminate urinary oxalate by the ailing kidneys.[19, 20] Since patients have chronic renal failure with hypercalcemia

from either receiving phosphate binder drug or parathyroid hormone and vitamin D abnormalities, that leads to calcium oxalate formation deposited in organs and may give rise to myocardial infarction, vascular access failure, and muscle weakness.[21, 22] A current dialyzer clearance approach developed by AA is a promising method for ensuring the efficacy of dialyzer reuse. Because some of AA on certain reprocessing was flushed out with NSS by the patient's blood replacement during the initiation of HD procedure and the remaining of AA which is a water-soluble small molecule, subsequently, it can be easily eliminated by diffusion process.[23] These properties will play a beneficial role in the degradation of excessive AA in human body during dialysis therapy. The AA injection during dialyzer reprocessing must be increased the quality of HD patients through the improvement of clinical practice by nurse practitioner at dialysis unit.

Conclusion

We suggested a novel dialyzer reprocessing by the AA 125 mg injection during pre-hemodialysis session. AA potentially eliminates toxic oxidants; thus, it may optimize dialyzer reprocessing procedure for improving quality of life in hemodialysis patients in the future.

Recommendation

The guideline recommendations by AA injection 125 mg during dialyzer reprocessing can reduced the tiny amount of PAA residual disinfectant even the toxic substances still exist inside of dialyzer membrane. It is a new alternative way to ensure the safety of dialyzer reused before providing an equipment to the dialysis patients.

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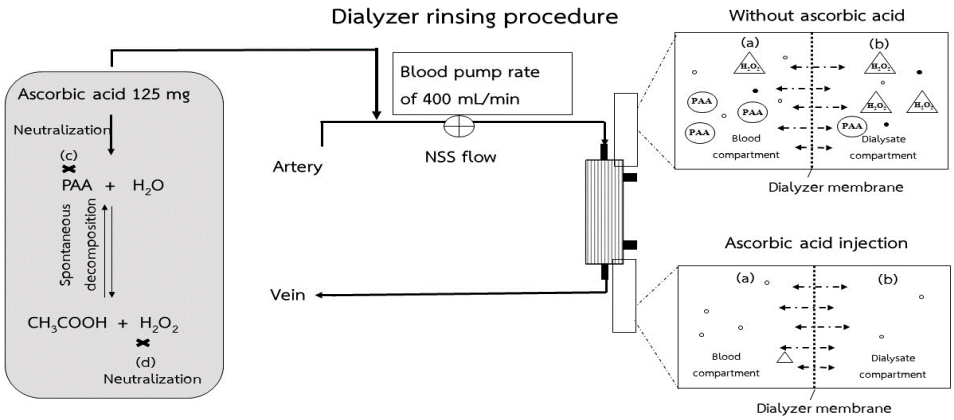

Figure 4 Illustrating the alternative dialyzer rinsing procedure through 125 mg ascorbic acid injection undergoing dialyzer reprocessing. a) Blood compartment, b) Dialysate compartment, c) Neutralization to PAA, and d) Neutralization to H2O2

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