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研 究 論 文
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In Vitro Evaluation of Reused Hollow Fiber Dialyzers

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= Abstract =

Air pressure decay(APD) rate and ultrafiltration rate(UFR) tests were performed on new and saline rinsed dialyzers as well as those reused in patients several times. C-DAK 4000(Cordis Dow) and CF 15-11(Baxter Travenol) reused dialyzers obtained from the dialysis clinic were used in the present study. The new dialyzers exhibited a relatively flat APD, whereas saline rinsed and reused dialyzers showed considerable amount of decay. C-DAK dialyzers had a larger APD(11.70 ± 1.32mmHg/min) compared to CF dialyzers(4.32 ± 0.55mmHg/min)($p < 0.05$). However, there was no observable difference in the UFR between the two dialyzers. Neither APD nor UFR showed any significant increase with an increasing number of reuses for up to more than 20reuses. A substantial number of failures observed in APD(larger than 20mmHg/min)on the reused dialyzers(2 out of 40 CF and 5 out 26 C-DAK) were attributed to the possible damage on the fibers. The CF 15-11 HFDs which failed APD test did not show changes in the UFR compared to normal dialyzers indicating that APD is a more sensitive test than UFR test to evaluate the integrity of the fibers.

I. INTRODUCTION

Treatment of patients with chronic renal failure with hemodialysis is a common practice today and hollow fiber dializers(HFD) are currently popular. Even though the HFDs are disposable and generally meant for one time use, the reuse of dialyzers presents a significant economic advantage to patients and is practiced in a number of dialysis clinics. More recently, 50% of hospital based and 80-90% of independent dialysis centers reuse the dialyzers on their patients[1]. Popli et al[2]. reported that severe hypersensitivity reactions occurring in new dialyzers were not associated with reused dialyzers and suggested that the incidence and severity of reactions to cuprophan capllary dialyzers may be lessened if care is taken to thoroughly rinse the dialyzers prior to use. However, the safety and the efficacy of the practice of reuse has prompted a number of studies to compare the performance characteristics of the new and reused HFDs. Luehmann et al [3] dscribed the details of reprocessing and compared the performance of the reused dialyzers both *in vivo* and *in vitro*. They concluded that the HFD performance has been retained and no adverse patient reaction occurred due to reuse. Kant et al.[4] compared the performance of C-DAK(Cordis Dow) dialyzers after reuse and concluded that multiple use of these dialyzers over a 15month period is safe, efficacious, and is not associated with an increased rate of infection, of morbidity or mortality. Favero et al.[5] reported that the risk of hepatitis in reuse

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centers was not higher than in single use centers.

On the other hand, reuse of HFDs also involves several potential hazards which include deterioration of the integrity of the membrane, infusion of blood proteins altered by the cleaning and disinfecting process into the blood stream, infusion of residuals of disinfecting agent used in the reprocessing, inadequate disinfection, and significant increase in ultrafiltration due to membrane deterioration[1]. The transportation for reprocessing dialyzers is a potential problem, since it might result in the failure of the dialyzer.

The aims of the present study was to assist the federal government in studying the effects of chemical sterilants on hemodialyzers under actual conditions by : determining the protocols for reprocessing and testing hemodilyzers in each participating dialysis facility ; to determine the maximum number of reprocessings of a single hemodialyzer within each participating center. This work was undertaken to analyze the effect of reuse and reprocessing on the integrity of the hollow fiber membrane. Air pressure decay(APD) and ultrafiltration rate(UFR) tests were performed on HFDs after various number of reuses in an *in vitro* experimental set up.

Ⅱ. METHODS

APD and UFR tests were performed on four types of dialyzers including CF 15-11, CF 12-11, CF 23-08 and C-DAK 4000HFDs, as shown in Table 1. The Cf capillary dialyzers are made of cuprophane fibers contained within a plastic shell and C-DAK 4000 dialyzers are made of cellulose acetate fibers. The new ones were provided to us in the original packing. NSR refers to those dialyzers which were rinsed with saline but not reprocessed or used in a patient. 0-reuse dialyzers were those reprocessed for use in a patient but dialysis was not performed. The other dialyzers were used a number of times as noted and reprocessed before being sent to us.

The reprocessing of the dialyzers in this center included rinsing with the RO/DI(reverse osmosis/deionized) water solution, reverse ultrafiltration cycling of bleach through the membrane and performance testing which included pressure leak test, UFR test and fiber bundle volume test. Finally, the dialyzers are disinfected and filled with formaldehyde. It should be noted that some of the dialyzers were

Table 1 Number of hemodialyzers for the present study

	CF capillary 15-11	C-DAK 4000	CF capillary 12-11	CF capillary 23-08
New	5	3		2
NSR	3	6		
0-reuse	5	4		1
1-reuse	6	5		
2-reuse	2	2	1	
3-reuse	1	2		
4-reuse	2	1	2	
6-reuse	2	2	1	
8-reuse	1	1	2	
10 to 20-reuse	7			
over 20-reuse	6			1
Subtotal	40	26	6	4

reprocessed several times between use. The reprocessed dialyzers provided to us passed the tests performed in the clinical center before being transported with care to our laboratory for testing. The time between reprocessing, transport from the medical center to our laboratory and testing did not exceed four days.

Once the dialyzers arrived in our laboratory, they were visually inspected and marked with our identification before test. The formaldehyde solution was removed from the dialyzer and the dialyzer was rinsed thoroughly(for about 30min) with RO/DI water. Subsequently, air at low pressure was forced through the dialyzer to remove the water before ADP tests were performed. A brief description of the test procedures are given below :

1. Air pressure decay(APD) test

Fig. 1 shows the schematic of APD test. The blood inlet of the dialyzer is connected to the pressure regulator through a 1/4 inch Tygon tubing, and a pressure gauge is connected to the other blood port of the dialyzer. The inlet and outlet ports of the dialysate are open to the atmosphere. The test was performed in the following steps :

a) The air source is opened and the dialyzer blood compartment is pressurized to 300mmHg, and the compartment pressure is monitored by the pressure gauge distal to the dialyzer. The air source is disconnected and the dialyzer left pressurized for 30 seconds in order to equilibrate the pressure in the blood compartment.

b) The pressure in the blood compartment is released.

c) The blood compartment is repressurized to 300mmHg.

d) The pressure decay rate in the blood compartment is measured for 10minutes at on minute intervals.

e) The procedure is repeated three times to assess the reliability of the data.

2. Ultrafiltration rate(UFR) determination test

After finishing APD test, UFR test was carried out on the same dialyzer. A schematic of the experimental set up for the ultrafiltration test is shown in Fig. 2 A rectangular water reservoir with two aquarium heaters was used for maintaining the constant temperature of 37℃. A cylindrical RO/DI water tank was placed inside the water reservoir. The outlet of this tank was connected to the blood inlet port of the dialyzer. The dialysate inlet port and the blood outlet port were capped by pinch clamps during this test.

A 3/4 inch diameter Tygon tubing was connected form the other dialysate port to the graduated cylinder outside the water reservoir as shown in the Fig. 2 Apressure gauge is connected to the blood inlet port of the dialyzer using a T-junction as illustrated so as to monitor the pressure of RO/DI water at the inlet. Any trapped air is removed from the dialyzer

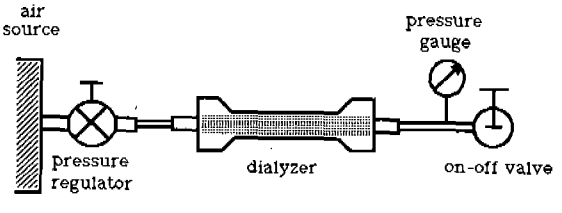

Fig. 1 The schematic of air pressure decay(APD) test

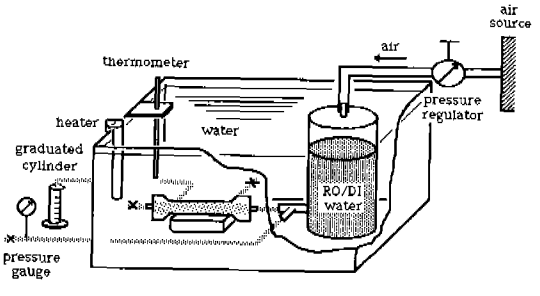

Fig. 2 The schematic of ultrafilatration rate(UFR) determination test

at the beginning of the experiment when the RO/DI water is filled in the blood compartment.

UFR test was performed in the following steps :

a) The air source was slowly opened and a pressure of 100mmHg/was applied in the RO/DI water tank for one minute to remove all air from the system.

b) The dialyzer compartment was pressurized by 100mmHg for 5 more minutes to stabilize the pressure in the dialyzer, and then the ultrafiltrate from the dialysate outlet port was collected in a graduated cylinder for one minute. The experiment was repeated two more times.

c) The experiment was repeated by applying pressures of 200 and 300mmHg in the RO/DI water tank.

A linear regression analysis was performed for the statistical analysis of both experiments.

Ⅲ. RESULTS AND DISCUSSION

Fig. 3 and 4 show the air pressure measured in APD tests. It can be observed that new dialyzers in general have a relatively flat pressure decay curve regardless of the type of the dialyzer, while reused or saline rinsed dialyzers exhibit a decay in pressure with time which is observed to be independent of

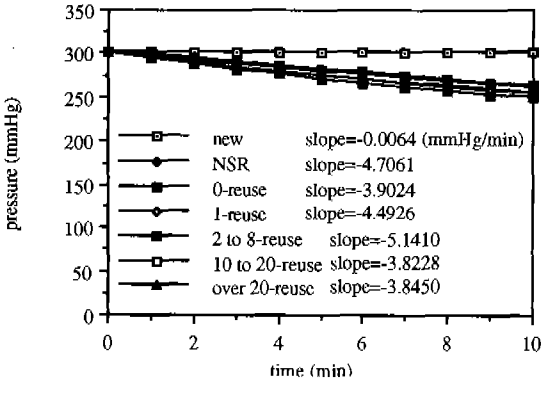

Fig. 3 Air pressure decay for CF capillary 15-11 dialyzers

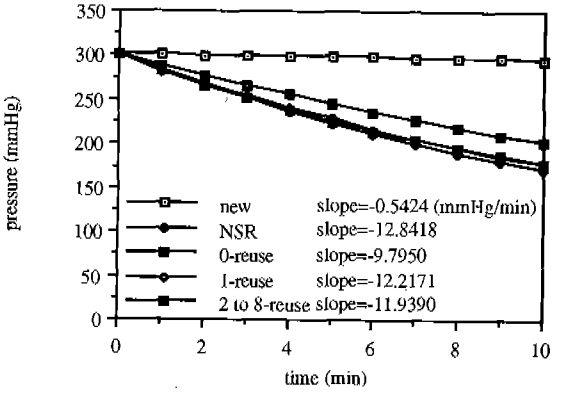

Fig. 4 Air pressure decay for C-DAK 4000 dialyzers

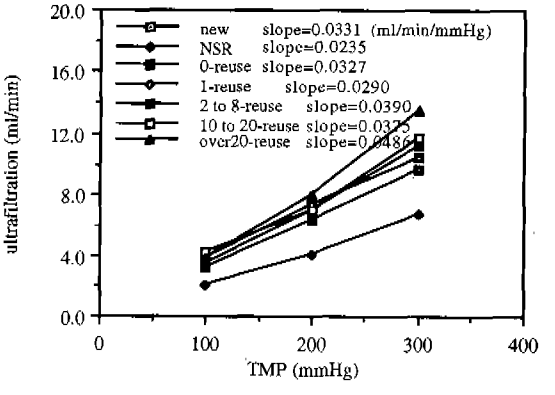

Fig. 5 Ultrafiltration rate for Cf capillary 15-11 dialyzers

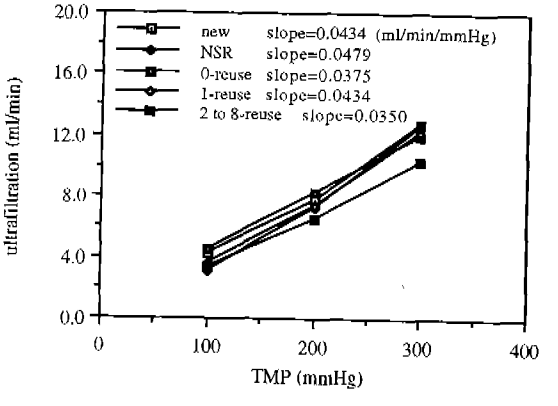

Fig. 6 Ultrafiltration rate for C-DAK 4000 dialyzers

the number of patients' reuses. It is also noted that C-DAK 4000 reused dialyzers show a larger pressure drip compared with CF reused dialyzer in APD test. Fig. 5 and 6 represent UFRs for various dialyzers and the UFR is observed to be linearly proportional to the applied pressure. It was also observed that C-DAK 4000 dialyzers show slightly larger UFR than CF capillary dialyzers. It is interestion to note that the saline rinsed CF capillary 15-11 dialyzers have lower UFR than the new or reused dialyzers. However, no such difference was observed in the C-DAK 4000 dialyzers.

In APD tests, we used a criterion that pressure decay rate exceeding 20mmHg/min would indicate failure of the dialyzer. Based on this criterion, the dialyzers which failed are included in Table 2. It should be noted that when the dialyzers failed they did not hold the air pressure for more than 30 seconds.

It is also interesting to note that UFR tests on the CF Capillary 15-11 dialyzer which failed in APD test did not show any significant differences from the other dialyzers. Only C-DAK 4000 dialyzers which failed in APD tests showed differences in UFR test. It can also be observed from the table that there is no trend indication the failure with increasing number of reuses.

It was interesting to observe that the new dialyzers did not exhibit any observable pressure decay at all compared to those which were wet(eitheer saline rinsed or reused and reprocessed). As the hollow fibers are expected to filter out the waste products during dialysis, it would be reasonable to exhibit some APD across the membrane. However, new dialyzers, when tested in the dry conditions, did not exhibith any pressure decay at all. Even with saline rinsing, there was a measurable pressure decay. It is probable that the new dialyzers may have residual substances on the membrane which blocks the pores and prevents air leaking across the membranes[6-8]. As soon as the dialyzer becomes wet (either due to saline rinsing or reprocessing), the pores on the membranes may become permeable to air or water. This may be the reason for the observable difference in APD between a new and reused dialyzer. *It is recommended that this fact be examined further and if proved to be true, the protocol for APD test be changed not to include any new dialyzers. Perhaps saline rinsed dialyzers can be used as a control study in the protocol.*

Table 2 Dialyzers failed in the air pressure leak tests

	CF capillary 15-11	C-DAK 4000	CF capillary 12-11	CF capillary 23-08
New	0	0	N/A	0
NSR	0	0	N/A	N/A
0-reuse	0	1	N/A	0
1-reuse	0	3	N/A	N/A
2-reuse	0	0	0	N/A
3-reuse	0	1	N/A	N/A
4-reuse	0	0	0	N/A
6-reuse	0	0	0	N/A
8-reuse	0	0	0	N/A
10 to 20-reuse	0	N/A	N/A	N/A
Over 20-reuse	2	N/A	N/A	0
Total failure	2	5	0	0

A larger pressure decay rate was observed rate was observed with the C-DAK 4000 dialyzers compared to that for the CF dialyzers within the 95% confidence interval. As pointed out earlier, the CF dialyzers were made of cuprophane fibers whereas the C-DAK dialyzers were made of cellulose acetate fibers. The difference in the pressure decay rate between the two dialyzers may be attributed to the material properties such as differences in the porosity or permeability of the different membranes.

This study also revealed thaat a sihnificant number of HFD's(2 out of 40 CF and 5 out of C-DAK) failed in APD tests. However, the statistical analysis for some failed dialyzers was not performed due to small number of data and the transportation problem which may make dialyzer fail in the air pressure leak test. However, there was no observable difference in UFR tests between the failed and normal CF dialyzers based on the air pressure leak test. It is also be noted that these same dialyzers tested at the clinic, before being shipped to our laboratory, did not fail. Similarly, there have not been any pubilished reports indicating failure of reused dialyzers in significant numbers. Hence, there may be other reasons for a significant number of failures observed in this study. Our postulated reason is that the membranes are damaged or dislodged from the seals during transport from the clinic to the University laboratory, especially if air pockets would have been present in filling the blood and dialysate compartments with formaldehyde soon after reprocessing. *To eliminate this variable in obscuring the results, it is strongly suggested that future tests be performed at the same site where reprocessing is performed.*

Once the reprocessed dialyzers were brought into the laboratory, the protocol called for the rinsing the blood and dialysate compartment with RO/DI water at a recommended rate of one liter perminute. Subsequently, the fluid from both compartments is to be dried by gently blowing pressurized air through them. It is possible that these procedures may aid in dislodging or disrupting the fibers which resulted in a shgnificant number of failures. It should also be noted that when the failed dialyzers were retested in the clinic, all of them failed the pressure leak test at the clinic also. *Hence, it is recommended that in future tests, the following protocol be followed. The formaldehyde from both the compartments be rinsed and filled with RO/DI water at a flow rate not to exceed 500ml/min in the blood compartment and 800ml/min in the dialysate compartment. As these flow rates are the maximum values used in the clinical situation, any damage to the fibers can be avoided. Morover, it is also recommended that pressure leak tests be performed under wet ccondition with RO/DI water in the blood compartment pressurized and in the dialysate compartment vented to the atmosphere.*

Ⅳ. SUMMARY

From APD and UFR determination tests on the CF 15-11 and C-DAK 4000 dialyzers described in this study, the following conclusions may be drawn. As con be observed from Table 1, th number of Cf 12-11 and CF 23-08 dialyzers were too small to find any meaningful conclusions.

1. New dialyzers showed a relatively flat pressure drop curve, whereas saline rinsed or patient reused dialyzers exhibited a decay in pressure with time.
2. The C-DAK 4000 dialyzers showed significantly larger pressure decay rate(11.70 ± 1.32mmHg /min) compared to the CF dialyzers(4.32 ± 0.55mmHg/min) in the air pressure leak test with the 95% confidence interval. On the other hand, there was no significantly observale difference in the UFR between the two dialyzers.
3. Using a criterion that pressure decay rate exceeding 20 mmHg/min indicates mechanical failure of the membrane, 2 out of 40 CF dialyzers and 5 out of 26 C-DAK dialyzers used

in this study failed APD test. However, CF dialyzers which failed APD tests were found to have the UFR similar to those which were observed to be normal. In the case of C-DAK dialyzers, the failed dialyzers also showed an increased the UFR compared to the normal.

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