Efficacy of Cellulose Triacetate Dialyzer and Polysulfone Synthetic Hemofilter for Continuous Venovenous Hemofiltration in Acute Renal Failure

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Objective: *To compare the clearance performances and biocompatibility between the modified cellulose membrane and the standard synthetic membrane in continuous renal replacement therapy (CRRT)*
Material and Method: *Seventeen patients with acute renal failure (ARF)were treated with separated continuous veno venous hemofiltration (CVVH) system conducted with the pre-dilution mode. The modified cellulose used was a Sureflux150E (cellulose triacetate) and the standard synthetic membranes used was an AV-400. Blood and replacement flow rate were kept at 100 and 20 mL/min, respectively. Ultrafiltraion rate was 1,200 mL/hr. Samplings of blood and ultrafiltrate were collected at baseline, 2, 8, 16, and 24 hr.*
Results: *Patients in both methods could similarly tolerate CRRT with only minor complications. Sureflux 150E and AV-400 provided comparable values of sieving coefficients and clearances of small solutes. The albumin loss in ultrafiltrate by Sureflux 150E was greater than AV-400 . The values of life span and biocompatability of both hemofilters were not different.*
Conclusion: *Because of the excellent efficacy and the much cheaper cost, the modified cellulose membrane could be an appropriate alternative to standard synthetic membrane in CRRT.*

Keywords: *Continuous renal replacement therapy, Modified cellulose membrane, Standard synthetic membrane*

J Med Assoc Thai 2006; 89 (Suppl 2): S65-72
Full text. e-Journal: *http://www.medassocthai.org/journal*

At present, continuous renal replacement therapy (CRRT) is a well-tolerated and efficient modality of treatment for acute renal failure (ARF) in critically ill patients[1,2]. Since solute clearance in CRRT is achieved by convection, hemofilter membrane used in the procedure should have high ultra filtration (UF) coefficient, low priming volume, low resistance to blood flow, adequate performance in diffusion of small molecular weight solutes, high porosity and high sieving coefficient for medium and large molecular weight solute, low tendency to clot or membrane fouling, and good compatibility[3]. A standard synthetic polymers membrane, AV-400 is generally used in CRRT. It is very efficient and biocompatible but is very expensive. Modified cellulose membrane has been recently developed with better properties in hydraulic permeability, sieving coefficient, and biocompatibility[4]. Of importance, the modified cellulose membrane is much cheaper than the synthetic membrane. The modified cellulose membrane has been widely used in standard hemodialysis. Whether the use of modified cellulose membrane in CRRT could provide comparable results with the synthetic membrane is still not established.

The present study was conducted to compare the clearance performances and biocompatibility between the modified cellulose membrane and the standard synthetic membrane in continuous venovenous hemofiltration (CVVH), the most popular modality of CRRT used in the treatment of ARF.

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Material and Method

Patients

This prospective study was conducted, at King Chulalongkorn Memorial Hospital, Bangkok Thailand, in 17 critically ill patients who suffered from ARF and were treated with CVVH. The present was approved by the Ethics Research Committee, Faculty of Medicine, Chulalongkorn University. Informed consent was obtained from each participating patient.

ARF was diagnosed when one of the following criteria was present: 1) fluid overload resulting from inadequate urine production despite administration of diuretic agents and maintenance of adequate blood pressure; 2) rise in serum Creatinine (Cr) above 2.5 mg/dL or doubling of baseline Cr; 3) serum potassium above 5.5 mEq/L. Exclusion criteria were immunodeficiency syndrome, previous extracorporeal treatment, and organ transplantation.

The severity of illness in each patient was assessed by the APACHEII Score system. Hemodynamics and life span of hemofilter were recorded for all subjects.

Study Design and CVVH Technique

The separated CVVH system was employed as previously described[5] in all patients. Hemofilters utilized in the present study were the modified cellulose membrane (Sureflux150E) and the standard synthetic membrane (AV-400). The manufacture data between Sureflux150E versus AV-400 delineated some discrepancies and these included surface area (1 vs 0.7 m^2), priming volume (90 vs 52 mL), and UF rate [2,050 mL/hr/100 mm.Hg vs 1300 mL/hr (blood flow rate = 150 mL/min, transmembrane pressure = 70 mm.Hg)].

A randomization of membrane assignment, Sureflux150E or AV-400 , was simply performed by the use of an alternative membrane for each patient in the order of recruitment.

Percutaneously introduced double-lumen venous catheters were used for vascular accesses. Each hemofilter was rinsed with 2 L. of pre-heparinized saline prior use. Blood flow rate infusing the extracorporeal circuit was kept at 100 mL/min. Filtration rate was approximately 20 mL/min. Replacement fluid used in the present was a bicarbonate based solution and was added in the pre-dilution mode. Anticoagulation was not utilized in the present study although there were no contraindications to use it in certain patients. Circuit clotting was prevented by flushing the circuit with 0.9% normal saline solution for every 30 minutes.

The comparison in clearance performances and biocompatibility between both hemofilters were performed during the first 24 hours of CVVH treatment. The small solutes studied in the present study were urea Cr, uric acid, and inorganic phosphate while the middle molecule solutes included albumin. The biocompatibility of each membrane was assessed by determining the values of white blood cell (WBC), neutrophil, and complement (C3) levels.

Sample Collection and Measurement

Blood samples from the prefilter (arterial line just before the branching for substitution fluid) as well as postfilter (venous line just after hemofilter) and ultrafiltrate samples were collected at baseline (0 min), 15 min, 2 hr, 8 hr, 16 hr, and 24 hr. All samples were stored at -80 C until assay.

The levels of small solutes, WBC, and neutrophil were determined by the standard laboratory method. The values of albumin were measured by immuno-turbidimetric kit. Solid phase Enzyme Linked Immuno Sorbent Assay (ELISA) was used to asses the levels of C3.

Sieving Coefficient (SC) was calculated by the formula

SC = filtrate concentration / plasma concentration.

Clearance of each solute was determined by the formula clearance = UF rate SC

Statistical analysis

All data were expressed as mean $\pm$ SD. The statistical difference among the values at each time point was analyzed by repeated ANOVA. All statistical testing were performed by using SPSS statistical package (version 11.0 for Windows, SPSS Inc, Chicago, IL). The results were statistically significant when $p < 0.05$.

Results

Basic patient characteristics

As demonstrated in Table 1, there were no significant differences in all basic clinical and laboratory parameters.

Filter performances

There were no significant differences in clearance of all mentioned small solutes at every time point during the 24-hour duration of CVVH treatment (Fig. 1-5). Also, no statistically significant differences in sieving coefficients of small solutes including urea, Cr, uric acid, and inorganic phosphate were noted between the two hemofilter groups (data not shown).

Table 1. Basic patient characteristics (N = 17)

	AV-400	Sureflux150E
Number	9	8
Gender male/female	5/4	5/3
Age (year)	60.3 ± 23.2	63.6 ± 15 ^{NS}
APACHE II Scoring System	20.7 ± 4.2	21.9 ± 4.5 ^{NS}
Mean arterial blood pressure (mm.Hg)	86.5 ± 30.3	76.7 ± 11.1 ^{NS}
Baseline BUN level (mg/dL)	81.4 ± 38.8	70.4 ± 34.4 ^{NS}
Baseline Cr level (mg/dL)	4.36 ± 0.92	4 ± 2.1 ^{NS}
Serum albumin (g/dL)	3.4 ± 0.3	3.5 ± 0.9 ^{NS}

Abbreviation: BUN = blood urea nitrogen, Cr = crea
NS = non significant when compared with AV -400
Data were presented as mean ± SD

As illustrated in Fig. 5, patients in the Sureflux150E group had greater amount of albumin loss in UF than the AV-400 group at all experimental time points. (5.3 ± 6.1 vs 0.6 ± 0.1 mg/L at 2-hour, $p < 0.05$; 4.3 ± 5.6 vs 0.61 ± 0.1mg/L at 8-hour, $p < 0.05$). The cumulative albumin loss in 24 hours was 17.47 mg/L in the Sureflux150E group and 0.9 mg/L in the AV-400 group ($p < 0.05$). Of interest, the maximum albumin loss in the UF in the Sureflux150E group occurred immediately after initiating the CVVH procedure but declined rapidly at 24-hours of CVVH treatment. The levels of serum albumin in both groups after 24 hours of CVVH treatment were not different (3.4 ± 0.7 vs 3.4 ± 0.5 g/dL, NS).

The values of C3 level in the Sureflux150E group were slightly, but not significantly, lower than the AV-400 group (Fig. 6), indicating no significant difference in complement activation by both hemofilters.

As illustrated in Fig. 7, there were no significant differences in the number of neutrophil and polymorphonuclear cells between both hemofilter groups.

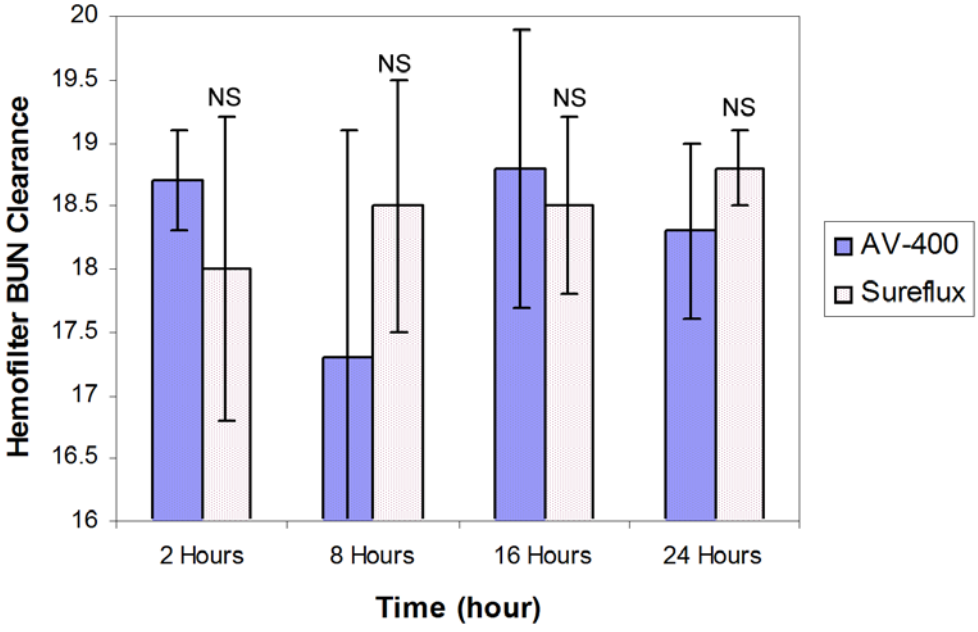

Fig. 1 Hemofilter blood ure nitrogen (BUN) clearance
NS = non significant when compared with the AV-400 group

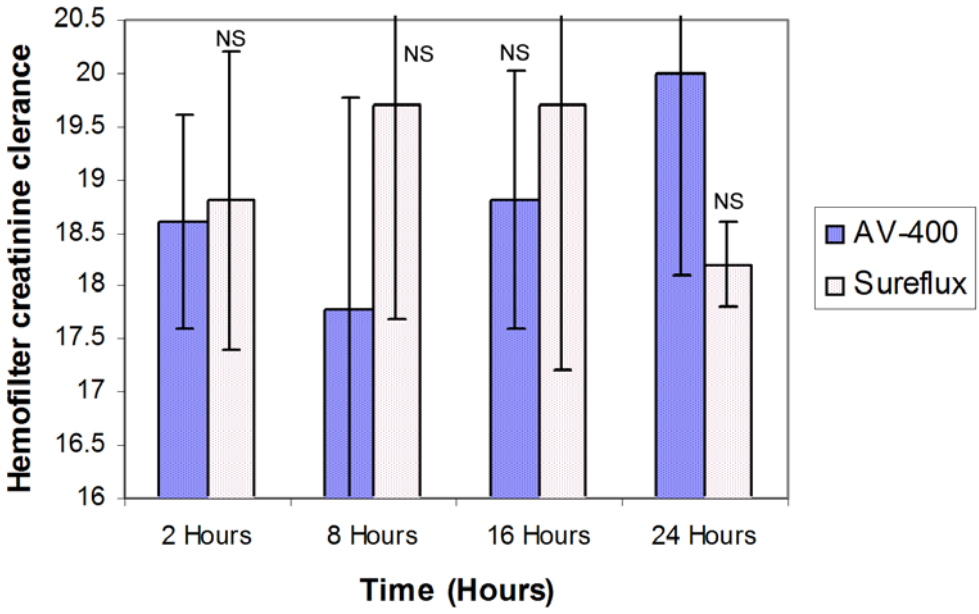

Fig. 2 Hemofilter creatinine (Cr) clearance
NS = non significant when compared with the AV-400 group

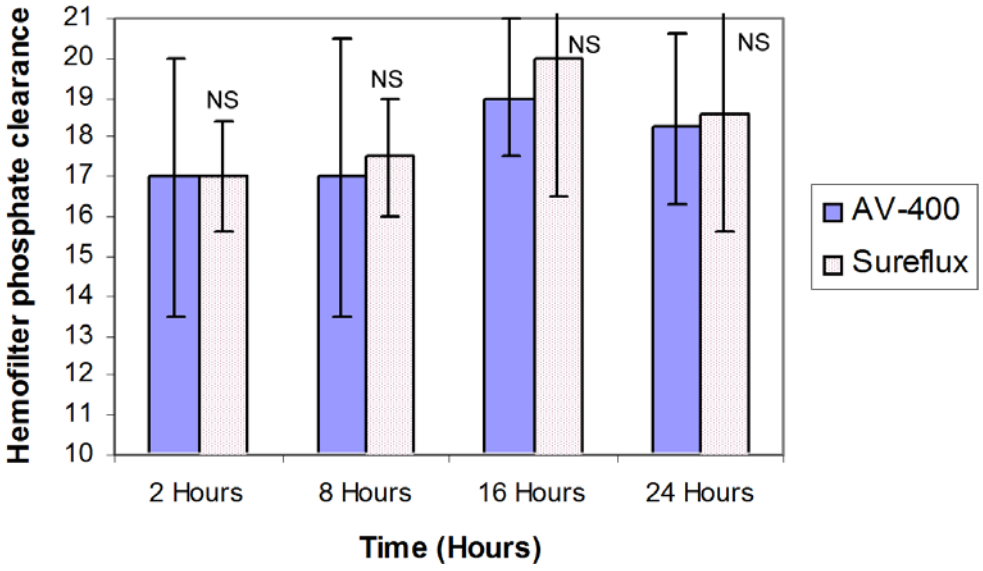

Fig. 3 Hemofilter phosphate clearance
NS = non significant when compared with the AV-400 group

Hemodynamic data

During the first 15 minutes of CRRT treatment, there were no significant hemodynamic changes from baseline in both groups. Patients in both groups showed good clinical tolerance and encountered minor complications throughout the CRRT sessions. The body temperature declined during the treatment by both filters and showed no difference between both groups (data not shown).

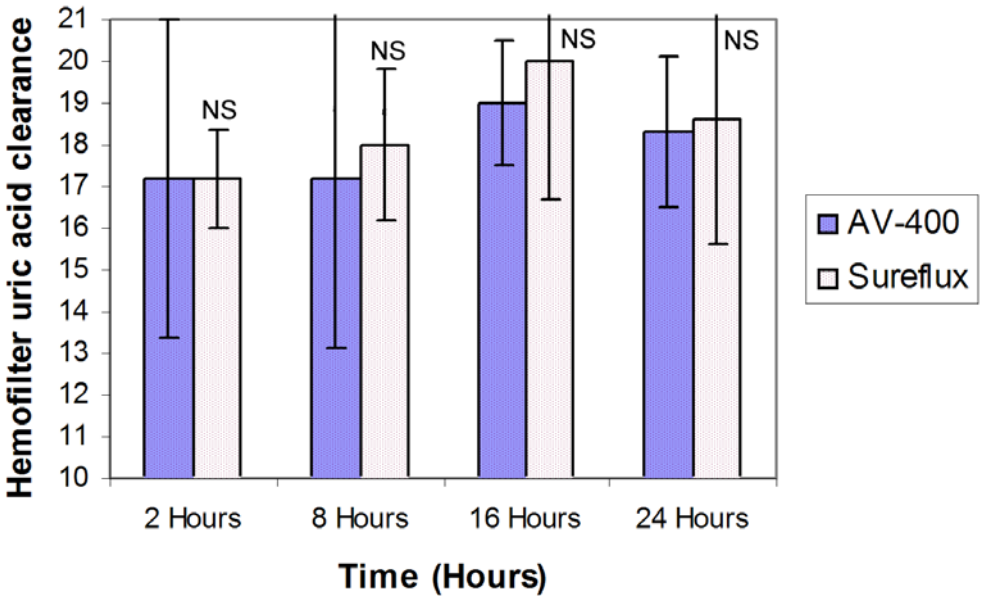

Fig. 4 Hemofilter uric acid clearance
NS = non significant when compared with the AV-400 group

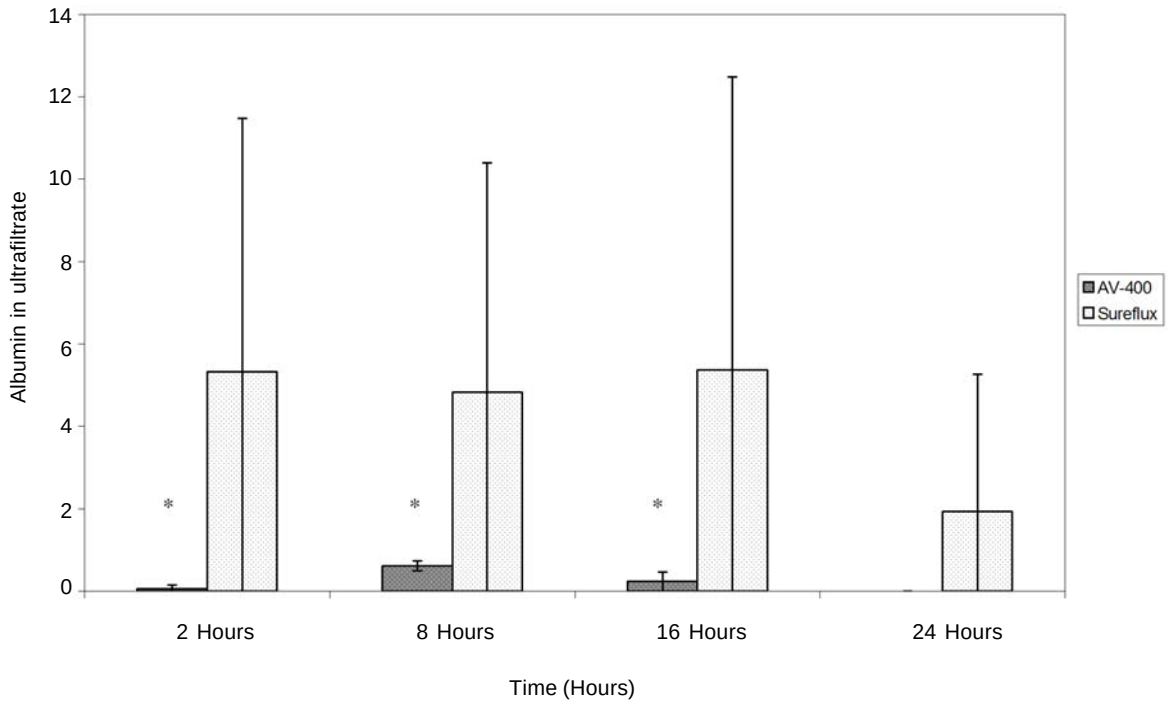

Fig. 5 Albumin loss in ultrafiltrate
* = $p < 0.05$ when compared with the AV-400 group

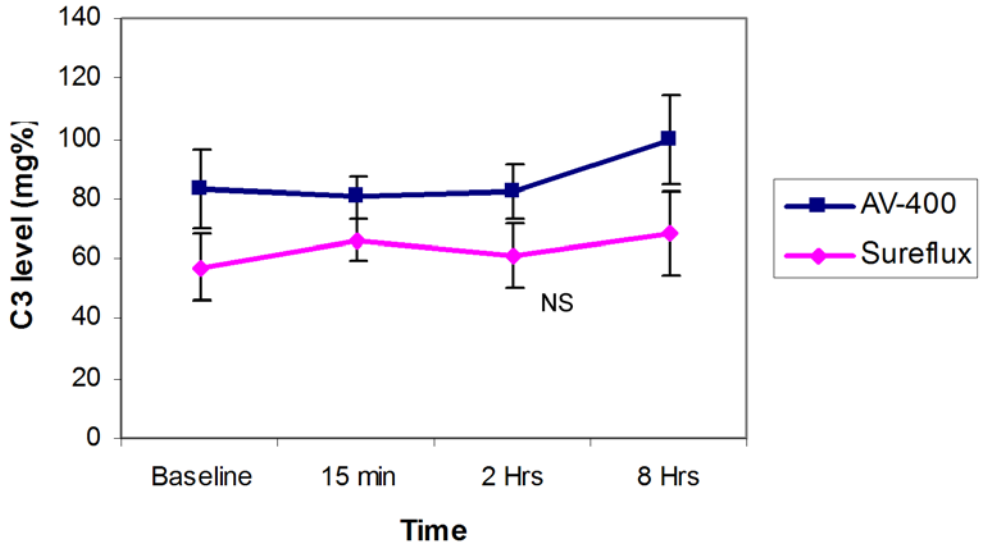

Fig. 6 Complement activation C3 level
NS = non significant when compared with the AV-400 group

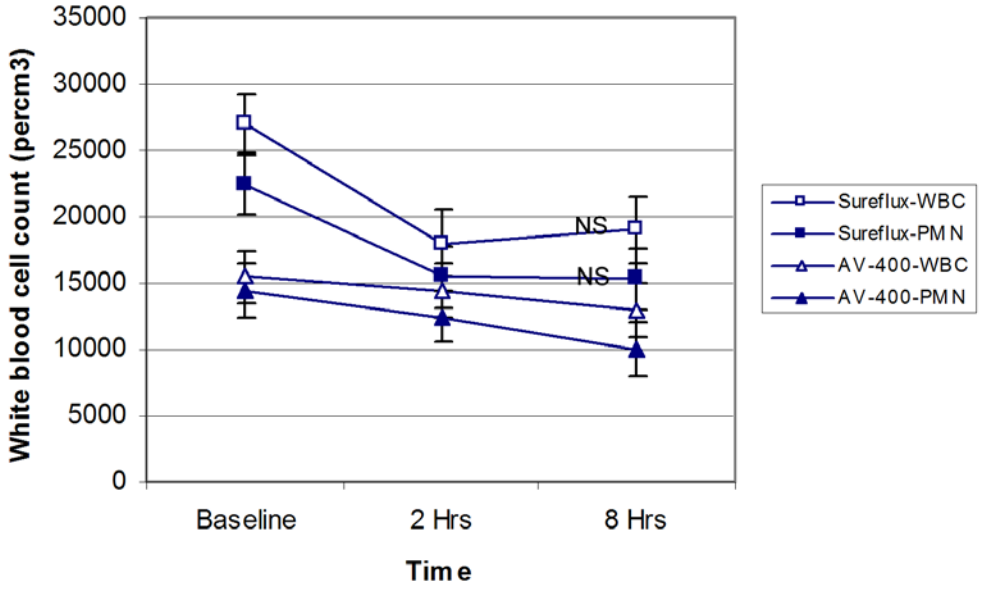

Fig. 7 Neutrophil and polymorphonuclear cell levels
NS = non significant when compared with the AV-400 group

Life span of hemofilter

Each kind of filter could be employed for almost 24 hours. The life time of Sureflux150E was 19.2 $\pm$ 3.2 hours while that of AV-400 was 18.9 $\pm$ 3.6 hours.

Discussion

In CRRT, several factors could have certain impact on outcome in ARF and these include delivery dose of dialysis[6], type and performance characteristics of dialysis membrane, timing of initiation of dialysis, and adequacy of dialysis[7-9]. In the present study, the use of modified cellulose membrane or Sureflux150E in CRRT could yield quite similar values of sieving coefficient, clearances of small solutes, and life span of

hemofilter when compared with the standard synthetic membrane or AV-400 (Fig. 1-5). Furthermore, CRRT by both membranes could provide comparable clinical tolerance and minor complications

Besides filter performance, the extracorporeal membrane used in CRRT for the treatment of critically ill patients with ARF is vitally important in the aspect of biocompatibility. Blood-membrane interaction could activate cellular and humoral components of blood. This would lead to the generation of several biological responses including activation of complement, coagulation cascade, monocyte, and neutrophil degranulation. Intense systemic complement activation leads to the release of the anaphylotoxin C3a and C5a, with generation and release of proinflammatory reactive oxygen species and other cytokines[10]. A previous study found that complement activation can retard the resolution of acute ischemic renal failure in rats[11]. The cellulose base membrane type seems to induce these reactions more than the synthetic membrane. In the present study, however, there was neither significant, hemodynamic change during the first 15 minutes or complement activation during the treatment in both membrane groups (Fig. 6, 7).

The values of albumin loss at every time point or daily were greater on the Sureflux150E than AV 400 (Fig. 5) while the serum albumin levels were unaltered. The albumin loss occurred mostly at the initial phase but decreased rapidly overtime. This might be explained by the deposition of the blood components in the pore of membrane and subsequent narrowing of the effective pore size. Indeed, the loss of albumin in the Sureflux150E group could easily be supplemented by daily nutritional support.

It is well established that the concentrations of several molecules such as urea, Cr, bicarbonate are lower in red blood cell than in plasma water. Consequently, changes in hematocrit in the filter, as induced by the CVVH pre-dilution mode modulates shifting of small molecules through the red cell membrane into the plasma and then the filtrate. Hence, in the CVVH post dilution mode, small molecule removal is significantly higher than in the CVVH pre dilution mode. The CVVH pre-dilution mode could reduce efficiency by 10-15%, but this could be easily overcome by the use of a relatively high UF rate[12]. Despite inferior efficiency, the CVVH pre-dilution mode could provide less circuit clotting when compared with the CVVH post-dilution mode. In the present study, however, the pre-dilution mode was selected on the purpose that it might provide a longer life span of hemofilter and would further reduce heparin requirement.

Indeed, Shigehiko et al[13] conducted a prospective observational study to assess the efficacy of CVVH with no anticoagulant, and found no significant difference in the mean circuit life among heparin and no anticoagulant group in 48 critically ill patients. As such, for the patients with a high risk of bleeding, CVVH without anticoagulant is feasible and safe and has no effect on circuit life time.

Because of the small sample size, the data from the present study were not sufficient to assess the significant mortality or morbidity rates from the use of both membranes.

In conclusion, the use of modified cellulose membrane in CRRT could provide comparable efficacy and minor complications with the standard synthetic membrane. Considering the lower cost of the modified cellulose membrane, cellulose triacetate could be an appropriately effective alternative to the standard synthetic membrane in continuous renal replacement therapy.

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การศึกษาประสิทธิภาพตัวกรองชนิดเซลลูโลสไตรอะซิเตท กับตัวกรองสังเคราะห์ โพลีซัลโฟน สำหรับการฟอกเลือดแบบต่อเนื่องในผู้ป่วยภาวะไตวายเฉียบพลัน

วรางคณา พิชัยวงศ์, อัษฎาศ์ ลีฬหวนิชกุล, สมชาย เอี่ยมอ่อง

วัตถุประสงค์*: เพื่อเปรียบเทียบประสิทธิภาพการขจัดของเสียและปฏิกิริยากระตุ้นกระบวนการอักเสบของร่างกาย ระหว่างตัวกรองชนิดเซลลูโลสไตรอะซิเตทและตัวกรองชนิดสังเคราะห์โพลีซัลโฟน ซึ่งเป็นตัวกรองมาตรฐานที่ใช้ในการฟอกเลือดแบบต่อเนื่อง*

วัสดุและวิธีการ*: ผู้ป่วย 17 ราย ที่มีภาวะไตวายเฉียบพลัน ได้รับการฟอกเลือดแบบต่อเนื่อง ทำการควบคุมวงจรการไหลเวียนโลหิตโดยใช้เครื่องหมุนเลือดดันผ่านทางเส้นเลือดดำ มีการเติมสารน้ำทดแทนกลับคืนที่ตำแหน่งก่อนเข้าตัวกรอง ตัวกรองที่ใช้ในการศึกษา ได้แก่ ตัวกรอง Sureflux ซึ่งเป็นตัวแทนของตัวกรองธรรมชาติที่ได้รับการดัดแปลง และตัวกรอง AV-400 เป็นตัวแทนของตัวกรองชนิดสังเคราะห์ กำหนดการไหลเวียนโลหิต 100 มิลลิลิตรต่อนาที อัตราการให้สารน้ำทดแทน 20 มิลลิลิตรต่อชั่วโมง ค่าอัลตราฟิวเตรชั่น 1,200 มิลลิลิตรต่อนาทีมีการเก็บตัวอย่างน้ำ, เลือด และอัลตราฟิวเตรทที่เวลาเริ่มการศึกษา, 2, 8,16, และ 24 ชั่วโมง*

ผลการศึกษา*: ผู้ป่วยทั้งสองกลุ่มสามารถดำเนินการฟอกเลือดอย่างต่อเนื่องโดยไม่มีภาวะแทรกซ้อน ไม่พบความแตกต่างของประสิทธิภาพการกำจัดสารที่มีโมเลกุลขนาดเล็ก แต่มีการสูญเสียอัลบูมินจากตัวกรองชนิด Sureflux มากกว่าตัวกรองชนิดสังเคราะห์ AV-400 ไม่มีความแตกต่างในด้านอายุเฉลี่ยของการใช้งาน และการกระตุ้นปฏิกิริยาการอักเสบของร่างกาย*

สรุป*: ตัวกรองธรรมชาติที่ได้รับการดัดแปลง มีประสิทธิภาพในการกำจัดสารได้ดีเทียบเท่ากับตัวกรองชนิดสังเคราะห์ มีความปลอดภัยที่จะนำมาใช้ในผู้ป่วยวิกฤตที่มีภาวะไตวายเฉียบพลัน มีราคาถูก การใช้ตัวกรองเซลลูโลสไตรอะซิเตท จึงเป็นทางเลือกหนึ่งที่มีความคุ้มทุนในการฟอกเลือดอย่างต่อเนื่องในผู้ป่วยภาวะไตวายเฉียบพลัน*