Contrast medium-removing effect of hemofiltration and hemodiafiltration

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Abstract: The contrast medium-removing effect of hemofiltration (HF) and hemodiafiltration (HDF) was experimentally investigated using a bovine blood tank model. HF and HDF were performed at a blood flow rate of 100 ml/min with a polysulfone hemofilter (PS filter-CF ; membrane area : 0.7 m^2). Two hundred milliliters of iomeprol (300 mgI/ml) was administered by a single injection into 4 liters of bovine blood. The blood half-lives of iomeprol were 1.0 hr for the high flow rate HDF group [replacement fluid flow rate (Q_F) : 10 ml/min and dialysate flow rate (Q_D) : 40 ml/min], 1.8 hr for the HDF group (Q_F : 10 ml/min and Q_D : 10 ml/min), and 3.8 hr for the HF group (Q_F : 10 ml/min). The mean clearance rates were 39.7 ml/min for the high flow rate HDF group, 21.4 ml/min for the HDF group, and 12.0 ml/min for the HF group. Iomeprol was mostly excreted in the waste fluid. It is concluded that HDF can remove contrast media more effectively than HF.

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Key words **:** *contrast medium, iomeprol, hemofiltration, hemodiafiltration*

INTRODUCTION

In recent years, opportunities to use contrast media have increased with improvements in various diagnostic imaging methods, including CT and angiography, as well as in intra-arterial therapy. Non-ionic contrast media with low osmotic pressure, including iomeprol, have been developed and come into use because they have less pronounced biological effects than conventional ionic contrast media with high osmotic pressure(1-4). All contrast media, however, are foreign matter to patients and experimental animals, and their use involves the risk of provoking adverse reactions, such as iododerma and nephrotoxicity (5,6). Since contrast media are mostly excreted in urine via the kidneys, they may accumulate in patients with renal failure (7,8). Furthermore, it has been reported that necrosis of the pancreas in the acute necrotic pancreatitis rat model exacerbated following the administration of a contrast medium (9) and that a patient with severe acute necrotic pancreatitis who underwent contrasted CT showed worsened prognosis (10). Therefore, contrast media should be used very carefully in patients with renal function disorders or necrotic lesions. Taking these findings into consideration, the supplementary removal of contrast media in blood appears to be highly desirable. Various blood purification therapies, such as hemodialysis (HD), hemofiltration (HF), and hemodiafiltration (HDF), are currently performed for patients with renal failure (11-13). HD, which may result in a decrease in blood pressure due to the rapid removal of solutes, is difficult to perform for seriously ill patients with multiple organ failure who frequently present with unstable hemodynamics (14). By contrast, HF has less effect on hemodynamics than HD (11). However, HF alone is not sufficient for removing substances of low molecular weight. For this reason, HDF, a method by which the dialysate circulates outside the HF filter and which has the advantages of both HD and HF, has been introduced (12, 13). HF and HDF are usualy performed for several hours at high

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flow rates with a large membrane area hemofilter. For critically ill patients with unstable hemodynamics, HF and HDF are often performed continuously at low flow rates with a small membrane area hemofilter [continuous hemofiltration (CHF) and continuous hemodiafiltration (CHDF)] to prevent a decrease in blood pressure and to continuously correct the water and electrolyte balance (15, 16). Contrast media with a molecular weight of less than 1,300 daltons have very low protein binding rates and are regarded as substances which are removable by HD (17-20). However, no in-depth studies have been made to date on the contrast medium-removing ability of blood purification therapies other than HD. In this study we investigate the efficacy of HF and HDF, at low flow rates with a small membrane area hemofilter, to remove iomeprol, a non-ionic contrast medium with low osmotic pressure. In addition, we studied the mechanism by which these therapies remove iomeprol.

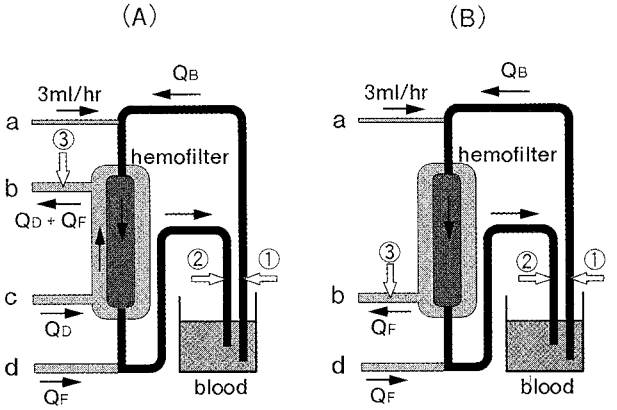

Fig.1. Schema of HDF (A) and HF (B) using a bovine blood tank. Four liters of the adjusted bovine blood was poured into a tank and warmed at 36℃ while being stirred with a stirrer. For HDF and HF, a PS filter CF (membrane area : 0.7㎡) was used. Five ml of blood was collected in the afferent tube (①) and in the efferent tube (②), and 5 ml of waste fluid was collected in the drainage tube (③). a : anticoagulant solution (10 mg/ml nafamostat mesilate solution), b : waste fluid, c : dialisate fluid, d : replacement fluid. Q_B : blood flow rate, Q_F : replacement fluid flow rate, Q_D : dialysate flow rate.

MATERIALS AND METHODS

A solution containing 140 milliliters of citrate-phosphate-dextrose (CPD) (21) was added to 1 liter of bovine blood immediately after collection, and the hematocrit and total protein of the mixture were adjusted to 38% and 6.0 g/dl, respectively, before the start of the present study. Four liters of the adjusted bovine blood was poured into a tank and warmed at 36℃ while being stirred with a stirrer (Figure 1). The console used for HF and HDF was a KM-8800 (Kuraray Co., Ltd., Osaka, Japan), and the filter : a polysulfone hemofilter (PS filter-CF ; membrane area : 0.7㎡ ; Kuraray). The replacement fluid and dialysate consisted of commercial replacement fluid which had previously been mixed with the CPD solution to obtain a concentration which was comparable to actual blood concentration. The bulk of the nafamostat mesilate (Torii Pharmaceutical Co., Ltd., Tokyo, Japan) was dissolved in the 5% glucose solution to obtain a concentration of 10 mg/ml, and the material was administered as an anticoagulant at a dose of 3 ml/hr (30 mg/hr) before filtration.

The test materials were divided into the following four groups : Group I (high flow rate HDF group, n=4) which underwent HDF at a blood flow rate (Q_B) of 100 ml/min, a replacement fluid flow rate (Q_F) of 10 ml/min, and a dialysate flow rate (Q_D) of 40ml/min ; Group II (HDF group, n=4) which underwent HDF at a Q_B of 100 ml/min, a Q_F of 10 ml/min, and a Q_D of 10 ml/min ; Group III (HF group, n=4) which underwent HF at a Q_B of 100 ml/min, and a Q_F of 10 ml/min ; and Group IV (control group, n=4) for which no blood purification method was used, and the blood in the tank was only stirred.

A non-ionic contrast medium with low osmotic pressure, iomeprol (612.4 mg/ml ; iodine content : 300mgI/ml ; molecular weight : 777 ; protein binding rate : 0% ; Eisai Co., Ltd., Tokyo, Japan) was used in the present study. Iomeprol was administered by one injection into the tank at 30 min after the start of HF and HDF. A 5-ml blood sample was collected in the afferent and efferent tubes, and a 5-ml waste fluid sample was collected in the drainage tube on a time-course basis (at 5 and 30 min, as well as at 1, 2, 4, and 6 hr after administration). These samples were centrifuged at 3,000 rpm for 10 min, and the isolated plasma and waste fluid were stored at -20℃ until the determination of iomeprol concentrations by high-performance liquid chromatography (HPLC).

The pharmacokinetic parameters were calculated, and data were analyzed with the least square method. Blood half-lives and elimination rates of iomeprol were calculated according to the following formulas:

Half-life (hr) = Ke / AUC ;

Elimination rate (%) = [Ca(t5)-Ca(t)]/Ca(t5)×100, where Ke is the elimination rate constant, AUC is the area under the curve, Ca (t5) is the blood iomeprol concentration in the afferent tube 5 min

after administration, and Ca(t) is the same concentration at t hours.

To investigate the elimination rate of iomeprol into the waste fluid and the adsorption rate on the HDF filter, the sieve coefficients, clearance rates, and adsorption rates of iomeprol were calculated according to the following formulas :

Sieve coefficient = Cd(t)/Ca(t) ;

Clearance rate (ml/min) = [Ca(t)-Cv(t)]/Ca(t)×Q_B;

Adsorption rate (%) = {[Ca(t)-Cv(t)]/Ca(t)-Cd(t) ×(Q_F+Q_D)/Ca(t)/Q_B}×100,

where Cd(t) is the iomeprol concentration in the waste fluid in the drainage tube at t hr after administration, Ca(t) is the iomeprol concentration in blood in the afferent tube at t hr after administration, Cv(t) is the iomeprol concentration in blood in the efferent tube at t hr after administration, Q_B is the blood flow rate, Q_F is the replacement fluid flow rate, and Q_D is the dialysate fluid flow rate.

For statistical analysis, blood iomeprol concentrations were expressed as the geometric mean± geometric SE, and other data were expressed as the mean or the mean±SD. Blood concentrations and parameters obtained for each model were compared by analysis of variance (repeated ANOVA) and Wilcoxon's rank sum test. A difference was considered statistically significant at a P value <0.05.

RESULTS

Five minutes after administration, the blood iomeprol concentration for Group IV (control group) was 41.0±0.2 mg/ml and no significant change was seen in this level. A semilogarithmic fit made of the concentration versus time data yielded a linear elimination curve for iomeprol in the blood purification groups (Figure 2). The blood purification groups showed a decrease in blood iomeprol concentrations, yielding the following half-lives : 1.0±0.04 hr for Group I (high flow rate HDF group) ; 1.8±0.1hr for Group II (HDF group) ; and 3.8±0.1 hr for Group III (HF group). Significant differences were seen in the kinetics of iomeprol concentration in the 4 groups ($p<0.001$). Four hours after administration, the blood iomeprol concentrations were 2.8±0.4 mg/ml for Group I, 9.7±1.2 mg/ml for Group II, and 17.9±0.4 mg/ml for Group III and, 6 hrs after administration, the corresponding concentrations were 0.7±0.1 mg/ml, 4.3±0.8 mg/ml, and 12.3±0.6 mg/ml, respectively.

Four hours after administration, the elimination rates were 93.1±1.2% for Group I, 75.4±2.8% for Group II, and 51.1±1.0% for Group III and, 6 hrs after administration, the corresponding rates were 98.4±0.4%, 88.1±1.6%, and 66.3±1.8% respectively (Figure 3). Significant differences were seen in the elimination rates of iomeprol from the blood in the 4 groups ($p<0.001$). The elimination rates were significantly higher in Group I than in Groups II and III ($p<0.001$), and in Group II than in Group III ($p<0.001$).

No changes were observed in sieve coefficient, clearance rate, or adsorption rate. The mean sieve coefficients were 0.73±0.07 for Group I, 0.90±0.10 for Group II, and 1.04±0.05 for Group III. The corresponding mean clearance rates were 39.7±

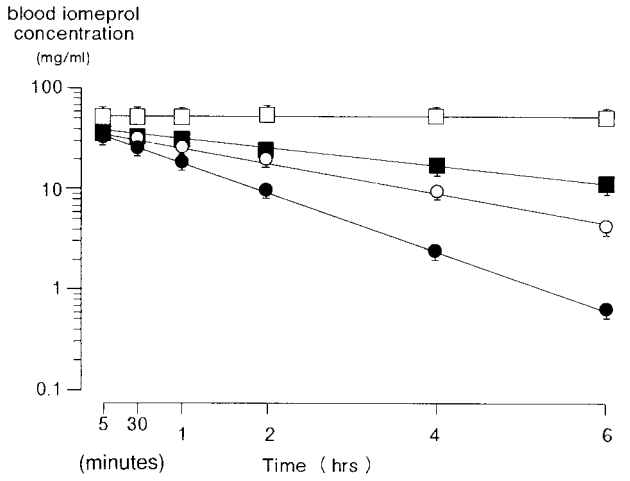

Fig.2. Time course of blood iomeprol concentration after the start of HDF or circulation for the high flow rate HDF group (●), the HDF group (○), the HF group (■), and the control group (□). Data represent the geometric mean±geometric SE (n=4).

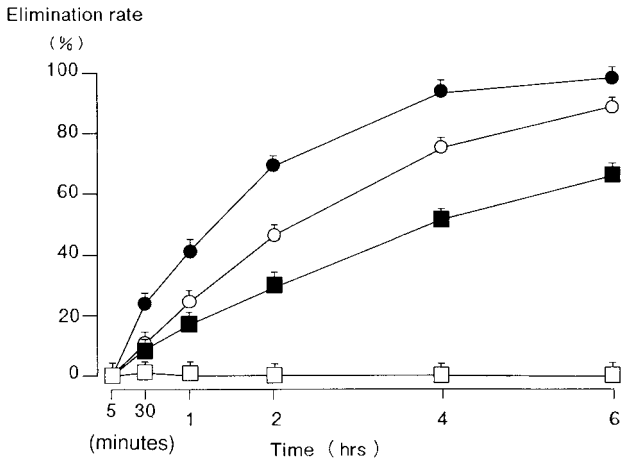

Fig. 3 . Elimination rates of blood iomeprol concentration after the start of HDF or circulation for the high flow rate HDF group (●), the HDF group (○), the HF group (■), and the control group (□). Data represent the mean±SD (n=4).

2.8ml/min, 21.4±4.0ml/min, and 12.0±1.1ml/min, respectively. As shown in Table 1, the clearance rates were significantly higher in Group I than in Groups II and III, and in Group II than in Group III. The adsorption rate accounted for 1.5 to 6.9%, and no significant differences were seen among the 3 groups.

DISCUSSION

CHF and CHDF have been used for critically ill patients with unstable hemodynamics to correct the imbalance of water and electrolytes (15, 16) and, in some reports, these therapies have been described as effective in removing chemical mediators related to the development of multiple organ failure (22, 23). HD removes substances of low molecular weight from blood by diffusion, and the clearance rate by HD is inversely proportional to the square root of the molecular weight of the substance in question (24). HF, on the other hand, filtrates substances of medium molecular weight (MW : <30,000 daltons) from blood by negative pressure (25). Thus, HF is generally more effective than HD in removing substances of medium molecular weight (MW:≧300 to 30,000 daltons) (26). However, the recent development of dialyzers with a high performance membrane has enabled substances of medium molecular weight (MW : <10,000) to be removed by HD as well (27). Iomeprol is a substance of medium molecular weight (MW : 777), with a very low protein binding rate, and a very low accumulation rate in tissue (8). Therefore, it has been reported that iomeprol can be removed from blood to the same extent in critically ill patients as in healthy subjects by HD, a method which utilizes a new type of dialyzer with a large membrane area consisting of a high performance membrane which can remove substances of medium molecular weight (MW : <10,000) (17).

HDF has the advantages of both HD and HF, and has greater ability to remove substances of low molecular weight than HF (12,13). In the present study, HDF removed iomeprol more effectively than HF at the same blood and replacement fluid flow rates (Q_B : 100ml/min ; and Q_F : 10ml/min). In blood purification therapy, the removal of a substance in blood is achieved not only by excretion in waste fluid but also by adsorption to membranes. However, the percentage of iomeprol removed by adsorption to membranes was less than 7%. Clearly, iomeprol was mostly excreted in waste fluid. The sieve coefficient, the ratio of the waste fluid iomeprol level to that of the blood, was 1.0 for the HF group. Therefore, it was considered that the efficacy of HF in the removal of iomeprol could be improved by increasing Q_B and Q_F, the latter nearly to Q_F max. Although the sieve coefficient is lowered by an increase in the Q_D of HDF, the clearance of iomeprol by HDF should be further enhanced by an increase in the Q_D since the volume of iomeprol excreted in the waste fluid will increase.

Contrast media administered to patients are mostly excreted in unchanged form in urine via the kidneys (7). Following the intravenous administration of 40 and 80 ml of iomeprol (816.5 mg/ml ; iodine content, 400mgI/ml) to healthy volunteers at a dose of 10ml/min, the blood half-life of iomeprol was 1.95 hr. Two

Table 1. Sieving coefficients, clearance rates, and adsorption rates of iomeprol after passage through the circuit at 2, 4, and 6 hrs after administration (n=4 for each group)

Time	Group	Sieving coefficient	Clearance rate (ml/min)	Adsorption rate (%)
2 hr	Group I	0.75±0.08*†††	40.3±1.1*†††	2.9±4.7
	Group II	0.92±0.07††	21.3±1.6††	2.9±2.4
	Group III	1.04±0.03**	11.9±0.8**	1.5±1.1
4 hr	Group I	0.71±0.04**††	41.8±1.8*†††	6.2±3.1
	Group II	0.99±0.06	23.0±3.2††	3.2±3.7
	Group III	1.01±0.09	11.1±0.6**	1.0±1.0
6 hr	Group I	0.75±0.01††	39.1±5.0*†††	1.7±4.9
	Group II	0.94±0.14	25.6±1.6††	6.9±4.1
	Group III	1.05±0.03	12.6±1.8**	2.1±1.6

Group I : high flow rate HDF group, Group II : HDF group, Group III : HF group, * : P<0.05 vs. Group II, ** : P<0.01 vs. Group II, †† : P<0.01 vs. Group III, ††† : P<0.005 vs. Group III

hours after administration, about 50% of the iomeprol administered was excreted in urine and, at 4hr, about 80% (8). In the present study, the blood half-life of iomeprol was 1.0 hr for the high flow rate HDF group and 1.8 hr for the HF group. The elimination rate of blood iomeprol, 4 hrs after administration, was 93.1% for the high flow rate HDF group, and 75.4% for the HDF group. It is predicted that the blood half-life and the elimination rate of HDF (Q_B:100ml/min ; Q_F : 10 ml/min ; and Q_D : 10 ml/min) would be comparable to that of healthy adults, and those of high flow rate HDF (Q_B : 100ml/min ; Q_F : 10ml/min ; and Q_D : 40ml/min) superior to that of healthy adults (8). A small volume (4 liters) of blood and a tank model were used in the present study, and the efficacy of iomeprol removal from blood only was assessed using a one-compartment model. As such, the effect of the distribution of iomeprol into extracellular fluids could not be taken into consideration. Consequently, it can be assumed that the half-lives and decreases in iomeprol following HF and HDF in clinical cases would be lower than the results obtained in the present study.

While the contrast medium-removing ability of HF or HDF in clinical cases has not been reported to date, several reports have described the efficacy of HD in the removal of contrast media. Generally, it can be predicted that more than 80% of a contrast medium administered is eliminated by HD which uses a dialyzer with a large membrane area at a blood flow rate of 200 ml/min. Ueda et al. have reported the efficacy of HD (Q_B : 200 ml/min and Q_D : 500 ml/min) using a hollow fiber dialyzer with an acetate cellulose diacetate membrane (membrane area : 2.1 ㎡) in the removal of iomeprol (714.4mg/ml ; iodine content : 350 mgI/ml) from patients with chronic renal failure (17). The clearance rate of iomeprol for the high flow rate HDF group was about 40 ml/min, i.e., about one-third the clearance rate (130 ml/min) of iomeprol by HD reported by Ueda et al (17). The clearance rate of a contrast medium is dependent upon its quality (molecular weight and protein binding rate), filter (material, type, and membrane area), and flow rate parameters (Q_B, Q_F, and Q_D). In the present study, the rate of iomeprol clearance by HF and by HDF was inferior to that by HD. This result was attributed to the following : 1) Q_B, Q_D, and Q_F of HF and HDF were set at low levels similar to CHF and CHDF cases ; and 2) a hemofilter with a smaller membrane area was used.

Despite the fact that newly developed low-osmolar and non-ionic contrast media affect renal function to a lesser extent and are better tolerated than conventional media (1-4), acute renal failure caused by these new contrast media has been reported (28, 29). The incidence of renal damage after angiographic procedures was reported to be over 20% in patients with a serum creatinin above 2mg/dl (30-32) and over 70% in diabetes mellitus patients with an abnormal renal function (33, 34). For this renal damage, standard conservative prophylactic therapies are not effective (32, 33, 35). Moon et al. reported that no further impairment of renal function was observed following the use of HD in any of 7 high-risk patients of developing contrast media nephropathy : serum creatinin above 4.5 mg/dl in 7 patients, diabetes mellitus in 5 patients, hypertension in 6 patients (36). They suggested that accelerated elimination of contrast media by prophylactic HD can be benefical in preventing further reduction in renal function after angiographic procedures in high-risk patients. On the other hand, Younathan et al. reported that after examinations with contrast media performed between regular HD in end-stage renal disease, there was no significant change in blood pressure, ECG, total serum protein, osmolarity, extracellular fluid volume, or body weight (37). They concluded that immediate dialysis after administration of non-ionic contrast agents is not necessary.

Continuous intra-arterial administration of a protease inhibitor to patients with severe acute necrotic pancreatitis has been used as an effective therapy (38, 39). However, it is necessary to confirm the necrotic area of the pancreas with contrasted CT before conducting this therapy, and the use of a contrast medium carries the risk of exacerbating renal function and necrosis of the pancreas (9, 10). The effects of contrast media on patients and experimental animals have not been examined in sufficient detail. The effects of accelerated elimination of contrast media by prophylactic blood purification therapies on necrotic lesions have not been examined. It is, therefore, necessary not only to investigate the effects of contrast media on patients and experimental animals but also to determine the time points and rates at which they should be removed from blood after administration. Furthermore, randomized control studies should be performed to evaluate the benefical effects of early contrast media removal in preventing side effects of contrast media .

We consider that HDF, at low flow rates with a small membrane area hemofilter, is a method which has less effect on hemodynamics and, as such, can

remove contrast media more safely in patients with unstable hemodynamics than HD and more effectively than HF. We found that the contrast medium-removing ability of HF and HDF, at low flow rates with a small membrane area hemofilter, is never superior to that of HD. However, the contrast medium-removing ability of HF and HDF would probably be improved, as compared with the result of the present study, by setting the blood flow rate, dialysate flow rate, and replacement fluid flow rate higher and by using a hemofilter with a larger membrane area. It is generally felt that opportunities to use contrast media for patients with renal function disorders or necrotic lesions will increase and that contrast media will be used more frequently for patients with unstable hemodynamics. We consider that it is possible to remove contrast media more safely and effectively by selecting the blood purification therapy most suited to a particular pathological process.

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REFERENCES

1. Harvey LA, Caldicott WJ, Kuruc A : The effect of contrast media on immature renal function. Comparison of agents with high and low osmolality. Radiology 148 : 429-432, 1983
2. Tornquist C, Holtas S : Renal angiography with iohexol and metrizoate. Radiology 150 : 331-334, 1984
3. Galloti A, Uggeri F, Favilla A, Cabrini M, de Haen C : The chemistry of iomeprol and physico-chemical properties of its adequeous solution and pharmaceutical formulations. Eur J Radiol 18 Suppl 1 : S 1-12, 1994
4. Cipolla P, Tirone P, Luzzani F, de Haen C : Pharmacodynamic effects of iomeprol for injection in experimental animals. Eur J Radiol 18 Suppl 1 : S 32-42, 1994
5. Vaillant L, Pengloan J, Blanchier D, de Muret A, Lorette G : Iododerma and acute respiratory distress with leucocytoclastic vasculitis following the intravenous injection of contrast medium. Clin Exp Dermatol 15 : 232-233, 1990
6. Berkseth RO, Kjellstrand CM : Radiologic contrast-induced nephropathy. Med Clin North Am 68 : 351-370, 1984
7. Smith HJ, Levorstad K, Berg KJ, Rootwelt K, Sveen K : High dose urography with renal failure. A double blind investigation of iohexol and metrizoate. Acta Radiol Diag 26 : 213-220, 1985.
8. Rosati G : Clinical pharmacology of iomeprol. Eur J Radiol 18 Suppl 1 : 51-60, 1994
9. Foitzik T, Bassi DG, Schmidt J, Lewandrowski KB, Fernandez der Castillo C, Rattner DW, Warshaw AL : Intravenous cvontrast medium accentuates the severity of acute necrotizing pancreatitis in rat. Gastroenterology 106 : 207-214, 1994
10. McMenamin DA, Gates LK Jr : A retrospective analysis of the effect of contrast-enhanced CT on the outcome of acute pancreatitis. Am J Gastroenterol 91 : 1384-1387, 1996
11. Quellhorst E, Schuenemann B, Doht B : Hemofiltration -a new method for the treatment of chronic renal insufficiency. Trns Am Soc Artif Intern Organs 23 : 681-682, 1977
12. Leger HW, Wizemann V, Goubeaud G, Rawer P, Schutterle G : Simultaenous hemofiltration/ hemodialysis : an effective alternative to hemofiltration and conventional hemodialysis in treatment of uremic patients. Clin.Nephrol 46 : 115-121, 1978
13. Sprenger KG, Stephan H, Kratz W, Huber K, Franz HE : Optimising of hemodiafiltration with modern membranes?. Contrib Nephrol 46 : 43-60, 1985
14. Schmidt M, Schoeppe W, Baldamus CA : Hemodynamics during hemodialysis with dialyzers of high hydraulic permeability. Contrib Nephrol 46 : 127-133, 1985
15. Kramer P, Bohler J, Kehr A, GroneHJ, Schrader J, Matthaei D, Scheler F : Intensive care potential of continuous arteriovenous hemofiltration. Trans Am Soc Artif Intern Organs 27 : 28-32, 1982
16. Voerman HJ, van Schijndel RJMS, Thijs LG : Continuous arterial-venous hemodiafiltration in critically ill patients. Crit Care Med 18 : 911-914, 1990
17. Ueda J, Furukawa T, Higashino K, Takahashi S, Araki Y, Sakaguchi K : Elimination of iomeprol by hemodialysis. Eur J Radiol23:197-200, 1996
18. Bahlmann J, Kruskemper HL : Elimination of iodine-containing contrast media by haemodialysis. Nephron 10 : 250-255, 1973

19. Evans JR, Cutler RE, Forland SC : Pharmacokinetics of iothalamate in endstage renal disese : J Clin Pharmacol 28 : 826-830, 1988
20. Kitamura E, Itoh T, Okada N, Nakanishi I, Tsubakihara Y, Ida N, Satoh K : Elimination of iohexol, a nonionic, low osmolality radiocontrast agent, by hemodialysis. Tousekikaishi 23:1123-1113, 1990
21. Gibson JG, Rees SB, MCManus TJ and Scheitlin WA : A citrate-phosphate-dextrose solution for the preservation of human blood. Am J Clin Path 28 : 569-578, 1957
22. Bellomo R, Tipping P, Boyce N : Continuous venovenous hemofiltration with dialysis removes cytokines from the circulation of septic patients. Crit Care Med 21 : 522-526, 1993
23. Hirasawa H, Sugai T, Ohtake Y, Oda S, Shiga H, Matsuda K, Kitamura N : Continuous hemofiltration and hemodiafiltration in the management of multiple organ failure. Contrib Nephrol 93, 42-46, 1991
24. Golper TA : Drug dosage adjustment in dialysis patients including continuous ambulatory peritoneal dialysis, the treatments of peritonitis, and continuous arteriovenous hemofiltration. In : Brenner BM, Stein JH, eds. Contemporary Issues in Nephrology 17, Churchill Livingstone, New York, 1987, pp.21-48
25. Baldamus CA, Pollok M : Ultrafiltration and hemofiltration. In : Maher JF,eds. Replacement of Renal Function by Dialysis. Practical Applications. Kluwer Academic Publishers, Dordrecht, 1989, pp 327-346
26. Henderson LW : Biophysics of ultrafiltration and hemomfiltration. In : Maher JF, ed. Replacement of Renal Function by Dialysis. Kluwer Academic Publishers, Dordrecht, 1989, pp 300-326
27. Floege J, Granolleras C, Deschodt G, Heck M, Baudin G, Branger B, Tournier O, Reinhard B, Eisenbach GM, Smeby LC : High-flux synthetic versus cellulosic memranes for β2-globulin removal during hemodialysis, hemomdiafiltration and hemmofitration. Dial Transplant 4 : 653-657, 1989
28. Edgren J, Laasonen L, Crcop PH, Groop L : Iohexol and metrizoate in urography of insulin-dependent patients. Acta Radiol Diagn 27 : 265-267, 1986
29. Cavaliere G, Arrigo C, D'Amico G, Bemasconi P, Schiavina C, Dellafiore L, Vergnaghi D : Tubular nephrotoxicity after intravenous urography with ionic high-osmolal and nonionic low-osmolal contrast media in patients with chronic renal insufficiency. Nephron 46 : 128-133, 1987
30 D'Elia JA, Gleason RE, Alday M, Malarick C, Godley K, Warram J, Kaldany A, Weinrauch LA : Nephrotoxicity from angiographic contrast material : A prospective study. Am J Med 72 : 719-725, 1982
31. Taliercio CP, Vlietstra RE, Fisher LD, Burnett JC : Risks for renal dysfunction with cardiac angiography. Ann Intern Med l04 : 501-504, 1986
32. Martin-Paredero V, Dixon SM, Baker JD, Takiff H, Gomes AS, Busuttil RW, Moore WS : Risk of renal failure afler major angiography. Arch Surg 118 : 1417-1420, 1983
33. Shafi T, Chou SY, Porush JG, Shapiro WB : Infusion intravenous pyelography and renal function. Arch Intern Med 138 : 1218-1221, 1978
34. Harkonen S, Kjellstrand CM : Exacerbation of diabetic renal failure following intravenous pyelography. Am J Med 63 : 939-946, 1977
35. Manske CL, Sprafka JM, Strony JT, Wang Y : Contrast nephropathy in azotemic diabetic patients undergoing coronary angiography. Am J Med 89 : 615-620, 1990
36. Moon SS, Back SE, Kurkus J, Nilsson-Ehle P : Hemodialysis for elimination of the nonionic contrast medium iohexol after angiography in patients with impaired renal function. Nephron 70 : 430-437, 1995
37. Younathan CM, Kaude JV, Cook MD, Saw GS, Peterson JC : Dialysis is not indicated immediately after administration of nonionic contrast agents in patients with end-stage renal disease treated by maintenance dialysis. Am J Roentgenol 163 : 969-971, 1994
38. Takeda K, Kakugawa Y, Kobari M, Matuno S : Continuous arterial infusion of protease inhibitor for severe acute pancreatitis. Gastroenterol Jpn 24 : 340, 1989
39. Takeda K, Matuno S, Sunamura M, Kakugawa Y. Continuous regional arterial infusion of protease inhibitor and antibiotics in acute necrotising pancreatitis. Am J Surg 11 : 394-398, 1996