Continuous haemodiafiltration during and after cardiopulmonary bypass in renal failure patients

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Purpose: Continuous haemodiafiltration (CHDF) is a technique enhancing the efficiency of solute clearance of continuous haemofiltration by infusing dialysis fluid through the haemofilter. It has been reported to control water and electrolyte balance continuously without haemodynamic instability in critically ill patients with renal failure. Therefore, we used CHDF during and after cardiopulmonary bypass (CPB) in two renal failure patients, and discuss its efficacy.

Clinical features: The first patient undergoing aortic valve replacement had dialysis-dependent renal failure. Chronic renal failure in the second patient undergoing mitral valve replacement and coronary revascularization was controlled preoperatively with diuretics. In both cases, CHDF was performed not only during CPB but also in the post-CPB period. Serum concentrations of potassium, urea and creatinine were well-controlled in spite of large amount of blood transfused in the post-CPB period (1000 ml fresh blood and 400 ml fresh frozen plasma in the fist patient, and 1400 ml fresh blood in the second patient). There was no difficulty in haemostasis during the use of nafamostat mesilate as an anticoagulant to keep activated clotting time at about 150 sec for CHDF in the post-CPB period.

Conclusion: Our initial experiences of CHDF during and after CPB suggest that the technique provides excellent electrolyte, metabolite and fluid management for the cardiac patients with chronic renal failure. Combined with nafamostat mesilate for anticoagulation, CHDF was simple and safe and did not increase the risk of bleeding.

Objectif : La technique de l'hémodiafiltration continue (HDFC) permet d'améliorer la clairance du soluté d'hémofiltration continue en perfusant le liquide de dyalise à travers un hémofiltre. Cette technique pourrait contrôler l'équilibre hydroélectrolytique en continu sans provoquer d'instabilité hémodynamique chez les insuffisants rénaux graves. L'utilisation de l'HDFC chez deux insuffisants rénaux pendant et après la circulation extracorporelle (CEC) nous offre l'occasion d'en discuter l'efficacité.

Éléments cliniques : Le premier patient opéré pour un remplacement valvulaire aortique souffrait d'une insuffisance rénale nécessitant dyalise. L'insuffisance rénale chronique du deuxième patient soumis à un remplacement valvulaire mitral et à une chirurgie de revascularisation myocardique était contrôlée en préopératoire par des diurétiques. Dans les deux cas, nous avons utilisé l'HDFC non seulement avant mais aussi après la CEC. Nous avons réussi à contrôler les concentrations sériques du potassium, de l'urée et de la créatinine malgré les grandes quantités de sang transfusées à la période post-CEC (1 000 ml de sang frais et 400 ml de plasma frais congelé pour le premier patient et 1 400 ml de sang frais pour le second patient). L'hémostase s'est maintenue pendant l'anticoagulation au mésilate de nafamostat administré à la période post-CEC de façon à conserver sous HDFC un temps de coagulation à 150 s environ.

Conclusion : Nos essais initiaux avec l'HDFC suggèrent que cette technique procure un excellent contrôle hydroélectrolytique et métabolique chez le patient cardiaque atteint d'insuffisance rénale chronique. Associée au mésilate de nafamostat pour l'anticoagulation, l'HDFC s'est avérée sécuritaire et n'a pas augmenté le risque de saignement.

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PATIENTS with chronic renal failure (CRF) have many coexistent complications such as hypertension, arteriosclerosis, fluid and electrolyte imbalance, anaemia and platelet dysfunction.[1] As cardiovascular complications are the cause of death in 50 to 65% of patients with CRF,[2] they are frequently candidates for open heart surgery. The CRF patient dependent on haemodialysis (HD) lacks compensatory mechanisms to respond to fluid and potassium loads.[3] Therefore, perioperative fluid and electrolyte management should be performed carefully when they undergo cardiac surgery with cardiopulmonary bypass (CPB). Several reports[3–6] indicated that HD or ultrafiltration during CPB may be useful in optimizing fluid, electrolyte and metabolic status in the CRF patients. However, there are no reports of post-CPB fluid, metabolite and electrolyte management despite the difficulties in the post-CPB period. Continuous haemodiafiltration (CHDF) is a technique enhancing the efficiency of solute clearance of continuous haemofiltration (CHF) by infusing dialysis fluid through the haemofilter.[7] It has been reported to be effective and safe for the treatment of acute renal failure in critically ill patients and its major advantage is the continuous control of water and electrolyte balance without haemodynamic instability.[8–10] Continuous haemodiafiltration may provide easier maintenance of fluid, metabolite and electrolyte balance with minimal haemodynamic adverse effects not only during CPB but also after the termination of CPB. Although Hong *et al.*[11] suggested that CHDF may be useful in patients who suffered from acute renal failure after open heart surgery, there are no reports of the use of CHDF during and after CPB for patients with chronic renal failure.

Therefore, we report its usefulness for fluid, metabolite and electrolyte management in two patients with CRF undergoing cardiac surgery.

Case reports

Case #1

A 43-yr-old woman with HD-dependent CRF caused by systemic lupus erythematosus had aortic stenosis. Her weight and body surface area were 33 kg and 1.19 m^2 respectively. She suffered a recent episode of congestive heart failure and was admitted for aortic valve replacement. Preoperative catheterization showed a cardiac output of 4.1 $l \cdot min^{-1}$ and a pressure gradient between the left ventricle and the aorta of 68 mmHg. The CRF and congestive heart failure were managed with HD three times a week, until the day before operation. Anaesthesia was induced with 60 $\mu g \cdot kg^{-1}$ midazolam and 12 $\mu g \cdot kg^{-1}$ fentanyl, and maintained with 30 $\mu g \cdot kg^{-1}$ fentanyl and isoflurane 0.25–0.75% in oxygen and air. Muscle relaxation was provided with vecuronium bromide as needed. Before CPB started, only 200 ml of potassium free solution were administered. Cardiopulmonary bypass was achieved with a disposable membrane oxygenator and the prime consisted of 800 ml whole blood, 400 ml fresh frozen plasma, 200 ml mannitol 20% and 200 ml glucose 5% solution to maintain an haematocrit of 24%. The cardioplegic solution included potassium at a concentration of 24 $mmol \cdot l^{-1}$. Total pump time was 220 min. After the start of the CPB, CHDF was induced with a haemoconcentrator using polypropylene membrane (HC-100M®, Senko Medical Instrument Manufacturing Co Ltd, Tokyo) and a roller blood pump at a blood flow of 200 $ml \cdot min^{-1}$. The dialysate (Na^+: 140 $mmol \cdot l^{-1}$, K^+: 2.0 $mmol \cdot l^{-1}$, Cl^-: 111.0 $mmol \cdot l^{-1}$, Ca^{2+}: 3.5 $mmol \cdot l^{-1}$, Mg^{2+}: 1.0 $mmol \cdot l^{-1}$, CH_3COO^-: 3.5 $mmol \cdot l^{-1}$, HCO_3^-: 35.0 $mmol \cdot l^{-1}$, glucose: 100 $mg \cdot dl^{-1}$) (Sublood-B®, Fukuwa Pharmaceutical Co Ltd, Osaka) was connected to a volumetric pump which delivered dialysate to the dialysate compartment of the haemoconcentrator. The dialysate flow was countercurrent to blood at a rate of 500 $ml \cdot hr^{-1}$. The CHDF circuit was connected between the shunt line and the reservoir of the extracorporeal circuit (Figure 1). Blood was taken from the shunt line of the extracorporeal circuit to the haemoconcentrator and then back to the reservoir by a separate roller pump. Diafiltrated fluid was obtained by a vacuum (−20 kPa). The electrolyte concentrations of diafiltrated fluid were similar to those of the plasma. The total amount of diafiltrated fluid during CPB was 2,850 ml. After the termination of CPB following heparin neutralization

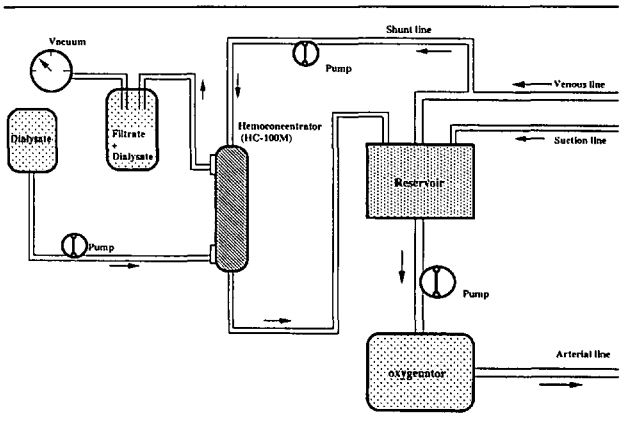

FIGURE 1 Haemodiafiltration circuit during cardiopulmonary bypass. The circuit was connected between the shunt line and the reservoir of extracorponeal circuit. Blood was taken from the shunt line of the extracorponeal circuit to the haemoconcentrator and then returned to the reservoir by a separate roller pump.

with protamine sulfate, the CHDF circuit was separated from the extracorporeal circuit, and then connected to another circuit (CHF-201®, Asahi Medical Co Ltd, Tokyo) primed with saline (Figure 2). At the same time, venous access was established via the left femoral vein with a 11 Fr double-lumen catheter for veno-venous CHDF at a blood flow of 60–80 ml·min^{-1}. Nafamostat mesilate (Futhan®, Torii Pharmaceutical Co Ltd, Tokyo), an anticoagulant, was administered at a rate of 5–7 μg·kg^{-1}·min^{-1} via the venous line to keep activated clotting time (ACT) around 150 sec. No difficulty in haemostasis was seen during infusion of nafamostat mesilate. The amount of diafiltrated fluid controlled by a vacuum producing negative pressures between 0 and −20 kPa was 2,200 ml from CPB termination to the end of surgery. Blood loss after the end of CPB was 370 ml. Fresh blood 1,000 ml and fresh frozen plasma 400 ml were given to maintain blood volume and haematocrit during the 150 min of post-bypass period. The serum concentrations of potassium, urea and creatinine (Table) were well-controlled with CHDF. The patient was transferred to intensive care unit with good cardiac function.

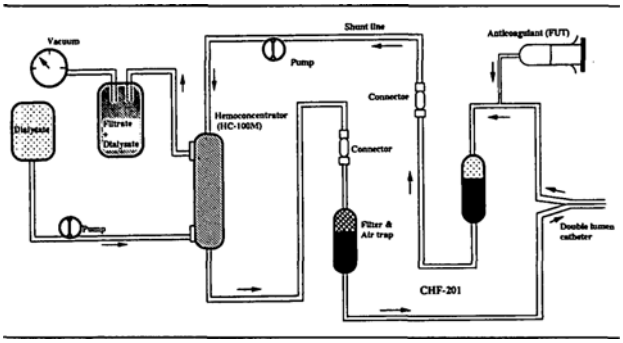

FIGURE 2 Haemodiafiltration circuit after cardiopulmonary bypass. After the termination of CPB, the circuit was separated from the extracorporeal circuit, and connected to another circuit primed with saline. At the same time, a venous line was established to the left femoral vein with a 11 Fr double-lumen catheter for veno-venous continuous haemodiafiltration.

Case #2

A 73-yr-old man was admitted after an acute episode of angina pectoris. The weight and body surface area were 54 kg and 1.53 m^2, respectively. Heart catheterization revealed mitral regurgitation (Grade III), coronary stenosis involving 50% stenosis of the left main coronary artery and 90% stenosis of the circumflex artery, and low cardiac output (2.47 l·min^{-1}). He had had a right nephrectomy due to tuberculosis about 40 yr ago. Although creatinine clearance was 6 ml·min^{-1}, the patient had been treated only with diuretics (40 mg·day^{-1} furosemide, 25 mg·day^{-1} spironolactone). Mitral valve replacement and coronary artery revascularization were performed. Anaesthesia, cardioplegia and CHDF were managed in the same way as in #1. In the pre-CPB period, 940 ml potassium-free solution and 40 mg furosemide were administered *iv* to prevent oliguria. Cardiopulmonary bypass was achieved with a disposable membrane oxygenator with a prime of 600 ml whole blood, 200 ml albumin 20%, 300 ml mannitol 20%, 300 ml glucose 5% solution and 1,000 ml hetastarch 6% solution. At the start of the CPB, CHDF was started as above. Furosemide (100 mg) was also administered. Total pump time was 222 min, urine output and total amount of diafiltrated fluid during CPB was 230 ml and 3,150 ml, respectively. At the end of CPB, CHDF was performed with continuous infusion of 6–8 μg·kg^{-1}·min^{-1} nafamostat mesilate keeping ACT around 150 sec. No difficulty in haemostasis was observed during infusion of nafamostat mesilate. Fresh blood was also given to maintain optimal levels of arterial blood pressure

TABLE Changes in serum concentrations of potassium, urea, creatinine and haematocrit.

	Anaes 0 hr	*CPB 0 hr*	*A-declamp*	*PCPB 0 hr*	*PCPB 1 hr*	*ICU*
K^+ (mmol·l^{-1})						
Case #1	3.9	3.6	3.5	4.5	4.0	4.1
Case #2	5.1	4.2	3.6	4.8	4.0	3.9
Urea (mg·dl^{-1})						
Case #1	35	31	27	26	27	28
Case #2	29	19	22	22	21	21
Creatinine (mg·dl^{-1})						
Case #1	4.5	3.4	3.2	3.0	3.0	3.3
Case #2	4.5	2.8	3.0	3.0	3.0	3.1
Haematocrit (%)						
Case #1	30.1	22.2	18.4	20.3	28.3	29.0
Case #2	29.0	13.8	15.6	17.2	25.8	32.5

Anaes 0 hr: before induction of anaesthesia, CPB 0 hr: immediately after cardiopulmonary bypass started, A-declamp: just before declamping of the aorta, PCPB 0 hr: just before CPB terminated, PCPB 1 hr: one hour after CPB terminated, ICU: immediately after ICU admission.

and haematocrit. The total amount of blood transfused was 1,400 ml during 120 min of post-CPB period. Urine output and total amount of diafiltrated fluid after CPB terminated were 340 ml with furosemide *iv* (total 100 mg) and 1,450 ml, respectively. The total amount of post-CPB blood loss was 447 ml. The serum potassium, urea and creatinine concentrations were well-maintained with CHDF (Table). The patient was transferred to intensive care unit with good cardiac function.

Discussion

Continuous haemodiafiltration is a widely accepted dialytic method in critically ill patients with renal failure.[7–10] It is as effective as continuous haemofiltration (CHF), but without the haemodynamic instability. It provides better clearance of solute than CHF by infusing dialysis fluid through the haemofilter counter current to the blood flow.[7] Continuous haemofiltration requires a large volume of replacement fluid to remove the inadequate solute, and has been reported not to be an ideal form of therapy in the treatment of acute hyperkalaemia.[12] Other dialytic methods such as haemodialysis and peritoneal dialysis may not be suitable for patients undergoing open heart surgery as conventional haemodialysis may cause haemodynamic instability due to the rapid and massive removal of fluid and solute, and peritoneal dialysis is less effective and respiratory depression may be caused by the large volume of dialysate which displaces the diaphragm upwards.[11,13] Therefore, we considered that post-CPB management of electrolyte, metabolite and fluid with CHDF would be easier, and used CHDF for the patients not only during CPB but also after CPB. Although blood was transfused after CPB to maintain optimal haematocrit and left ventricular filling pressure in both cases, pulmonary congestion and hyperkalaemia, which are relatively common complications in patients with renal failure during the post-bypass period, did not occur.

Anticoagulant-induced bleeding, a serious complication of CHF[14] or CHDF,[11] may limit the use of CHDF during operation. However, there was no difficulty in haemostasis in two cases during CHDF with nafamostat mesilate, a synthetic serine protease inhibitor, as an anticoagulant. Its anticoagulant activity is due to inhibitory effects on endogenous clotting factors (FXIIa, FXa and thrombin) and not by binding to antithrombin III like heparin.[15] Nafamostat mesilate has been used during extracorporeal circulation in patients with a high risk of bleeding.[16,17] Ohtake and his colleagues compared the incidence of bleeding complications during CHF and CHDF among various anticoagulants.[16] They found that the incidences of bleeding with heparin, low molecular weight heparin and nafamostat mesilate were 67, 29 and 4%, respectively. Akisawa *et al.* also reported that, in 107 haemodialysis patients with high risk for intradialytic bleeding, the exacerbation of bleeding by haemodialysis with nafamostat mesilate was noted in only 3.7%.[17] This low risk of bleeding with the use of nafamostat mesilate may be explained by its short half-life time (5–8 min) producing increased clotting times only in the extracorporeal circuit.[16] These studies strongly suggest that CHDF using nafamostat mesilate even during surgical procedures could be performed without the risk of massive bleeding.

Clotting formation and haemolysis are expected as the problems associated with the increased circuitry and machinery required in CHDF during post-CPB period. Matsuo *et al.* reported that nafamostat mesilate was less effective than heparin in suppressing thrombin generation.[15] Therefore, although we did not experience it, attention should be paid to clot formation during CHDF with nafamostat mesilate: ACT should be checked frequently (hourly after CPB) and be kept >150 sec by controlling the infusion rate of nafamostat mesilate. The length of CHDF circuit should also be minimal and the filter trapping the clots had better be applied in the venous chamber.

Recently, it has been reported that continuous intravenous infusion of nafamostat mesilate may cause hyperkalaemia in patients with pancreatitis and disseminated intravascular coagulation.[18] The mechanism is thought to be due to decrease in urinary potassium excretion, suppression of aldosterone secretion, direct action on the apical membrane of the collecting duct cells and inhibition of potassium influx to erythrocyte.[19] Moreover, Ookawara *et al.* reported that a patient suffering from acute renal failure showed hyperkalaemia during haemodiafiltration using nafamostat mesilate.[20] However, hyperkalaemia is probably rare during haemodiafiltration as potassium is removed continuously, and the incidence of hyperkalaemia during extracorporeal circulation using nafamostat mesilate is only 0.02%, compared with 4.53% and 0.19% in the treatment of disseminated intravascular coagulation and pancreatitis, respectively. (Unpublished data, from Torii Pharmaceutical Co Ltd, Japan).

In conclusion, our initial experiences of CHDF during and after CPB suggest that the technique provides excellent fluid, metabolite and electrolyte management for patients undergoing cardiac surgery without the risk of bleeding.

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