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The haemodynamic effects of intermittent haemofiltration in critically ill patients

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Abstract. The haemodynamic effects of intermittent high volume venovenous haemofiltration were studied in 13 critically ill patients. The mean negative fluid balance during filtration was 1.2 l and the mean duration of treatment 3 h 40 min. The cardiac index fell initially (4.5 ± 0.2 to 3.8 ± 0.2 l/min/m^2; $p < 0.05$) but then remained stable throughout treatment before returning to baseline at the end of haemofiltration. The mean arterial pressure was unchanged with an increase in the systemic vascular resistance (651 ± 33 to 765 ± 65 dyne·s/cm^5; $p < 0.05$) suggesting that vascular responsiveness is maintained during haemofiltration.

Key words: Acute renal failure – Haemofiltration – Oxygen transport

The adverse haemodynamic effects, particularly hypotension, of intermittent haemodialysis have prompted interest in other techniques of renal replacement therapy for critically ill patients. These techniques usually involve haemofiltration which has been shown to be associated with greater haemodynamic stability in patients with chronic renal failure [1, 2]. There has, however, been little attempt to study the haemodynamic effects of haemofiltration in critically ill patients with multiple organ failure. These patients are especially prone to cardiovascular instability and are particularly vulnerable to its consequences. We therefore prospectively studied the haemodynamic responses to high volume haemofiltration (HVHF) in 13 such patients.

Methods

After approval by the local Ethics Committee, 13 patients undergoing intermittent, pump driven high volume venovenous haemofiltration were each studied on one occasion. Clinical details of the patients, including admission APACHE II scores, are given in Table 1. Haemofiltration was undertaken as treatment for acute renal failure in 11 patients and in an attempt to improve gas exchange in 2 patients with severe ARDS. The patients were all sedated with an infusion of papaveretum and receiving full mechanical ventilation. They all had arterial cannulae and thermodilution pulmonary artery catheters in situ for routine clinical monitoring. In all patients cardiovascular status had been optimised using fluids and catecholamines as appropriate. The aim of this therapy was to achieve the goals (CI > 4.5 l/min/m^2, DO2 > 600 ml/min/m^2 and VO2 > 170 ml/min/m^2) advocated by Shoemaker for critically ill patients [3], while maintaining a mean arterial pressure (MAP) of greater than 70 mm·Hg.

The study period was from immediately before haemofiltration commenced until one hour after its termination. During this period, other interventions were avoided if possible. There were no changes to sedation or to ventilator settings. No patient received additional fluids although all continued to receive maintenance fluids, including enteral or parenteral nutrition, at an unchanged rate of between 80 and 100 ml/h. Catecholamine infusions, which are detailed in Table 2, were unaltered in 12 patients. The dose of dobutamine was increased from 35 to 40 μg/kg/min towards the end of the period of haemofiltration in patient 2.

Table 1. Haemodynamic effects of haemofiltration: patient details

No.	Age	Sex	Apache	Diagnosis	Outcome
1	63	M	20	*Pneumocystis pneumonia*; ARDS	Died
2	80	M	33	*Staph. pneumonia*; ARDS septic shock	Died
3	71	M	28	*Staph. septicaemia*; septic shock; ARDS	Died
4	53	F	27	Pneumococcal pneumonia; septic shock; ARDS	Died
5	73	M	30	Septic shock; ARDS	Died
6	67	M	43	Pneumococcal pneumonia; septic shock; ARDS	Died
7	59	M	32	*Strep. septicaemia*; septic shock	Survived
8	40	M	32	Paracetamol overdose; fulminant hepatic failure	Died
9	81	M	29	Bowel infarction; septic shock; ARDS	Survived
10	63	F	43	Rhabdomyolysis; shock	Survived
11	68	F	29	Pulmonary TB; ARDS	Died
12	52	F	23	Pneumococcal septicaemia; pneumonia; ARDS	Survived
13	80	M	32	Septic shock; ARDS	Survived

Table 2. Details of haemofiltration treatments studied

No.	Catecholamine (dose μg/kg/min)	Duration (h)	Fluid exchange (l)	Net fluid removal (l)	Overall balance (l)	Pre		Post
						Urea (mmol/l)	Creatinine (μmol/l)	Urea (mmol/l)
1	Dopamine 3	4.00	17	2.5	−2.1	35.3	360	34.1
2	Dobutamine 35−40	3.30	17	0.5	−0.1	38.1	440	29.6
3	Dobutamine 20 Noradrenaline 0.6	6.30	24	2.0	−1.4	29.3	550	22.5
4	Dobutamine 15 Dopamine 2	4.00	17	1.01	−0.7	22.00	690	16.9
5	Adrenaline 0.15 Noradrenaline 0.6	2.20	12	1.5	−1.25	35.3	542	25.3
6	Adrenaline 0.25 Noradrenaline 0.3	3.00	17	1.5	−1	33.4	580	29.5
7	Dobutamine 15	4.50	17	1.5	−1	29.2	590	19.0
8	Dopamine 3	3.30	14	2.0	−1.7	43.7	960	25.9
9	Adrenaline 0.15	3.45	17	2.0	−1.6	37.7	670	27.4
10	None	2.30	13	1.0	−0.8	25.4	430	18.9
11	Dobutamine 10 Noradrenaline 0.15	4.00	13	1.5	−1.4	13.6	50	Post filtration values not measured for patients not in renal failure
12	Dopamine 10 Noradrenaline 0.03	3.00	13	2.0	−2.0	7.0	25	
13	Adrenaline 0.1	3.00	10	1.0	−0.8	33.7		26.7

Table 3. Effects of haemofiltration of haemodynamics and oxygen transport (mean ± SEM)

	Pre	1 h	2 h	3 h	Post	Probability	
						Pre: 1 h	Pre: post
HR	110 ± 5	107 ± 5	103 ± 6	108 ± 6	106 ± 5	NS	NS
CVP (mmHg)	15 ± 1.4	13 ± 1.4	13 ± 1.6	16 ± 1.1	15 ± 1.7	$p<0.01$	NS
PAOP (mmHg)	14 ± 1.1	12 ± 1.4	12 ± 1.7	16 ± 1.3	12 ± 1.4	NS	NS
CI (l/min/m^2)	4.5 ± 0.2	3.8 ± 0.2	4.0 ± 0.3	3.8 ± 0.2	4.3 ± 0.2	$p<0.05$	NS
MAP (mmHg)	81 ± 3.5	76 ± 3.3	75 ± 3.7	79 ± 4.4	80 ± 3.4	NS	NS
SVR (dynes·s·cm^{-5})	651 ± 33	765 ± 65	713 ± 38	750 ± 37	682 ± 48	$p<0.05$	NS
DO_2 (ml/min/m^2)	684 ± 33	605 ± 55	668 ± 56	606 ± 39	651 ± 41	NS	NS
VO_2 (ml/min/m^2)	152 ± 9	145 ± 10	138 ± 11	161 ± 6	151 ± 7	NS	NS
Qs/Qt (%)	32 ± 2.8	28 ± 3.0	32 ± 3.4	28 ± 3.4	31 ± 2.4	$p<0.01$	NS

Haemofiltration was performed using a Gambro AK10 system with a FH-77 hollow fibre filter and vascular access through a double lumen catheter in a subclavian or internal jugular vein. A blood flow rate of 200−300 ml/min and transmembrane pressure of 300−400 mmHg, were used to achieve an initial filtration rate of 100−120 ml/min. The filtration rate tended to decline as treatment progressed, and was in the region of 70−80 ml/min by the end of some treatments. Anticoagulation was with heparin administered in the afferent limb of the circuit to achieve an ACT 30 s above baseline or greater than 180 s. The replacement fluid was Haemofiltrasol 22 (Gambro) (Na^+ 140 mmol/l, Ca^{++} 1.6 mmol/l, Mg^{++} 0.75 mmol/l, Cl^- 100 mmol/l, lactate 45 mmol/l) with potassium added as required. Details of the treatment for each patient are given in Table 2. The mean duration of treatment was 3 h 40 mins (range 2 h 20 min − 6 h 30 min), the mean volume exchanged 15.5 l (10−24 l) and mean volume of fluid removed 1.6 l (0.5−2.5 l). This resulted in a negative fluid balance, allowing for maintenance fluids of 1.2 l (range 0.1−2.1 l).

Immediately before the start of haemofiltration, heart rate, mean arterial pressure (MAP), mean central venous pressure (CVP), mean pulmonary artery pressure (MPAP) and end expiratory pulmonary artery occlusion pressure (PAOP) were recorded. Cardiac output was measured by thermodilution (average of 3 injections of 10 ml ice-cold 5% glucose). Cardiac index (CI) and systemic vascular resistance (SVR) were calculated using standard formulae. In 10 of the 13 patients, simultaneous samples of arterial and mixed venous blood were also taken. These were analysed for oxygen tension (PO2), oxygen saturation (SO2), carbon dioxide tension (PCO2), hydrogen ion concentration ($[H^+]$) and haemoglobin concentration using a Corning 278 blood gas analyser and Corning 2500 co-oximeter. In these patients, oxygen delivery (DO2), oxygen consumption (VO2) and shunt fraction Qs/Qt) were calculated from standard formulae. All measurements were repeated hourly during haemofiltration and again 1 h after cessation of haemofiltration. Statistical analysis was by a Wilcoxon signed rank test comparing pretreatment values with those at each hour during treatment and following treatment.

Results

The responses of the 11 patients treated for acute renal failure and the 2 treated for ARDS were similar and therefore the results are presented for all patients together. They are summarised in Table 3 and Fig. 1; all values given are means ± SE. There was no significant change in heart rate throughout the study. There was a small fall in both CVP and PAOP early in treatment although only the former was statistically significant ($p<0.01$). Despite a mean fluid removal of 1.6 l and negative fluid balance

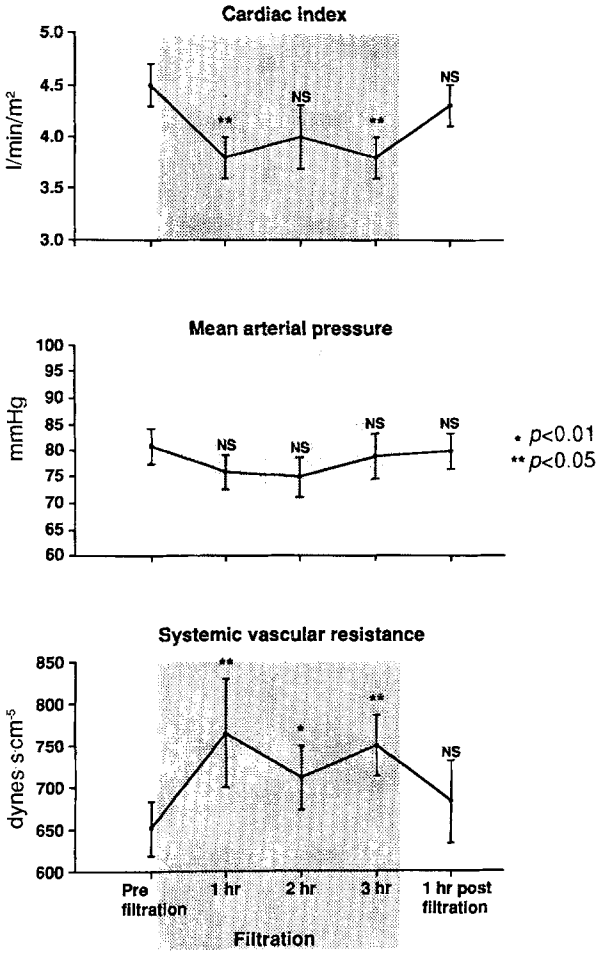

Fig. 1. Effects of haemofiltration on cardiac index, mean arterial pressure and systemic vascular resistance. *$p<0.01$, **$p<0.05$ (vs prefiltration value)

of 1.2 l, the post-treatment filling pressures were not significantly different from baseline values. The CI fell by 15% at the onset of haemofiltration ($p<0.05$), remained at this level during the treatment period and then returned to the baseline value when haemofiltration was discontinued. There was no significant change in MAP at any point in the study. The SVR rose at the start of haemofiltration ($p<0.05$) and remained elevated until the end of treatment when it returned to baseline value (Fig. 1).

In 10 of the 13 patients, data was available to allow the calculation of DO2, VO2 and Qs/Qt. The 11% reduction in DO2 largely paralleled the reduction in CI but fell just short of statistical significance ($p<0.053$). There was no significant change in VO2. Qs/Qt was reduced during treatment ($p<0.01$). All of these values returned to baseline at the end of treatment.

Discussion

The results of this study show that intermittent pump driven high volume veno-venous haemofiltration can be performed safely in appropriately resuscitated critically ill patients. Mean arterial pressure remained stable throughout haemofiltration despite a mean fluid removal of 1.6 l. Cardiac index fell by 15% at the start of haemofiltration and then remained stable before rapidly returning to baseline value after treatment. There was a significant rise in SVR during filtration.

These findings are in keeping with the results of studies carried out in patients undergoing haemofiltration for chronic renal failure in which a number of workers have shown that, in contrast to haemodialysis, haemofiltration is associated with maintenance of blood pressure in the face of fluid removal and a decrease in cardiac output [1, 2].

There have been conflicting reports on the effects of haemofiltration on cardiac output. In patients with chronic renal failure Baldamus and co-workers [1] noted a progressive decline in cardiac output throughout treatment. They also found that, despite a higher noradrenaline clearance during haemofiltration than during haemodialysis, the plasma noradrenaline concentration was actually higher during filtration, suggesting a more appropriate sympathetic response to fluid removal. In contrast Brazilay [4] and co-workers claimed that haemofiltration was associated with an increase in cardiac output in a group of critically ill patients with multiple organ failure and presumed the improvement to be due to removal of toxic mediators. Their study was uncontrolled, over a relatively long time scale and other interventions which they do not discuss in detail were also undertaken concurrently. The precise haemodynamic effects of haemofiltration cannot therefore be confidently inferred from their study.

There are several possible explanations for the reduction in cardiac output which we observed during haemofiltration. We feel it is unlikely to be due simply to fluid removal since the reduction in filling pressures was not large, the reduction in cardiac output was not progressive with increasing fluid removal, and furthermore, it appeared to occur before significant fluid volume was removed. In addition, cardiac output returned to its baseline value after treatment was completed, at a time when fluid loss was greatest. There may be a specific negative inotropic effect of haemofiltration, possibly associated with toxicity of membrane or lactate fluid replacement, or due to removal of catecholamines. As 12 of the 13 patients in our study were receiving catecholamines (Table 2), the latter may be the most likely explanation but we did not measure either clearances or plasma levels and so this is uncertain.

It is possible that the observed haemodynamic responses to haemofiltration depend on the circumstances in which it is carried out. Where an actual haemodynamic benefit is claimed it is usually on the basis of removing mediators [4] and in the early stages of experimental endotoxic shock [5]. None of our patients was in the early stage of their illness in as much as all had established multiple organ failure. It may be that the theoretical haemodynamic benefits of mediator removal are less if haemofiltration is not undertaken at an early stage.

Although the fall in DO2 during haemofiltration did not reach statistical significance ($p = 0.053$), it is likely that there is a true reduction and that it is a consequence

of the reduction in cardiac output. The decline in DO2 of 11% is of slightly lesser magnitude than that in CI because of the fall in Qs/Qt and the consequent improvement in oxygenation. This improvement is in contrast to previously reported findings in haemodialysis [6]. The VO2 did not fall in response to the reduction in DO2.

Haemodynamic instability is common in critically ill patients undergoing renal replacement therapy, particularly haemodialysis. The reasons for this, which are complex and only partially understood, have recently been reviewed [7]. They include changes in circulating volume and in concentrations of electrolytes, other solutes and vasoactive substances, as well as the effect of bio-incompatible membranes, dialysate buffer and the impaired sympathetic response to fluid removal. The use of more bio-compatible membranes and of bicarbonate buffered dialysate have reduced, rather than prevented, this instability during haemodialysis [8–10]. The resulting hypotension may require not only plasma volume expansion but also catecholamine support [11, 12]. These problems have led to interest in continuous techniques [13, 14] and in convective rather than diffusive solute removal.

The use of haemofiltration in two patients of this series with severe ARDS, but without evidence of renal failure was on the basis of presumed inflammatory mediator removal [4]. In one patient it had no effect on outcome, but in the other patient (No 12) it led to an immediate reduction in shunt fraction from 45 to 33% with consequent improvement in oxygenation and ultimate survival.

No technique of renal replacement therapy has been shown to clearly improve outcome. Our 63% hospital mortality for the 11 patients with acute renal failure compares favourably with the 72% reported by Abreo and colleagues [15]. Biochemical and acid base status was satisfactorily controlled in all patients using daily haemofiltration. At present the choice of renal replacement technique depends on local expertise and on weighing up potential side effects of each technique. Continuous techniqes have the attraction of appearing more physiological but do have drawbacks. Suitably experienced staff must be immediately available throughout the 24 h period. The patient must be continuously connected to an extracorporeal circuit which must be anticoagulated. Although prostacyclin may reduce the risks of bleeding associated with heparinisation, its continuous systemic administration may result in adverse haemodynamic and oxygen transport effects [16]. The system requires either a large bore arterial cannula or a continuously running blood pump with attendant risk of disconnection and severe haemorrhage. Fluid balance calculations may be subject to error with the large volumes of filtrate, dialysate and replacement fluid involved.

Intermittent high volume veno-venous haemofiltration avoids many of these logistical problems. It can be undertaken in a few hours allowing continuous close supervision by experienced staff. The use of an automatic weighing machine avoids errors in fluid balance. Despite relatively rapid fluid removal it is well tolerated haemodynamically. The clinical significance of repeated short term reductions in CI and DO2 with regard to perpetuation of organ dysfunction is unclear and requires further investigation. It may be that with close monitoring and short term titration of increased doses of inotrope that these reductions may be avoided. Further studies are also required into the causes of the changes in cardiac output with particular reference to concentrations of catecholamines and possibly to the mediators of multiple organ failure.

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