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THE EFFECTS OF DIFFUSION AND ULTRAFILTRATION ON CARDIAC OUTPUT AND ORGAN BLOOD FLOWS

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Summary

The effects of diffusion and ultrafiltration on cardiac output (CO) and organ blood flow (BF) in the uraemic dog were studied by a modified microsphere technique. In the diffusion phase of sequential therapy, a decrease in mean arterial pressure (MAP) and total peripheral resistance (TPR) was noted despite no change in circulatory plasma volume (CPV) and CO. In the ultrafiltration (UF) phase, MAP recovered with an increase in TPR despite the decrease in CPV and CO. Muscle vascular resistance increased in UF phase but not in the diffusion phase. The results suggest that the decrease in CPV through UF resulted in CO decrease, but that the compensation mechanism for the decrease is impaired by diffusion.

Introduction

Haemodialysis (HD) in chronic renal failure is based on two processes: solute removal by diffusive mass-transfer and fluid removal by ultrafiltration (UF). Symptomatic hypotension and dialysis induced disequilibrium are major adverse reactions of HD. However, much higher fluid removal rates are tolerated when UF and diffusion are separated [1, 2]. We studied the individual and the combined influence of UF and diffusion on cardiac output (CO) and organ blood flow (BF) in the dog.

Materials and methods

Mongrel dogs were anaesthetised with Nembutal® (20–30mg/kg i.v.). A catheter for microsphere injection was placed in the left ventricle through the carotid artery. Femoral artery and vein were cannulated for access for extracorporeal circulation (EC). After bilateral nephrectomy, 2.6 per cent of urea solution in dose of 5 per cent BW was intravenously infused to give dogs the same BUN

values and fluid overload as those of HD patients.

After 30 minutes of EC, four groups, each of five dogs, were studied by the following protocols: 1) Two hour EC only; 2) One hour HD; 3) One hour UF; 4) One hour diffusion followed by one hour isolated UF.

Toray Filtryser A-l-SS with 0.31m^2 of PMMA membrane was used for all experiments. Blood flow was set at 80ml/min. The dialysate composition was as follows: Na^+:139, K^+:3, Ca^+:3.5, Mg^+:1.5, Cl^-:109, Acetate$^-$: 38mEq/L, glucose:200mg/dl with osmolarity:305mOsm/L. Dialysate flow was 100ml/min. At the end of each phase in the four protocols, CO and BF to the organs were determined simultaneously by the modified microsphere method [3, 4]. About 10μCi (about 400,000 beads) of carbonised microsphere (15 ± 3μm) labelled with ^{141}Ce (3M Co., St Paul, Minn.) was administered into the left ventricle and the reference blood was simultaneously withdrawn via the brachial artery at the rate of 10ml/min for one minute. ^{95}Nb labelled and ^{51}Cr labelled microspheres were used for the second and third injections, respectively. After the completion of the protocol the organs were dissected out for radioactivity counting in an autogamma counter (Packard autogamma scinti. spectrometer 5320, USA). Blood chemistry including serum electrolytes was measured by an auto-analyser (Hitachi 716, Japan). All values are expressed as mean ± SE and statistical comparison was made by Student's t-test and paired t-test.

Results

The results of four groups are shown in Table I and Figure 1.

Changes in blood chemistry

In the HD group and the diffusion phase of sequential (Seq) group, serum urea nitrogen (SUN), serum potassium (K) and serum inorganic phosphate (P) significantly decreased while serum calcium (Ca) significantly increased. No change in SUN was seen in UF phase, but slightly significant increase was noted in K, Ca and P. Mean UF volume in the HD and UF groups and in the UF phase of Seq group, in all a significant increase in Hct was noted, were 203ml (1.46% of BW), 250ml (1.83% of BW) and 122ml (1.0% of BW), respectively.

MAP, CO and TPR

MAP, CO and TPR showed no change in the EC phase of each group. MAP significantly decreased in the HD group and the D phase of the Seq group, while no change was seen in other groups. CPV measured with ^{125}I-RISA significantly decreased in the HD and UF groups, and the UF phase of the Seq group. Although CO significantly decreased with the decrease in CPV, it did not show any change in the EC group and D phase of the Seq group. Accordingly, TPR significantly increased in the UF group and the UF phase of the Seq group. TPR also tended to increase in the HD group, but not significantly.

Regional BF (Table I)

Hepatic arterial flow (HAF) was obtained from microspheres trapped in the liver while portal organ blood flow was calculated by adding BFs to the spleen, pancreas

TABLE I. Cardiac output and organ blood flow during extracorporeal circulation, haemodialysis, ultrafiltration, and sequential haemodialysis with ultrafiltration

		EC group		HD group		UF group		Seq group		
		EC	EC	EC	HD	EC	UF	EC	D	UF
CO (ml/min)	Mean	1327	1132	1245	583***	1223	593***	761	781	518*††
	SE	371	334	142	206	193	102	122	75	80
Brain (ml/min)		25.5	20.3	25.7	23.4	21.4	17.2**	12.6	14.4	13.1
		2.7	2.8	3.2	5.9	2.7	2.6	1.9	1.3	1.8
Heart (ml/min)		114.6	110.8	73.0	40.1	80.4	47.0***	56.3	79.7	52.3†††
		33.2	32.4	4.9	10.5	9.8	8.7	13.8	4.5	9.2
Hepatic artery (ml/min)		69.2	40.8	76.2	67.4	109.6	66.7	58.5	134.4***	92.4
		36.7	17.0	39.9	26.8	59.3	18.8	20.4	35.5	31.6
Spleen (ml/min)		49.5	28.3	50.2	4.7**	31.4	9.9*	33.8	27.0	5.6*
		16.9	11.1	10.0	1.6	9.9	5.7	11.1	13.5	2.8
Pancreas (ml/min)		7.3	10.2	7.9	2.0*	8.3	3.5***	4.3	3.3***	1.6*
		2.2	4.4	2.2	0.5	2.4	1.9	0.7	0.6	0.2
Stomach (ml/min)		45.1	45.7	30.2	20.2	55.9	16.1	12.6	19.9*	12.6†††
		14.7	13.9	7.6	8.7	17.3	2.3	1.6	2.5	2.1
Small intestine (ml/min)		154.0	193.1	126.0	53.4	158.2	70.4**	63.4	56.8	46.5**
		40.9	63.4	33.0	16.0	29.6	20.0	7.9	5.5	9.5
Colon (ml/min)		20.1	17.3	23.0	7.9*	34.4	11.5*	17.0	15.8	10.7
		5.8	7.8	4.1	2.9	10.8	2.9	2.6	2.8	3.1
Omentum (ml/min)		21.4	12.3	14.5	3.3	10.5	3.1*	17.0	12.4	5.3†
		8.2	4.6	2.5	1.9	3.9	1.5	6.0	4.0	3.5
Mesentery (ml/min)		12.8	7.1	12.3	3.4*	12.7	4.2***	8.4	6.8	2.0†
		4.4	2.6	1.7	1.9	3.8	2.2	2.3	1.5	0.6
Portal vein (ml/min)		310.2	314.0	261.0	94.2*	311.2	118.6***	156.6	141.8	84.6*
		86.3	104.3	47.0	27.8	61.8	35.1	17.6	18.5	17.4
Muscle (ml/min) per 100g		12.2	7.0	6.7	3.2	4.1	2.0*	7.4	7.5	4.4*†
		4.3	2.4	1.6	1.6	1.3	0.5	0.9	1.2	1.5
Skin (ml/min) per 100g		2.7	2.8	1.0	0.2*	2.0	0.6*	1.0	0.9	0.6†
		0.9	1.5	0.2	0.1	0.7	0.3	0.3	0.1	0.1

* $p < 0.05$; ** $p < 0.02$; *** $p < 0.01$ compared to EC phase. † $p < 0.05$; †† $p < 0.02$; ††† $p < 0.01$ compared to D phase
CO: cardiac output; EC: extracorporeal circulation; HD: haemodialysis; UF: ultrafiltration; Seq: sequential HD and UF

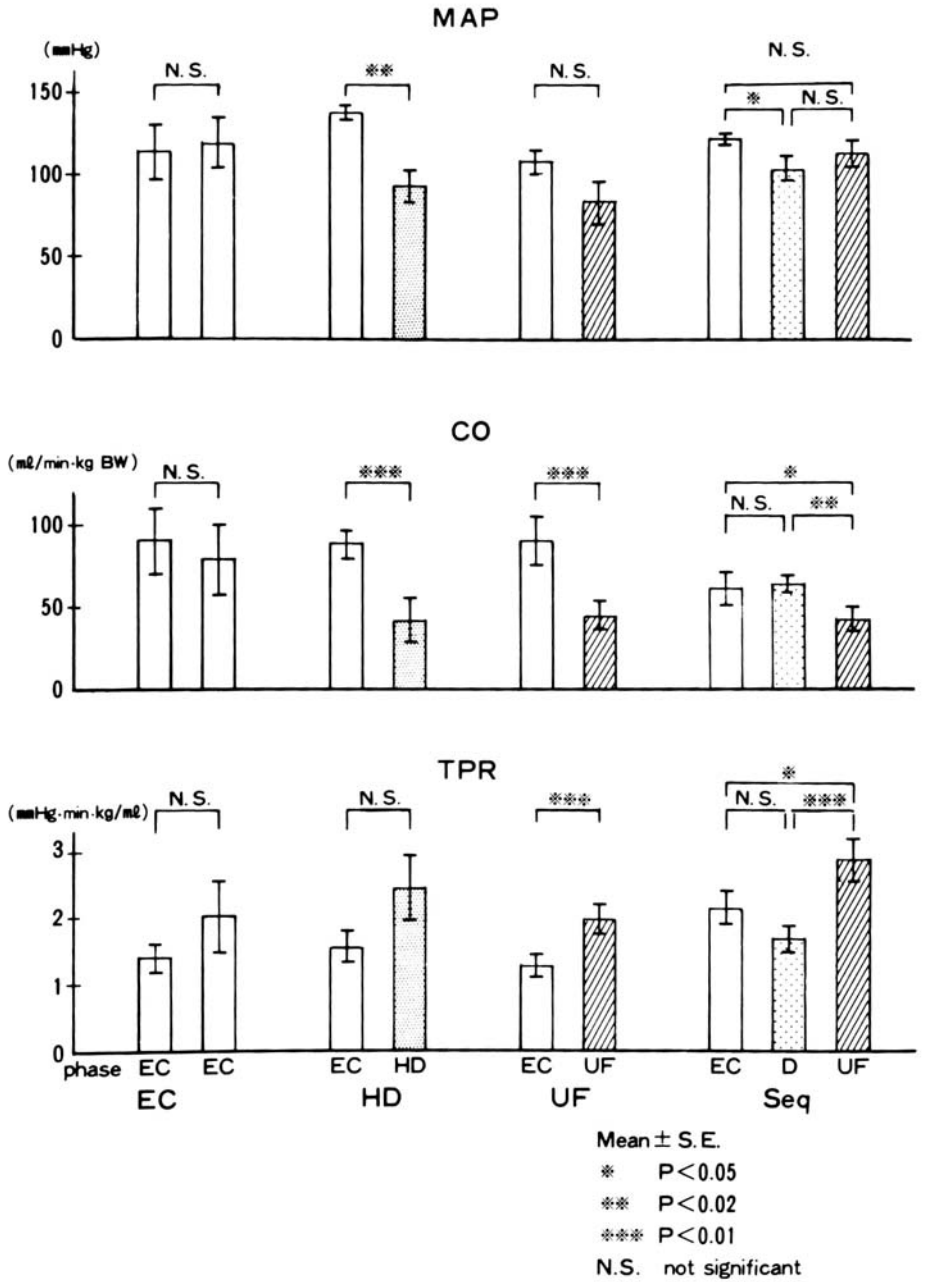

Figure 1. Changes in mean arterial pressure, cardiac output and total peripheral vascular resistance during extracorporeal circulation, haemodialysis, ultrafiltration and sequential haemodialysis and ultrafiltration in dogs. MAP: mean arterial pressure; CO: cardiac output; TPR: total peripheral vascular resistance; EC: extracorporeal circulation; HD: haemodialysis; UF: ultrafiltration; Seq: sequential haemodialysis (D) and ultrafiltration (UF)

and gastrointestinal tract (portal organs). BF to the brain was maintained almost constant during all experiments except in the UF group, where it decreased slightly but significantly. Change in BF to the heart was parallel to that of CO. HAF increased significantly during the D phase of the Seq group while it showed no change in the other phases. Portal organ blood flow significantly decreased in the HD and UF groups, and the UF phase of the Seq group, but no change was noted in the D phase of the Seq group. BF to the muscle significantly decreased in the UF group and the UF phase of the Seq group, but no significant change was seen in the HD and D phase of the Seq group.

During the HD phase, regional vascular resistance significantly increased in the portal organs only. On the other hand, it significantly increased in the portal and muscular system in the UF group and the UF phase of the Seq group.

Discussion

Similar changes in blood chemistry and systemic haemodynamics to those of HD patients were observed during HD and UF in the experimental model. Since no significant change in MAP, CO, TPR and BF to organs was seen in the EC group, EC itself may not have much effect on systemic haemodynamics. UF was carried out in the HD and UF groups, and the UF phase of Seq group, in all of which CO decreased. The decrease in CPV due to UF might have decreased preload, resulting in the decrease in CO. The decrease in CO was similar in HD and UF groups. In the UF group, TPR significantly increased with no significant decrease in MAP, while a significant decrease in TPR was seen concomitantly with a significant decrease in MAP in the HD group. The compensatory mechanism against the CO decrease increased TPR, resulting in stable MAP. However, in the HD group where diffusion effects occurred, such a compensatory mechanism was ineffective so that MAP decreased. As to TPR distribution, vascular resistance in portal organs significantly increased when a significant decrease in CO occurred in the HD and UF groups, and the UF phase of the Seq group. Although vascular resistance in muscle significantly increased in the UF group and UF phase of the Seq group, it did not increase significatly in the HD group and D phase of the Seq group. Regional vascular response to the decrease in CO was not homogenous. When CO decreases, the increase in portal and muscle vascular resistance has an important role in the cardiovascular adjustment. Since approximately 40 per cent of CO is distributed to muscle, the change in muscle vascular resistance contributes much to the change in TPR. Such cardiovascular adjustment does not work well in HD, resulting in hypotension. The following are suggested as responsible: 1) pharmacological effects of acetate used as alkalising agent in dialysate [5–7]; 2) abnormalities in baroreceptor and vasomotor nervous system as the result of imbalance in osmotic pressure and electrolytes between intracellular and extracellular components caused by solute removal [2, 8–11]; 3) removal of humoral vasoactive factors such as adrenalin and noradrenalin by dialysis.

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