Clinical Significance of Renal Hemodynamics in Severe Congestive Heart Failure: Responsiveness to Ultrafiltration Therapies

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Isolated ultrafiltration, hemodialysis & peritoneal dialysis (Tx) were recently used in the treatment of intractable heart failure (HF). We examined the relation between the response of HF to Tx and the residual kidney functions. Tx was carried out in 17 patients (Pts) with HF who did not respond to aggressive medical treatment. Ten Pts (R) responded to Tx and 7 Pts (N) did not. Serum urea nitrogen (UN), creatinine (Cr), uric acid (UA), sodium (Na), potassium (K), and chloride (Cl) concentrations on admission and before Tx were not different between R and N. Urine UN, Cr, Na, K, and Cl on admission and before Tx were also not significantly different. Fractional sodium excretions (FENa), renal failure indices (RFI), and urine/plasma Cr ratios (U/P Cr) on admission were 2.0 ± 1.6 , 2.7 ± 2.2 , and 30.5 ± 20.0 in R and 5.9 ± 4.2 , 8.2 ± 6.0 and 11.5 ± 3.8 in N. They were significantly different ($p < 0.05$). However, these did not differ before and after Tx. These data show that FENa, RFI and U/P Cr might be useful indices in predicting the responsiveness of intractable HF to Tx.

THE traditional treatment for severe heart failure has been salt and water restriction, vasodilators, diuretics, and digitalis. Positive end expiratory pressure (PEEP) for intubated patients or intra-aortic counter pulsation for severe low-output patients have been tried and have shown benefits in the treatment of refractory congestive heart failure.¹

Iso-osmotic water removal by extra-renal ultrafiltration using peritoneal dialysis, hemodialysis, or isolated filtration have been routinely done for the treatment of over-hydrated uremic patients.² The efficacy and safety of water

removal by these ultrafiltration therapies has been established in patients with chronic renal failure.³ Hemodialysis, peritoneal dialysis and isolated filtration for severe congestive heart failure patients have been mentioned frequently⁴ but the outcome of these therapies is not well known. This paper reported that patients with refractory congestive heart failure who had a relatively good renal functional reserve might show a favorable response to ultrafiltration therapies.

PATIENTS AND METHODS

We reviewed the clinical records of patients with severe congestive heart failure who were admitted to the Musashino Red Cross Hospital from April 1983 to August 1987. All patients with severe congestive heart failure were initially treated by loop diuretics, vasodilators, and

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Fig.1. Indices of renal hemodynamics of patients with severe heart failure on admission, before isolated filtration, peritoneal dialysis, or hemodialysis (Tx), and after Tx. Urine plasma creatinine ratio (U/P Cr), fractional sodium excretion (FENa), and renal failure index (RFI) were calculated by the equations shown in Methods.

digitalis. Patients who did not respond to these therapies were then treated by non-renal sodium and water removal by peritoneal dialysis, hemodialysis, or isolated ultrafiltration (ultrafiltration therapies). They were divided into two groups. Responders included patients who obtained some improvement of congestive heart failure by ultrafiltration therapies and who were temporarily or permanently released from the therapy; non-responders included patients who did not respond to the ultrafiltration therapies and died during the course of the therapies. Blood urea nitrogen, serum creatinine, serum sodium concentration, urine creatinine, and urine sodium concentrations were measured by routine laboratory autoanalyzer methods. Fractional sodium absorption (FENa), renal failure index (RFI) and urine/plasma creatinine ratio (U/P Cr) were calculated by the following equations.⁵

$$\text{FENa (\%)} = \frac{(\text{urine sodium}) \times (\text{serum creatinine})}{((\text{serum sodium}) \times (\text{urine creatinine}))} \times 100$$

$$\text{RFI} = \frac{(\text{urine sodium})}{((\text{urine creatinine}) / (\text{serum creatinine}))} \times 100$$

$$\text{U/P Cr} = \frac{(\text{urine creatinine})}{(\text{plasma creatinine})}$$

These parameters were compared on admission, at the start of ultrafiltration therapy and at the end of the therapies between the two groups. Statistical significance were estimated by Student's non-paired t test.

RESULTS

Eighteen patients were treated with ultrafiltration therapies because of severe heart failure. One patient was also treated with intra-aortic counterpulsation, and has not been included in this study. Ten patients responded to the ultrafiltration therapies (*Responders*). Four of them survived and were discharged. Their admission period was 47 ± 25 days. Six patients responded to ultrafiltration therapies but were lost after temporary improvement of congestive heart failure because of arrhythmias or recurrent myocardial infarct. Their admission period was 52 ± 15 days. Seven patients did not respond to ultrafiltration therapies and died after 17 ± 17 days of admission (*Non-responders*). Patient characterizations of the two groups are shown in Table I. Average age and sex were not significantly different between responders and non-responders. The frequency of patients complicated with diabetes mellitus, hypertension, or kidney diseases were not different between the two groups. Blood urea nitrogen, creatinine, and uric acids on admission, before ultrafiltration therapies, and after ultrafiltration therapies were not significantly different between responders and non-responders. Serum sodium, potassium, chloride, and phosphate concentrations on admission, before ultrafiltration therapies, and after ultrafiltration therapies were not significantly different between responders and non-responders (Table II). Urine biochemistries of

TABLE I

Case	Age Sex	Original diseases	Complications			Treatments	Outcome
			D.M.	H.T.	K.D.		
Responders							
1	71M	Old myocardial infarction	—	—	—	I.F., H.D.,	alive
2	66M	Angina, Hypertension	—	+	+	H.D.	alive
3	39M	Hypertensive cardiomyopathy	—	+	+	H.D.	alive
4	39M	Hypertensive cardiomyopathy	+	+	+	H.D.	alive
5	64F	Acute myocardial infarction	+	—	+	H.D., P.D.	dead
6	70F	SSS, Old myocardial infarction	—	+	—	H.D.	dead
7	72F	Atrial fibrillation	—	+	—	H.D.	dead
8	77M	Angina pectoris	+	—	+	P.D.	dead
9	66M	Acute myocardial infarction	+	—	+	H.D.	dead
10	72F	SSS, Old myocardial infarction	—	+	—	H.D.	dead
mean	63.6		4/10	6/10	6/10		
Non-responders							
1	74F	Angina pectoris, old myocardial infarction	+	—	+	P.D.	dead
2	56M	Acute myocardial infarction	+	+	+	H.D.	dead
3	76M	Dissecting aneurysm, angina pectoris	—	+	—	H.D., P.D.	dead
4	72M	Hypertrophic cardiomyopathy, dissecting aneurysm	—	+	—	H.D.	dead
5	74M	SSS, angina pectoris	+	—	—	I.F., H.D., P.D.	dead
6	69F	Hypertensive cardiomyopathy	+	—	+	H.D.	dead
7	80F	Hypertensive cardiomyopathy	—	+	+	I.F., H.D.	dead
mean	71.6		4/7	4/7	4/7		

Patients profiles with severe heart failure treated by peritoneal dialysis (P.D.), hemodialysis (H.D.), and isolated filtration (I.F.). They were divided into two groups, Responders and Non-responders. Responders included patients who responded to P.D., H.D. or I.F. and released from these therapies. Non-responders included patients who did not respond these therapies and died during these therapies. (D.M.; Diabetes mellitus, H.T.; Hypertension, K.D.; Kidney diseases, S.S.S.; Sick sinus syndrome).

patients on admission, before ultrafiltration therapy, and after ultrafiltration therapy are shown in Table III. They were not significantly different between two groups.

Indices of renal hemodynamics of patients on admission, before ultrafiltration therapies, and after ultrafiltration therapies are shown in Table IV. Indices of non-responders after ultrafiltration therapies are not shown because insufficient numbers of blood and urine samples were taken simultaneously. U/P creatinine ratio on admission of responders was significantly greater than that of non-responders ($p < 0.05$). This difference disappeared when ultrafiltration therapies were started. Fractional excretion of sodium by responders on admission was $2.0 \pm$

1.5%, and it was significantly ($p < 0.05$) smaller than that of non-responders ($5.9 \pm 4.3\%$). This difference also disappeared when ultrafiltration was started. The renal failure indices of responders on admission were smaller than those of non-responders ($p < 0.05$). This difference also disappeared at the time when ultrafiltration therapy was started.

DISCUSSIONS

The traditional treatments for severe heart failure are salt and water restriction, vasodilators, diuretics, and digitalis. Positive end expiratory pressure (PEEP) for intubated patients or intra-aortic counter pulsation for severe low-output

TABLE II

Group	BUN (mg/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)	Sodium (mEq/l)	Potassium (mEq/l)	Calcium (mg/dl)	Chloride (mEq/l)	Phosphate (mg/dl)
<i>Responders</i>								
on admission	64.2 (40.8)	4.3 (3.3)	7.4 (3.5)	135.2 (3.4)	4.9 (0.9)	8.0 (0.6)	107.2 (4.4)	4.3 (1.1)
before Tx	72.9 (23.7)	6.5 (2.4)	9.1 (3.8)	131.8 (6.4)	4.6 (0.8)	8.0 (0.5)	102.0 (6.0)	5.0 (0.6)
after Tx	54.6 (15.9)	5.0 (2.0)	6.3 (2.0)	136.1 (4.1)	4.1 (0.8)	8.1 (0.7)	105.4 (6.4)	4.0 (1.0)
<i>Non-responders</i>								
on admission	57.2 (21.0)	3.4 (1.1)	6.9 (2.0)	138.7 (2.9)	4.3 (1.1)	7.9 (0.6)	107.6 (6.6)	4.0 (0.8)
before Tx	81.9 (22.0)	5.3 (3.0)	10.3 (3.9)	137.1 (5.1)	4.4 (0.6)	7.3 (0.8)	102.7 (7.9)	6.2 (2.6)
after Tx	85.4 (23.3)	6.5 (2.2)	10.6 (7.4)	142.0 (9.3)	4.5 (1.4)	7.3 (0.7)	110.8 (7.0)	8.1 (6.0)

Serum biochemistries of patients with severe heart failure on admission, before isolated filtration, peritoneal dialysis, or hemodialysis (Tx), and after Tx. Data shown are mean (S.D.) values. BUN stands for blood urea nitrogen.

TABLE III

Group	Urea nitrogen (mg/dl)	Creatinine (mg/dl)	Sodium (mEq/l)	Potassium (mEq/l)	Chloride (mEq/l)
<i>Responders</i>					
on admission	435 (143)	67 (24)	57 (29)	38 (14)	59 (31)
before Tx	262 (71)	57 (19)	57 (13)	33 (12)	58 (11)
after Tx	270 (124)	50 (19)	68 (15)	27 (12)	63 (15)
<i>Non-responders</i>					
on admission	364 (60)	43 (8)	75 (23)	38 (16)	65 (18)
before Tx	323 (122)	41 (11)	69 (25)	32 (22)	64 (12)
after Tx	348 (100)	40 (10)	60 (19)	31 (23)	66 (14)

Urine biochemistries of patients with severe heart failure on admission, before isolated filtration, peritoneal dialysis, or hemodialysis (Tx), and after Tx. Data shown are mean (S.D.) values. UN stands for urea nitrogen.

patients have been tried and have shown benefit in the treatment of those patients with severe congestive heart failure who were non-responsive to the conservative medical treatments.¹ The one year survival of refractory congestive heart failure was less than 30%.^{3,6}

Ultrafiltration therapy by hemodialysis, peritoneal dialysis and isolated filtration was been widely applied to dialysis patients as treatment for overhydration.² Ultrafiltration therapies were recently recommended for patients with severe congestive heart failure who do not

TABLE IV

Group	U/P Cr	FENa (%)	RFI (%)
<i>Responders</i>			
on admission	30.5 (20.1)	2.0 (1.6)	2.8 (2.2)
before Tx	10.8 (6.1)	5.4 (3.1)	7.1 (4.1)
after Tx	10.9 (5.4)	5.5 (2.1)	7.5 (2.8)
<i>Non-responders</i>			
on admission	11.5* (3.9)	5.9* (4.3)	8.2* (6.0)
before Tx	8.6 (5.1)	7.0 (5.1)	9.7 (7.4)

Indexes of renal hemodynamics of patients with severe heart failure on admission, before isolated filtration, peritoneal dialysis, or hemodialysis (Tx) and after Tx. Urine plasma creatinine ratio (U/P Cr), fractional sodium excretion (FENa), and renal failure index (RFI) were calculated by the equations shown in Methods. Data of Non-responders after Tx were not shown because simultaneous collections of urine and blood were not available. Data are shown as mean (S.D.) values. Asterisks () stand for significant differences ($p < 0.05$) compared with those of Responders by the Student's non-paired *t* test.*

respond to diuretics, vasodilators, or digitalis.^{3,4} Clinical surveys concerning the results of patients who were treated by ultrafiltration therapies were not available.

The purpose of this study was to elucidate the factors that might predict the outcome of refractory congestive heart failure with decreased renal function. Our patients with severe congestive heart failure showed decreased renal blood flow and glomerular filtration rate as estimated by serum creatinine concentration. Patients were divided by the immediate response to ultrafiltration therapy into two groups, the responders and the non-responders. The responders showed significantly higher urine/plasma creatinine ratio, lower fractional excretion of sodium and lower renal failure index than those of the non-responders on admission. Other indices such as urine sodium concentration, urine creatinine concentration and urine urea concentration did not reflect the responsiveness or treatment outcome of these patients.

Fractional excretion of sodium and renal failure index were assessments of the tubular

reabsorption of sodium. Pre-renal azotemia is the most common and initial form of renal complication occurring with congestive heart failure.⁵ Fractional excretion of sodium and renal failure index in this condition might be low, reflecting increased tubular sodium reabsorption to increase circulating blood volume and cardiac output. Longer and more severe decrease of renal blood flow in refractory congestive heart failure might cause intrinsic renal tubular damage and defective tubular sodium reabsorption. Fractional excretion of sodium and renal failure index in this condition might be high, reflecting defective sodium reabsorption by the damaged tubule. Fractional excretion of sodium less than one percent strongly indicates pre-renal azotemia. When administered, all our patients showed more than one percent of fractional sodium excretion. The lower value of fractional sodium excretion of the responders might indicate a less severe decrease of renal circulation or a shorter duration of decreased renal circulation and a favorable outcome would be expected in these patients. The non-responders might have had more severely damaged renal circulation and also systemic circulation which reflected an increase in fractional excretion of sodium and renal failure indices.

Urine/plasma creatinine ratio is an assessment of renal glomerular filtration of plasma creatinine and renal tubular reabsorption of water. This is always more than one as long as tubular reabsorption of water is not completely disrupted. Ratios greater than 40 strongly point toward pre-renal acute renal failure, while ratios less than 20 are equally strong indicators of intrinsic and post-renal acute renal failure. All patients except one showed a urine/plasma creatinine ratio less than 40. Decreases of the ratio might indicate an injured tubule which reabsorbs water. Responders showed larger urine/plasma creatinine ratio than non-responders on admission. The difference of urine/plasma creatinine ratio on admission between responders and non-responders might reflect the difference of renal circulation and so the difference of cardiac function of the two groups.

In conclusion, fractional excretion of sodium, renal failure index, and urine/plasma creatinine ratio of patients with severe congestive heart failure and decreased renal function might be useful indices in predicting the responsiveness to ultrafiltration therapy and its outcome. The mechanism of the relationship between residual

renal function and outcome should be examined further.

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