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Original Contributions

Ultrafiltration in the Treatment of Refractory Congestive Heart Failure*

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Summary: Artificial subtraction of fluids and solutes was evaluated in the course of acute and chronic heart failure when it became refractory to standard intensive medical treatment. A group of 19 patients (mean age 57 years), 9 with ischemic, 2 amyloidotic, 4 valvular, and 4 idiopathic cardiomyopathy, were treated. In 17 patients extracorporeal ultrafiltration (UF) by means of a polysulfonate ultrafilter was adopted along 125 sessions (105 assisted by a roller pump and 20 as a slow continuous ultrafiltrate). In two patients continuous peritoneal dialysis was adopted. In every case UF was well tolerated. Ultrafiltrate volumes ranged from 1680 to 3500 ml for every session with corresponding Na losses ranging from 194 to 434 mEq/session. Improved clinical and functional status with reduction of edema was observed in 17 of 19 patients. In 12 patients UF could be discontinued due to restored response to diuretics; 5 of these patients could subsequently undergo heart surgery (1 transplant, 3 valve replacement, 1 coronary bypass). The remaining 7 patients survived on medical therapy alone for an average of 228 days. In 7 of 19 cases, UF could not be discontinued, and these patients died after an average of 23 days of treatment. In conclusion, UF proved to be effective in eliminating salt-fluid overload and restoring response to medical treatment. Patients who are potential surgical candidates seem to be the most suitable for UF.

Key words: ultrafiltration, heart failure

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Introduction

The late stage of congestive heart failure (CHF) is characterized by refractoriness to standard intensive medical treatment. The increasing sodium and water body content, unresponsive to diuretics, leads to progressive weight gain and worsening clinical status. In such situations extracorporeal ultrafiltration (UF) has been suggested for its effectiveness in removing fluid and solutes.[1-10] However, its use in cardiology has been limited and only a few series with short follow-ups have been reported. The aim of our study was to further evaluate in patients with CHF (a) the efficacy of UF in removing fluid and solute overload, (b) the tolerance to UF therapy, (c) the complexity of the technique, and (d) the long-term clinical relevance of the water and solutes depletion achieved with UF.

Patients and Methods

Nineteen patients with CHF were admitted to the study: 3 females and 16 males, with a mean age of 57 years (range 28–78). The underlying heart disease was coronary artery disease (CAD) in 9, valvular in 4, and cardiomyopathy in 6 (2 amyloidotic). All patients had extreme heart enlargement, pulmonary congestion, and anasarcatic edema. Criteria for inclusion were New York Heart Association functional class IV and refractoriness to intensive therapy with inotropic drugs, vasodilators, and diuretics in various combinations. Namely, inefficacy of diuretic therapy was defined when increased doses (up to 750 mg) of intravenous furosemide could not elicit an effective diuretic response, thus failing to induce body weight loss, edema reduction, and increase in urinary sodium content. The basal urinary sodium daily losses were always low despite "normal" diuresis volume. The treatment's schedule is described in Table I. In 15 cases the blood access to the extracorporeal circulation was performed surgically, by local anesthesia, inserting a teflon vessel tip connected to a silastic tube into both the radial artery and a contiguous vein.[11] The tubes were connected to the extracorporeal circuit during the UF session, and to each other at the end of the session, allowing arteriovenous shunting of the blood. In three other cases, the critical con-

TABLE I UF treatment schedule

Ultrafiltration:	patients 17/19
Vascular access:	radial shunt: 15
	femoral-subclavian venous catheter: 3
Filter:	Amicon 20 (polysulfonate)
Blood flux:	100–300 ml/min
Positive pressure:	50–150 mmHg
Filtration rate:	pump-assisted 20ml/m/min
	spontaneous 5-7ml/m/min
Heparin infusion:	continuous 5-15 UI/m/min
	intermittent 500 UI
Total number of sessions = 125	
Continuous peritoneal dialysis patients 2/19	
Total number of sessions = 11	

ditions of the patients urged the percutaneous insertion of the catheter into a femoral vein, using the Seldinger technique. The catheter was then connected to the filter and the return of the blood to the patient was assured via a subclavian catheter.

A total number of 125 UF sessions were performed, 114 during hospitalization and 11 on ambulatory basis. A total of 105 UF sessions were performed in extracorporeal circulation assisted by a blood roller pump. At a flow rate of 200–300 ml/min and a positive pressure of 50–150 mmHg, blood was pumped and ultrafiltrated through a polysulfonate hollow fiber filter (Amicon 20). It was then returned to the patient by passing through a drip-chamber connected to the pressure monitor. A blood volume of about 100 ml was required to prime the line. No heater was needed due to the minimal heat loss along the extracorporeal pathway. The system was set to give an ultrafiltration rate not greater than 20 ml/min by suitable modifications of blood flow rate and pressure.[12] It was empirically planned not to exceed 2–3 liters subtracted per session, since we considered this value safely comparable to a physiologically tolerable daily diuresis. In this way each session lasted about 2 hours. Anticoagulation was performed by infusion of heparin, either continuous 5–15 UI/min, or intermittent 500 UI when clotting time was shorter than 5 min. In 4 cases, in which a very slow UF rate was advisable because of severe hypotension, 20 sessions were performed by "spontaneous" filtration, connecting the filter directly to the radial artery, cannulated by a permanent shunt. The UF rate was 5–7 ml/min.

Furthermore, in two other cases with severe hypotension, peritoneal dialysis was adopted as an alternative method to perform a slow continuous isotonic ultrafiltration. A Tenckhoff peritoneal catheter was inserted percutaneously and hypertonic glucose solution (2.3%) was infused and drained intermittently. A total number of 11 sessions were performed. Data obtained on these patients were analyzed together with the others. All previous drugs were maintained along the course of UF treatment and diuretics were eventually reduced according to clinical conditions. The sessions were performed mostly on alternate days, but their frequency was adapted to the clinical status of the patients. UF treatment was discontinued when a restored response to diuretics was observed, namely both when body weight remained constant on the days following the last session and increased urinary sodium losses were observed.

In each patient, the UF treatment was monitored as follows:

1. Overall water and sodium losses at the end of each session
2. Daily body weight (basal value = mean 74.6 ± 11 kg)
3. Daily plasma sodium (basal value = mean 132 ± 6.6 mEq/l)
4. Daily plasma creatinine (basal value = mean 1.58 ± 0.83 mg%)
5. Arterial pressure, measured by sphygmomanometry every day (basal value = 107 ± 16 mmHg) and every 15 minutes during the UF sessions
6. Daily diuresis volume (basal value = mean 2030 ± 1127 l)
7. Daily urinary sodium losses (basal value = 22 mEq/24h)

Because the UF method was shown to be well tolerated even in the most critically ill patient, routine invasive hemodynamic monitoring was not included in the study protocol.

The clinical status of the patients has been followed from the start of the UF treatment, for periods ranging from 4 to 997 days (mean = 133 days).

Results

Mean duration of UF treatment was 14 days (range 1–57). On the basis of the previously planned 2–3 l of maximum ultrafiltrate volume subtracted at each session, total number of sessions followed the amount of fluid that had to be removed. Effective subtraction of water and sodium was obtained in the majority of the patients. Mean UF volumes ranged from 1680 to 3500 ml/session; mean sodium losses from 194 to 434 mEq/session.

Differences in body weight pre- (mean value 74.6 ± 11 kg) and posttreatment (mean value 68.1 ± 11 kg) were statistically significant ($p < 0.01$).

Mean plasma sodium concentration before treatment was 132 ± 6.6 mEq/l and did not change at the end of the UF period (mean value 133 ± 8.6 mEq/l) despite a total mean sodium loss of 1188 mEq. Mean total fluid loss at the end of the treatment was 11 liters. A trend toward increasing plasma sodium values was evident during the first days of treatment: the hypotonic diuresis constantly observed during the same period can account for this figure. In the patients who underwent longer treatments, the initial rise of plasma sodium was followed by a reduction during the subsequent days. During the entire period of UF, sodium was never supplemented to the patients.

The course of the UF sessions has been free from major complications. Hypotensive episodes, arrhythmias, or acute episodes requiring the interruption of the session were never recorded; in only three cases sudden clotting of the extracorporeal circuit occurred. Otherwise, constant monitoring of blood pressure and heart rhythm never revealed important variations.

Daily diuresis constantly showed a distinct decrease during the treatment, while plasma creatinine increased significantly ($p<0.05$) from a mean value of 1.58 mg% pretreatment to 2.72 mg% at the end of the UF period. In two cases, in which systemic amyloidosis was present, renal function showed a marked deterioration, requiring substitutive support by intermittent sessions of hemofiltration. In one of these cases, the abrupt onset of renal failure was related to the start of captopril therapy. As long as the UF treatment went on, two cases showed a marked thirst increase: one of these patients showed mental deterioration and refused to continue the extracorporeal treatment. Compliance to the treatment was good in the other patients.

TABLE II Short-term results

Clinical improvement (with reduction of anasarca)	17/19
Correction of hyponatremia	5/19
Restored response to diuretics (UF discontinued)	12/19
Death	7/19

Short-term results are shown in Table II: clinical and functional improvement with reduction or disappearance of edema were observed in 17 of 19 patients, correction of the hyponatremia in 5 of 19, restored responsiveness to diuretics in 12 of 19 patients.

Seven patients died during the period of UF treatment, 5 because of progressive heart failure, 2 during a pneumonia episode (Table III).

Table IV depicts the clinical outcome in 12 patients in which UF could be discontinued. Mean duration of UF

TABLE III Mortality during UF treatment

n	Sex/age	Diagnosis	UF duration (days)	Cause of death
1	M61	A	19	+(Pneumonia)
2	M62	CAD	55	+(Pneumonia)
3	F70	IDC	4	+(Heart failure)
4	M77	CAD	16	+(Heart failure)
5	M64	A	41	+(Heart failure)
6	M51	CAD	25	+(Heart failure)
7	M38	V	13	+(Heart failure)

Abbreviations: V: valvular; A: amyloidotic; IDC: idiopathic dilated cardiomyopathy; CAD: coronary artery disease; +: death.

TABLE IV Clinical outcome in patients in which UF could be discontinued

n	Sex/age	Diagnosis	Follow-up duration (days)	NHYA class post-UF	Outcome at the end of follow-up
1	M40	IDC	30	II	+ Sudden death
2	M28	CAD	7	III	+ Cerebral thrombus
3	F78	IDC	970	II	Alive
4	M57	V	—	III	MV bioprosthesis
5	F55	V	—	I	MV bioprosthesis
6	M53	CAD	183	II	Alive
7	M41	CAD	186	II	Alive
8	M53	V	—	III	MV bioprosthesis
9	M45	IDC	—	I	Heart transplant
10	M70	CAD	61	I	Alive
11	M52	CAD	39	III	Alive
12	M65	CAD	—	II	CABG

Abbreviations: MV: mitral valve; CABG: coronary artery bypass graft; —: follow-up ended at surgery. Other abbreviations as in Table III.

treatment in this group of patients was much shorter than in patients who died (mean 8 vs. 23 days). Five patients could undergo heart surgery and 7 survived on standard medical therapy for mean 228 days (range 11–997).

Discussion

Extracorporeal UF is a method originally employed in patients with renal failure and fluid overload.[12,13] In contrast to other renal substitution forms of therapy, in isolated UF the dialysate is absent and plasma water is filtered directly across the membrane. The structure of the membrane restricts the passage of solutes with a molecular weight greater than about 20.000–30.000, giving a filtrate almost isotonic to the plasma. These characteristics allow rapid subtraction of great amounts of fluid and make the technique well tolerated. For these reasons, Silverstein and co-workers several years ago suggested UF for the treatment of fluid overload in the cardiac patient.[1] CHF, when it becomes refractory to standard medical therapy, carries a very poor prognosis and contraindicates any surgical attempt to correct the underlying heart disease. The need to overcome the impasse imposed by the inefficacy of diuretics may be fulfilled by UF.[3,4,6,10]

Our study is primarily observational. It confirms the results obtained by other authors[3-10] and it extends the evaluation of the patients well beyond the period of UF treatment. UF proved effective in removing water and sodium overload in patients with refractory CHF, and it was well tolerated and relatively safe: in most cases, during repeated UF sessions a significant decrease in body weight has been obtained without blood pressure modifications. In nearly half of the patients the procedure resulted in more than temporary symptomatic improvement and profoundly affected their outcome and prognosis. Five patients could undergo surgical correction of their heart disease, with three long-term survivors, and five patients survived on medical therapy alone, following the discontinuation of UF. In the evaluation of these results it must be taken into account that all these patients were in terminal conditions. Seven patients died during the treatment. In this latter group the mean duration of treatment was much longer than in the patients who survived because no persistent improvement was observed during the treatment. In our view this finding reflects the importance of a significant cardiac functional reserve still available before UF treatment that was uncovered and recruited by UF. In any case, death could not be directly related to the UF treatment itself.

Plasma sodium modifications along the UF treatment showed an initial phase of increasing values, presumably due to the correction of a dilutional hyponatremia, followed by a longer course of a slow decrease that could be related to the depletion induced by UF. Based on this experience, we avoid sodium supplements during the first days of UF treatment, even in the hyponatremic patient. Sodium can be given in some cases of longer UF treatments, performed for long-term maintenance of the "dry weight" achieved during the earlier sessions.

A slow, progressive, deterioration in renal function during UF was observed in some cases: therefore, close monitoring of the renal function is mandatory during the treatment.

Conclusions

In conclusion, in patients with CHF refractory to standard intensive medical therapy, UF (1) proved effective in removing sodium and water overload, (2) was well tolerated, and (3) appeared safe and easy to perform.

Based on our experience there is a proven indication for UF therapy in patients suitable for surgical correction of their cardiac abnormality. Further experience is needed in other cases of refractory heart failure.

References

1. Silverstein ME, Ford CA, Lysaght MJ, Henderson LW: Treatment of severe fluid overload by ultrafiltration. *N Engl J Med* 291, 747 (1974)
2. Misler S, Nidus BD: Long term ultrafiltration as a treatment of refractory congestive heart failure. *NY State J Med* 84, 518 (1984)
3. Page E, Machecourt J, Dechelette E, Wolf JE, Bourland P, Denis B: Traitment des insuffisances cardiaques avec oedemes refractaires par ultrafiltration extracorporelle. *Arch Mal Coeur* 77, 9 (1984)
4. Magilligan JD: Indications for ultrafiltration in the cardiac surgical patient. *J Thorac Cardiovasc Surg* 89, 183 (1985)
5. Fauchald P, Forfang K, Amlie J: An evaluation of ultrafiltration as treatment of therapy resistant cardiac edema. *Acta Med Scand* 219, 47 (1986)
6. Bergerone S, Tognarelli G, Pacitti A, Segoloni G, Pozzi R, Dalmasso M, DiLeo M: Ultrafiltration in the treatment of congestive heart failure. In *CAVH—Proceedings of the International Symposium on Continuous Arteriovenous Hemofiltration.* (Eds. LaGreca G, Fabris A, Ronco C). Wichtig, Milano (1986) 247-253
7. Donato L, Biagini A, Contini C, L'Abbate A, Emdin M, Placenti M, Palla R: Treatment of end-stage congestive heart failure by extracorporeal ultrafiltration. *Am J Cardiol* 59, 379 (1987)
8. Simpson IA, Rae AP, Simpson K, Gribben J, Boulton Jones JM, Allison MEM, Hutton I: Ultrafiltration in the management of refractory congestive heart failure. *Br Heart J* 55, 344 (1986)
9. Konig P, Geissler D, Lechleitner P, Spielberger M, Dittrich P: Improved management of congestive heart failure. Use of continuous ambulatory peritoneal dialysis. *Arch Intern Med* 147, 1031 (1987)
10. Smith SA, Tan L: Ultrafiltration and haemofiltration for refractory congestive cardiac failure. (Letter) *Lancet* 1390 (1987)
11. Ramirez O, Swartz C, Onesti G, Mailloux L, Brest AN: The winged in line shunt. *Trans Am Soc Artif Intern Org* 12, 220 (1966)
12. Kramer P, Kaufhold G, Grone HJ, Wigger W, Rieger J, Matthaei D, Stokke T, Burchardi H, Scheler F: Management of anuric intensive-care patients with arteriovenous hemofiltration. *Int J Artif Org* 3, 225 (1980)
13. Bosch JP: Continuous arterial-venous hemofiltration. In *CAVH—Proceedings of the International Symposium on Continuous Arteriovenous hemofiltration.* (Eds. LaGreca G, Fabris A, Ronco G). Wichtig, Milano (1986) 9-35