ULTRAFILTRATION AS A THERAPEUTIC OPTION FOR REFRACTORY CONGESTIVE HEART FAILURE

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BACKGROUND

Chronic kidney disease is frequently associated with cardiovascular disease, particularly among elderly patients, and this combination complicates the management of severe congestive heart failure (CHF).1•2 Even with adequate renal function, end-stage cardiomyopathy of any etiology can at times result in severe hemodynamic alterations leading to volume overload that is unresponsive to conventional diuretic therapy.7 Moreover, aggressive diuretic programs inevitably lead to acid/base and electrolyte-metabolic imbalance that further compounds the clinical scenario. Simultaneous correction of intractable fluid overload and metabolic disarray in these patients can be achieved by using different ultrafiltration modalities, including continuous venovenous hemofiltration/dialysis, sustained low-efficiency dialysis, sustained continuous ultrafiltration and continuous cyclic peritoneal dialysis. While the duration of these therapies varies, patients who do not have a favorable response within 30 days usually have a poor prognosis.3

THE KIDNEY IN HEART FAILURE

Heart failure leads to several hemodynamic and hormonal changes char affect the kidneys' ability to handle sodium and water. As such, the kidneys play a pivotal role in rhe pathogenesis ofCHF.

In heart failure, decreased kidney blood flow increases sympathetic nervous system activity and activates the renin-angiotensin-aldosterone system, which in rum causes decreased kidney perfusion pressure and intrarenal vasoconsrriction. In advanced CHF, there is vasoconstriction of both afferent and efferent glomerular arterioles, which decreases glomerular filtration rate (GFR) and results in pre-renal azotemia.4 Consequently, the decreased GFR increases rhe tubular reabsorption of sodium and warer, particularly at rhe proximal tubular level where approximately 60-70% is reabsorbed. About 20-30% of sodium reabsorption occurs in the ascending limb of the loop of Henle; this increases in CHF, with additional reabsorption raking place in the distal nephron.5 Redistribution of renal blood flow and hemodynamic changes in the pericubular capillaries also contribute co enhanced tubular sodium and water reabsorprion during CHF.6,7

Early CHF increases renal rentn production due co arterial underfilling, which in turn stimulates the release of a hepatic decapeptide angiorensin I. The angiorensin-converting enzyme present in blood vessels, kidneys and lungs converts chis compound to occapepride angiotensin II, a potent vasoconscrictor. Angiocensin II stimulates adrenal secretion of aldosrerone that is respon-

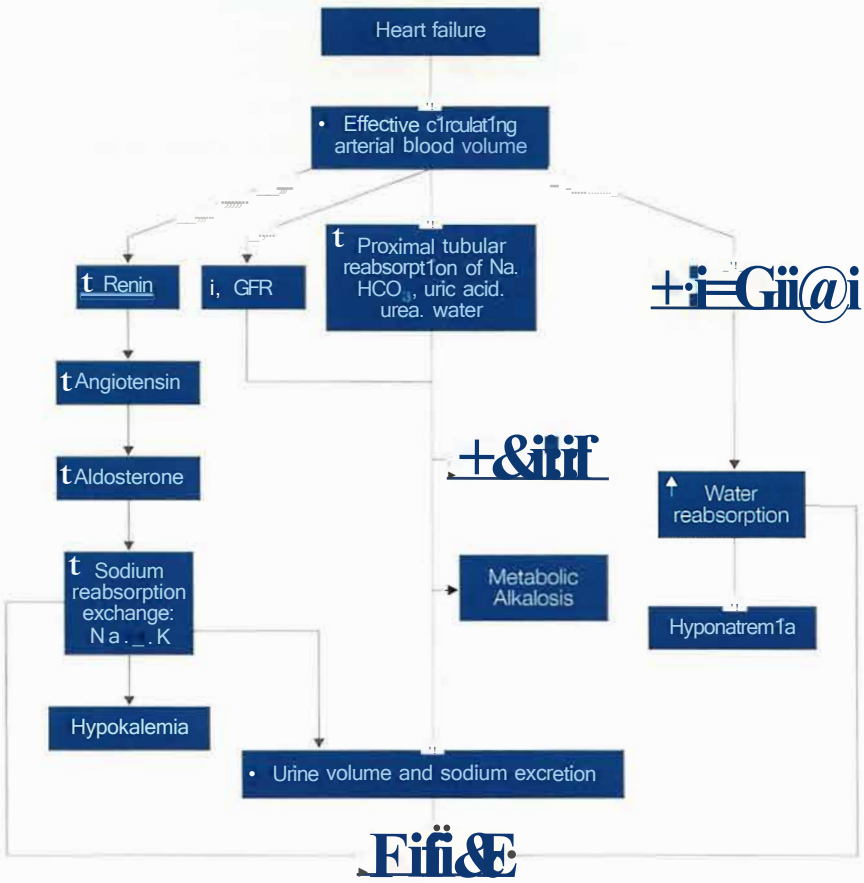

Figure 1. An overview of the hemodynamic and hormonal changes caused by CHF

sible for sodium and water reabsorpcion in che distal tubule and enhanced potassium excretion. Baroreceptor scimulacion releases anti-diuretic hormone (ADH), which contributes to increased water reabsorption distally and is partly responsible for the dilucional hyponacremia seen among CHF patients. The hemodynamic and hormonal changes in CHF are summarized in Figure 1.

USE OF DIURETICS IN CONGESTIVE HEART FAILURE

Fluid rescriccion at a race of 20 ml/kg/day and sodium restriction are essential when rreacing CHF. Hospicalized acutely/chronically ill patients with CHF-related anasarca usually have failed conventional diuretic programs in the outpatient setting and require intravenous (IV) diurecic intervention. When choosing aggressive IV therapy, it is importanc to know how and where different diurecics act in the nephron (Figure 2). Combining different compounds that ace at different sites can produce a synergistic effect chat results in normovolemia.q

Under close supervision and if clinically warranted, the patient should receive a bolus of IV furosemide (1.0-1.5 mg/kg) followed by a furosemide drip at 10 mg/hr to inhibit Na reabsorption in the loop of Henle ascending limb. The lack of response co any type of loop diuretic prohibits the use of another loop diuretic; instead, a thiazide diuretic such as hydrodiuril (250 mg IV every 12 hours) could be added to block the distal ascending loop of Henle.[10] Since kaliuresis induced by promoting Na-K exchange results in hypokalemia, and since these pacients have aldosterone excess (Figure 1), an aldoscerone receptor blocker such as spironolactone should be added to potentiate the ocher diuretics acting ac the distal convoluced tubule and to preserve potassium by inhibiting Na-K exchange.

If no significant diuretic response is achieved (<100 ml/hr) after chree to four hours, dopamine at 2-3 mcg/kg/min should be initiated to enhance renal blood flow and suppress proximal tubular reabsorption of Na. This frequently results in a brisk diuresis,11 although tachyarrythmias could be a limiting faccor with the use of dopamine.

Rapid mobilization of intravenous volume causes contraction alkalosis and enhances proximal tubular reabsorption of HCO3. Moreover, the kaliurecic and chloruretic effects of diuretics also contribute to metabolic alkalosis.12 If significant alkalosis develops (HCO3 >35 mEq/L), a carbonic anhydrase inhibitor (acetazolamide) could be used at a dose of250 mg IV ql2hrs, usually for 24-48 hours only. The proximal tubular action of chis diuretic can result in profound hypokalemia by enhancing distal HCO3-K exchange. Before using acetazolamide, pH and PCO2 should be obtained to rule out a mixed acid-base disorder since elevated HCO3 can at times be compensatory to respiratory acidosis to maintain a normal pH.

Finally, there are new compounds such as conivapcan that act in the collecting duce co inhibit ADH effect and promote water diuresis. While very few patients need a sequential nephron blockade, chose who do should be closely monitored for severe metabolic disarray and have blood work at regular 8-12 hour intervals.

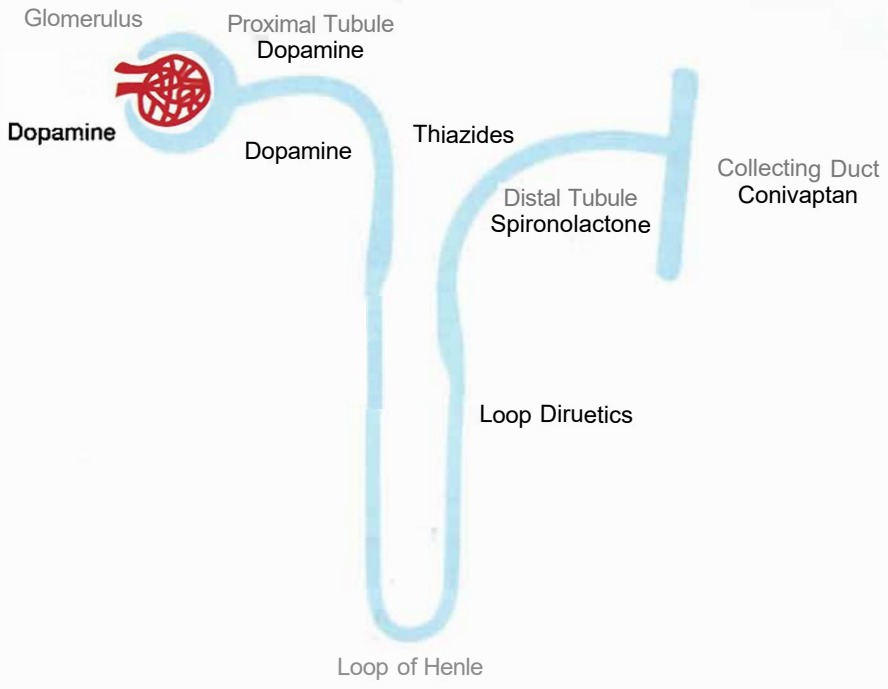

Figure 2. Diuretic sites of action within the nephron

Complications of Aggressive Diuresis:

Hypokalemia	Hypomagnesemia
Hyponatremia / Hypernatremia	Hyperuricemia
Hyperglycemia	Metabolic Alkalosis
Azotemia	Hypotension

Although studies have shown increased mortality among patients created wich aggressive long-term diuretic therapy, the exact role of diuretics is unclear since patients requiring the most aggressive diuretic programs are typically those with advanced end-stage heart disease.[8]

If diuretic combinations fail to enhance fluid mobilization or if severe metabolic and acid-base imbalance ensues, the program should be discontinued and the patient started on ulcrafiltration.

TECHNIQUES AND DESCRIPTIONS OF ULTRAFILTRATION MODALITIES

For che last 20 years, ulrrafilcracion (UF) has been used for CHF because it removes isotonic rather than hypotonic fluids, resulting in less eleccrolyre/metabolic abnormalities chan when using diurecics.14-15

Once a pacient with CHF has failed intensive medical management, extracorporeal ultrafiltracion is a safe and effective means of removing fluid and solures.13 The most frequencly used ulcrafilcrarion modalities are continuous venovenous hemofilcracion/dial$_{ys}$is (CVVHD), suscained low-efficiency dialysis {SLED), sustained continuous ulcrafiltracion (SCUF) and continuous cyclic peritoneal dialysis (CCPD).

CVVHD provides slower solute clearances and ulcrafiltration rates over 24 hours. It is used instead of intermicrenc hemodialysis to creat critically ill patients in whom hemodynamic instabili$_{ty}$ is a problem wich high ultrafilcracion races. CVVHD is performed by a specially trained ICU nurse and requires placement of a central venous cachecer for vascular access and a specialized blood pump. In addition co ultrafilcration, CVVHD removes solutes by means of convection and diffusion across a semipermeable membrane found in a polysulfonate ultrafilter. CVVHD provides hemodynamic stability due to slower ulrrafilcration and better steady-state control of azotemia, and it requires close attention co electrolytes (potassium, magnesium, phosphorus and calcium). Anticoagulation is a key component co CVVHD to prevent cloccing of the extracorporeal circuit and requires pre-filter calcium chelating trisodium citrate with a pose-filter calcium chloride infusion to offset hypocalcemia. Complications of CVVHD are listed at right.

Suscained low-efficiency dialysis (SLED) is another common mechod used for ulcrafiltration in refractory fluid overload. Unlike CVVHD, SLED uses a conventional hemodialysis blood pump instead of a specialized CVVHD pump, although it requires che same central venous vascular access as CVVHD. It also provides excellent control of electrolytes and good ulcrafiltracion tolerance and is much less expensive than CVVHD.16 SLED is considered a hybrid therapy because ic uses scandard hemodialysis equipment and accessories buc with slower soluce clearances and ulcrafilcracion races maintained for prolonged periods of time (usually 6-12 hours). A hemodialysis nurse needs only ro initiate and discontinue treatment and be available to non-dialysis nursing staff during therapy in case of problems. Limitations of chis modality are primarily clotting of che hemodial$_{yz}$er and require anticoagulation using trisodium citrate solution or heparin.

While used less frequently, continuous cyclic peritoneal dialysis (CCPD) is superior to CVVHD and SLED in individuals who have problems with vascular access. This treacment uses a tunneled abdominal wall (Tenckhoff) catheter co prevent peritonitis from complicating direct cutaneo-peritoneal access. Morbid obesity, multiple abdominal surgeries, ileostomy, colostomy and unknown intra-abdominal pathology would contraindicate its use. It may also be contraindicated for chose with severe chronic obstructive pulmonary disease since increased intra-abdominal pressure can lead to impaired lung function.

The crearment consists of using frequent hypertonic dextrose exchanges to enhance fluid mobilization due to an osmotic gradient established in the peritoneal membrane. Hyperglycemia can complicate chis treatment, particularly in critically ill diabetic patients. However, this remains an acceptable treatment if the previously mentioned therapies are not suitable fur the clinical condition.

A less frequenrly used ulcrafiltration modali$_{ty}$ is the arterio-venous sustained continuous ulcrafilrration (SCUF), a treatment requiring no pump or special equipment ocher than an anerio-venous access and a hollow fiber device. SCUF uses the patient's arcerial pressure as a means to achieve conveccion, leading co ukrafiltration without soluce clearance. Hypotension (which is frequently the case in these patients) becomes a limiting factor in achieving adequate ulcrafiluation. Since both CVVHD and SLED use a pump, blood flows are precisely regulated and lead to more reliable and steady ultrafilcracion compared co SCUF.

In a large study (Ulcrafiltration vs. Intravenous Diurecics for Patients Hospicalized for Acute Decompensated Heare Failure, UNLOAD) presented as an abstract at the American College of Cardiology annual scientific session in March 2006, 200 patients were compared using conventional diuretic therapy versus early ultrafilrration. Those treated with ulcrafiltrarion had a shorter hospital course, faster symptom improvemem and fewer readmissions over a 90-day period. The procedure is performed by placing a 16-gauge, 35mm catheter in the antecubical fossa (withdrawal line), and blood is returned via a standard peripheral IV line utilizing a minimally invasive hollow fiber

Complications of Continuous Venovenous Hemodialysis

Vascular access malfunction	Blood flow reduction and circuit clotting
Line disconnection	Air embolism
Fluid and electrolyte imbalance	Loss of filter efficiency
Bleeding	Thrombosis
Infection/sepsis	Biocompatibility and allergic reaction
Hypothermia	Nutrient losses
Inadequate blood purification	

device. Although this modali$_{ry}$ appears to have favorable results, more studies are needed to identify which patients are beccer candidates for early initiation of ultrafilcration as the first choice of therapy.

CONCLUSIONS

Refractory CHF wirh severe fluid overload requires an understanding of basic pathophysiologic events, which include hemodynamic and endocrinologic mechanisms responsible for increased sodium and water retention. Many of these changes affect renal physiology and result in significant metabolic disarray. Diuretic therapy should be the initial treatment of choice. However, if diuretics fail to achieve normovolemia or result in complications, ulcrafiltrarion procedures such as CVVHD, SLED, SCUF and CCPD should be considered to simultaneously correct fluid retention and metabolic imbalance.

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