

# Aggressive Diuresis for Severe Heart Failure in the Elderly\*

Patricia A. Howard, PharmD, BCPS, FCCP; and  
Marvin I. Dunn, MD, Master FCCP

**Study objective:** To determine the efficacy, safety, and economic benefit of continuous IV infusion of furosemide as a treatment modality for elderly patients with class IV heart failure.

**Design:** Prospective trial of consecutively admitted elderly patients > 65 years old with class IV heart failure.

**Setting:** A single cardiovascular service in a university medical center.

**Patients:** Seventeen male and female patients > 65 years old consecutively admitted to a cardiovascular service.

**Results:** High-dose, continuous IV infusion of furosemide was successful in providing a 9- to 20-L diuresis in an average of 3.5 days without causing clinical complications or aberrations in blood chemistry. The length of stay was 2.3 days shorter than a contemporary group of class III and class IV elderly patients with heart failure managed on other medical services. The Medicare reimbursement for heart failure was \$6,047. Patients receiving IV bolus diuretic therapy incurred billing charges of \$10,193, or a loss of \$4,146 per patient to the hospital. Patients receiving diuretic infusion therapy incurred billing charges of \$4,944. This was a difference of \$5,249 per patient treated by continuous IV infusion compared to bolus therapy and a profit per Medicare patient of \$1,103. Therefore, a \$4,146 billing loss was converted to \$1,103 profit.

**Conclusion:** IV furosemide infusion therapy for class IV heart failure in the elderly is a safe, effective, and economic mode of therapy. (CHEST 2001; 119:807-810)

**Key words:** congestive heart failure; economic saving; IV furosemide infusion

**Abbreviations:** ACE = angiotensin-converting enzyme; CHF = congestive heart failure; LOS = length of stay; NYHA = New York Heart Association

Congestive heart failure (CHF) is a major national health problem that affects almost 5 million Americans<sup>1</sup> and is the only major cardiovascular disorder that is increasing in both incidence and prevalence.<sup>2</sup> The tremendous increase in the prevalence of CHF is the result of the aging population and improved survival for patients with coronary heart disease who have experienced angina and myocardial infarction. The prevalence of CHF increases from approximately 1% for those aged 50 to 59 years, to 6 to 10% for those > 65 years of age.<sup>1,2</sup> CHF is the most common medical diagnosis-related group for hospitalized patients aged  $\geq$  65 years.<sup>3</sup> Among the 1 million patients hospitalized annually for CHF, approximately 75% are  $\geq$  65 years old.<sup>1,2</sup>

Total direct costs for CHF have been estimated at \$20 to \$40 billion annually. The greatest expenditure is for hospitalization costs, which have been estimated at \$8 to \$15 billion dollars annually.<sup>2</sup> The estimated cost for each hospitalization is approximately \$6,000 to \$12,000.<sup>3</sup> As a consequence, heart failure is a major economic burden on the health-care system. In 1992, Medicare paid \$2.4 billion for 654,000 CHF hospitalizations; however, the actual charges were \$5.6 billion, more than double this amount.<sup>4</sup> Medicare reimbursement is based on an average hospital length of stay (LOS) of 4.8 days. Studies have shown, however, that the national average for LOS is approximately 6 to 8 days. Therefore, even in uncomplicated hospital admissions, reimbursement will fall short of the charges for treatment and hospitals incur a financial penalty for managing these patients.

\*From the Department of Pharmacy (Dr. Howard) and Division of Cardiovascular Medicine (Dr. Dunn), University of Kansas Medical Center, Kansas City, KS.  
Manuscript received April 12, 2000; revision accepted August 31, 2000.

Correspondence to: Patricia A. Howard, PharmD, BCPS, FCCP, Department of Pharmacy, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160-7231

## MATERIALS AND METHODS

Seventeen consecutive elderly patients were admitted to the Cardiovascular Service at the University of Kansas Medical

Center with New York Heart Association (NYHA) class IV heart failure. The patients had a history of both ischemic and nonischemic cardiomyopathy. All patients had peripheral edema, an estimated central venous pressure of at least 16 to 18 cm, marked hepatomegaly, ascites and/or pleural effusion, and an estimated fluid excess of approximately 15 to 30 kg. These represented both initial and recurrent episodes of heart failure. The mean age was 71 years (range, 65 to 74 years). There were 12 men and 5 women, of whom 9 were white and 8 were black. All patients were receiving a maintenance regimen of digoxin, an oral diuretic, and 16 patients were also receiving an angiotensin-converting enzyme (ACE) inhibitor. These were compared to 42 age-matched control subjects who were admitted to other general medical services in the same hospital during this same time period. Many of these patients were NYHA class III rather than class IV. All were admitted with heart failure after attempts at outpatient diuresis failed.

Following admission to the hospital, oral diuretic treatment was discontinued. The patients were given furosemide as a 100-mg IV bolus followed immediately by a 24-h continuous infusion. The infusion was started at 20 to 40 mg/h and doubled every 12 to 24 h (to a maximum of 160 mg/h) as needed to achieve a diuresis of not less than 100 mL/h. The patients were on a regular hospital floor. The heart rhythm was monitored by telemetry. Serum electrolytes, BUN, creatinine, and vital signs were monitored every 8 to 12 h. Patients were weighed daily and fluid intake and output recorded. Patients were interviewed by a pharmacist for drug tolerance and adverse effects. Diuresis was continued until jugular venous pressure became normal; peripheral edema disappeared; hepatomegaly, ascites, and pleural effusions resolved by physical examination and radiographic evaluation; or the patient returned to baseline weight or had laboratory signs of volume contraction by a rise in BUN or creatinine. Since hypochloremia can lead to loop diuretic resistance, patients with serum chloride concentrations < 95 mEq/L were treated with either arginine hydrochloride, 5 to 10 g tid or qid, in salt-poor tomato or fruit juice and/or acetazolamide, 500 mg bid. Treatment with both of these drugs was continued until the serum chloride level was > 95 mEq/L. Eight of the 17 patients required chloride replacement therapy.

Charges were obtained from the patients' bill and were the charges conventionally assessed during the hospitalization, such as room charge, medications, disposable supplies, special equipment, and special services such as ECG and radiographs, etc. These charges, usually approved by Medicare, were obtained from the itemized computer printout of individual patient charges provided by the billing department. Physicians' professional fees were not included.

## RESULTS

The magnitude and time course for diuresis is summarized in Table 1. The mean furosemide infusion rate

**Table 1—Efficacy of 24-h Continuous Infusion of Furosemide**

Variables	Mean	Range
Magnitude of total diuresis, L	13.9	8.6–21.2
Diuresis in first 24 h, L	5.0	3.7–12.0
Diuresis in first 48 h, L	9.2	5.9–20.0
Time for complete diuresis, d	3.5	1.5–5.9
Furosemide infusion rate, mg/h	87.0	40–120

was 87 mg/h. Continuous infusion was very effective for rapidly removing large amounts of fluid particularly during the first 24 to 48 h. In four patients, a diuresis in excess of 20 kg was achieved within the first 48 h following hospital admission with no adverse effects. In addition to the high degree of efficacy, the most notable aspect of this method of diuresis was the absence of any significant adverse drug effects or laboratory abnormalities. As Table 2 illustrates, serum BUN did increase slightly; however, only one patient required a dosage reduction due to a BUN > 50 mEq/L. In some, the BUN elevation was due to the concomitant administration of arginine or acetazolamide. Serum potassium was remarkably stable, and no patients who were taking an ACE inhibitor required potassium supplementation. The one patient who was not receiving an ACE inhibitor was given oral potassium supplementation. No patients reported musculoskeletal cramping or pain. Uric acid levels increased; however, no patient developed symptoms of gout or required treatment. The rapid diuresis was not associated with hypotension. No patient required a dosage reduction, discontinuation of therapy, or IV fluids for volume replacement. Ototoxicity did not occur in any patient.

The control patients received care from a number of physicians with different medical backgrounds, *eg*, general internists, internists with a specialty other than cardiology, and family medicine physicians. All received bolus furosemide, and most were receiving an ACE inhibitor. The patients were both first-time hospital admissions and readmissions. Since the ability of these physicians to accurately assess jugular venous pressure, hepatomegaly and ascites, and pleural effusions was variable, it was not possible to verify information abstracted from the charts of these patients. The final diagnosis, however, specifically stated that these patients were NYHA class III or class IV. In the conventionally treated group (control subjects), furosemide was administered two to three times daily as 40-mg to 160-mg boluses. No patient received > 640 mg/d.

Comparative hospital charges for patients treated

**Table 2—Effect of High-Dose Diuretic Continuous Infusion on Laboratory Values\***

Laboratory Tests	Before Diuresis	After Diuresis
BUN, mg/dL	24 ± 10.6	32 ± 18.7
Creatinine, mg/dL	1.3 ± 0.34	1.5 ± 0.33
Sodium, mEq/L	139 ± 3.7	136 ± 3.2
Chloride, mEq/L	101 ± 3.3	99 ± 3.6
Potassium, mEq/L	3.9 ± 0.3	3.8 ± 0.4
Uric acid, mg/dL	8.8 ± 2.4	10.4 ± 2.6

\*Data are presented as mean ± SD.

by either infusion or bolus diuretic therapy are shown in Table 3. All charges were obtained from the patients' itemized billing statements. Charges for patients receiving continuous infusion therapy were substantially lower due to the reduced length of hospital stay.

All patients receiving IV infusion therapy were individually titrated to achieve a rapid diuresis. The amount of furosemide administered could not be given conveniently as a bolus. For example, our average infusion rate was 87 mg/h, which was 2,088 mg for 24 h. If this were divided into three doses (every 8 h), each dose would be 696 mg or 70 mL. This would be a difficult "bolus" to administer technically and safely. Therefore, IV infusion therapy is a unique technique for infusing high-dose furosemide. There is no other practical method of achieving this.

Furthermore, the purpose of this study was not to compare the efficacy of bolus therapy vs IV infusion therapy. Rather, it was to show that IV therapy could be administered safely, with a shorter hospitalization, and incurring lesser charges.

## DISCUSSION

Patients admitted to the hospital with NYHA class III or class IV heart failure typically present with severe congestion of the lungs, liver, spleen, as well as ascites, pleural effusions, and peripheral edema. This excess fluid must be removed in order to control symptoms and return the patient to a compensated state. Diuretics are the primary agents used to control sodium and volume overload in patients with CHF. Because patients with advanced CHF have reduced renal function, potent loop diuretics are required. These agents increase the fractional excretion of the filtered sodium load by up to 25% in the loop of Henle.<sup>5</sup> With IV bolus diuretic therapy, however, the usual rate of diuresis is only about 2 to 3 kg/d. Since many patients have 15-kg to 20-kg fluid weight gain, this slow diuresis prolongs hospitalization and results in a loss of revenue for the hospital.

Another factor that may prolong hospitalization is

the development of diuretic resistance. Numerous factors may contribute to diuretic resistance, including inadequate diuretic dosage, increased sodium intake, decreased GI absorption, decreased drug delivery to the nephron, and compensatory sodium retention during the diuretic-free interval.<sup>6,7</sup> Since loop diuretics function by inhibiting active chloride reabsorption in the loop of Henle, hypochloremia may also decrease the efficacy of loop diuretics and must be corrected to achieve a good diuresis. Two effective methods for overcoming diuretic resistance are combination diuretic therapy and continuous IV infusions of loop diuretics. The most frequently used combination regimen is that of a loop diuretic and a thiazide agent such as metolazone.<sup>6</sup> In hospitalized patients with severe edema, however, this approach may be burdensome. The thiazide agents must be given orally, and the relatively longer half-lives of these drugs result in slower onsets of action and longer durations of action, thus making dosage titration more difficult. In contrast, the administration of loop diuretics by continuous IV infusion offers many advantages, including rapid onset, ease of dosage titration, continuous delivery of drug to the nephron, and rapid offset if adverse problems occur.

The efficacy of continuous loop diuretic infusions has been demonstrated in studies<sup>8-10</sup> of patients with CHF and renal insufficiency. One study<sup>10</sup> found that patients with severe refractory CHF may require doses of furosemide as high as 4,000 mg/d. The safety of continuous infusions of furosemide in doses up to 160 mg/h has been demonstrated.<sup>8,10</sup> The loop diuretic bumetanide has also been studied as a continuous infusion medication; however, in our experience, infusion rates > 2 mg/h are often associated with the development of disabling musculoskeletal pain.<sup>11</sup> The continuous infusion of a loop diuretic has been shown to provide a more efficient delivery of diuretic to the nephron, eliminate the diuretic-free interval during which compensatory sodium retention occurs, and decrease the development of tolerance.<sup>9</sup> It has also been suggested that the lower peak drug concentrations associated with continuous IV infusion may allow the administration of high daily doses while minimizing the risk of ototoxicity and other adverse effects.<sup>12</sup>

At our institution, CHF was the diagnosis associated with the greatest loss of revenue annually. In order to reduce the length of hospitalization for patients with severe CHF, we have embraced this method of rapid diuresis that is highly effective and well tolerated by all patients, including those > 65 years of age.

The average length of hospitalization for these 17 patients was 3.4 days. By comparison, the average LOS for the 42 control CHF patients at our hospital

**Table 3—Impact of Rapid Diuresis on Hospitalization Charges\***

Variables	IV Bolus Diuretic Therapy	24-h Continuous Diuretic Infusion
Mean LOS, d	5.7	3.4
Mean charge*	\$10,193	\$4,944
Medicare reimbursement	\$ 6,047	\$6,047
Net difference	-\$ 4,146	+\$1,103

\*Charges based on itemized patient billing statements.

receiving conventional diuresis was 5.7 days. Table 3 shows the potential impact of rapid diuresis and shortened hospitalizations on the costs for treating heart failure patients in our institution. The findings translate into potential savings of > \$500,000 for every 100 heart failure patients treated in this manner.

### Limitations

There are two major limitations to this study. One is the small number of patients treated. Although more patients have been treated in this manner and many of the 17 included in this study have been treated on several occasions, changes in medical staffing patterns prohibited a study period of longer duration.

The second limitation is that this was not a prospective, blinded study. Blinding this type of therapy would have been difficult technically and ethically. This was a prospective study, and the patients were selected sequentially, which should serve to avoid selection bias. However, these patients were compared to a large contemporary cohort of patients who were managed in the more conventional manner. The contemporary cohort did not match the IV infusion group in all characteristics but were the same age and apparent severity of heart failure. They served as "controls" primarily for comparing billing charges and length of hospitalization.

Since IV infusion therapy is the only practical method of delivering large doses of furosemide in a short period of time, comparison with bolus therapy was not possible. Furthermore the dose required must be titrated individually and varies from patient to patient, as well as in the same patient from hospitalization to hospitalization.

### CONCLUSION

CHF is a common condition among the elderly that is associated with significant morbidity and mortality, resulting in high health-care charges. In order to reduce the economic burden of frequent hospitalizations, strategies must be developed that

minimize the length of hospitalization for patients admitted to the hospital with severe heart failure. Our clinical experience has shown that aggressive high-dose diuresis using continuous IV infusions can be safely administered to elderly patients and may significantly shorten the hospitalization and reduce charges. Additional studies are needed to confirm these observations and document the cost-effectiveness of this approach.

### REFERENCES

- 1 Gheorghiadu M. Epidemiology, prevalence, treatments, and clinical trials: treatment of heart failure: a managed care perspective. *Am J Managed Care* 1998; 4(suppl 2A):S316-S328
- 2 Packer M, Cohn JN. Consensus recommendations for the management of chronic heart failure: evaluation of heart failure; clinical features. *Am J Cardiol* 1999; 83(suppl 2A): 2A-8A
- 3 Mills RM, Young JB. Practical approaches to the treatment of heart failure. Baltimore, MD: Williams & Wilkins, 1998; 2-17
- 4 Konstam M, Dracup K, Baker D, et al. Heart failure: evaluation and care of patients with left ventricular systolic dysfunction; clinical practice guideline No. 11. Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services, June 1994; AHCPR publication No. 94-0612
- 5 Taylor SH. Refocus on diuretics in the treatment of heart failure. *Eur Heart J* 1995; 16(suppl F):7-15
- 6 Dormans TPJ, Gerlag PGG, Russel FGM, et al. Combination diuretic therapy in severe congestive heart failure. *Drugs* 1998; 55:166-172
- 7 Brater DC. Resistance to loop diuretics: why it happens and what to do about it. *Drugs* 1985; 30:427-443
- 8 Gerlag PG, van Meijel JJ. High dose furosemide in the treatment of refractory congestive heart failure. *Arch Intern Med* 1988; 148:286-291
- 9 Rudy DW, Voelker JR, Greene PK, et al. Loop diuretics for chronic renal insufficiency: a continuous infusion is more efficacious than bolus therapy. *Ann Intern Med* 1991; 115: 360-366
- 10 Van Meyel JJM, Smits P, Dormans T, et al. Continuous infusion of furosemide in the treatment of patients with congestive heart failure and diuretic resistance. *J Intern Med* 1994; 235:329-334
- 11 Howard PA, Dunn MI. Severe musculoskeletal symptoms during continuous infusion of bumetanide. *Chest* 1997; 111: 359-364
- 12 Yelton SL, Gaylor MA, Murray KM. The role of continuous infusion loop diuretics. *Ann Pharmacother* 1995; 29:1010-1014



## Aggressive Diuresis for Severe Heart Failure in the Elderly\*

Patricia A. Howard and Marvin I. Dunn

*Chest* 2001;119; 807-810

DOI 10.1378/chest.119.3.807

**This information is current as of February 18, 2010**

<b>Updated Information &amp; Services</b>	Updated Information and services, including high-resolution figures, can be found at: <a href="http://chestjournal.chestpubs.org/content/119/3/807.full.html">http://chestjournal.chestpubs.org/content/119/3/807.full.html</a>
<b>References</b>	This article cites 8 articles, 3 of which can be accessed free at: <a href="http://chestjournal.chestpubs.org/content/119/3/807.full.html#ref-list-1">http://chestjournal.chestpubs.org/content/119/3/807.full.html#ref-list-1</a>
<b>Open Access</b>	Freely available online through CHEST open access option
<b>Permissions &amp; Licensing</b>	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://www.chestjournal.org/site/misc/reprints.xhtml">http://www.chestjournal.org/site/misc/reprints.xhtml</a>
<b>Reprints</b>	Information about ordering reprints can be found online: <a href="http://www.chestjournal.org/site/misc/reprints.xhtml">http://www.chestjournal.org/site/misc/reprints.xhtml</a>
<b>Email alerting service</b>	Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.
<b>Images in PowerPoint format</b>	Figures that appear in CHEST articles can be downloaded for teaching purposes in PowerPoint slide format. See any online article figure for directions

A M E R I C A N C O L L E G E O F



P H Y S I C I A N S<sup>®</sup>