Clinical Outcomes of a Furosemide Infusion Protocol in Edematous Patients in the Intensive Care Unit

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BACKGROUND—Many critically ill patients have severe volume overload due to vigorous fluid resuscitation. Optimal fluid management strategies to clear tissue edema are unclear.

OBJECTIVE—To assess safety and effectiveness of a clinical application of a furosemide infusion protocol in edematous critically ill patients.

METHODS—A prospective, cohort study of consecutive adult critically ill patients who received furosemide infusion by protocol from June 2003 to July 2004.

RESULTS—The mean total dose of furosemide was 2240 mg. The mean cumulative fluid balance therapy was -3376 mL. Electrolyte values in the critical laboratory range were 3.3% for potassium, 0.2% for sodium, and no critical values for magnesium. The mean change in creatinine level was +0.2 mg/dL during furosemide infusion therapy, but the mean creatinine level returned to baseline by 3 days after the furosemide infusion. A minimum mean arterial pressure less than 55 mm Hg occurred 12% of the time during the furosemide infusion.

CONCLUSIONS—Furosemide infusion therapy was associated with moderately negative cumulative fluid balances, electrolyte shifts, and mild transient worsening of renal function. (Critical Care Nurse. 2012;32[6]:25-34)

Many critically ill patients with capillary leak develop severe volume overload as a result of vigorous fluid resuscitation attempts. Although survival is enhanced by early goal-directed therapy in patients with sepsis,1 tissue edema is a frequent consequence of vigorous fluid resuscitation. Once capillary leak subsides during recovery, general interstitial edema remains and may impair organ function. In the case of acute lung injury, results of a randomized study indicate that a “conservative” fluid management strategy improves lung function and shortens the duration of mechanical ventilation and stay in the intensive care unit (ICU) without increasing nonpulmonary organ failure, compared with a “liberal” fluid strategy.2

Clearance of edematous fluid in the ICU may be difficult. Optimal fluid management strategies to accomplish this goal remain unclear. The purpose of this study is to assess outcomes of a clinical furosemide infusion protocol in edematous critically ill patients.

Methods
Consecutive critically ill adult patients from the respiratory ICU who received furosemide infusion by protocol between June 2003 and July 2004 were included in this prospective cohort study. The protocol was initiated at a physician's discretion and was used by ICU nurses to manage patients' fluid balance. Patients were excluded if they were treated with dialysis. Patients typically admitted to the respiratory ICU at LDS Hospital are those who require care for refractory respiratory failure after initial treatment in...
another ICU at LDS Hospital. Respiratory ICU patients typically stay in the unit several weeks. However, during the study period, the respiratory ICU also functioned as a general ICU to meet patient flow demands, so some critically ill patients without primary respiratory failure were also admitted to the respiratory ICU. LDS Hospital’s institutional review board approved this study, and informed consent was waived.

Data collected included age; sex; daily serum level of urea nitrogen; daily creatinine level; score on the Acute Physiology and Chronic Health Evaluation (APACHE) II; admission diagnosis; daily fluid balance; levels of sodium, potassium, and chloride; total carbon dioxide; duration of intubation; number of ventilator-free days; disposition destination; and survival. The lowest value for mean arterial blood pressure (MAP) for each patient was recorded each day. The lowest daily potassium and magnesium values and the highest daily sodium values were recorded.

Furosemide Infusion Protocol

LDS Hospital’s furosemide infusion protocol is a standardized set of orders for initiating and titrating intravenous infusions of furosemide in patients with peripheral edema (Table 1). Furosemide is a loop diuretic that may result in a markedly negative fluid balance, but also has the potential to create electrolyte and intravascular volume depletion and may worsen renal function. The protocol was developed before this study and was available to ICU nurses as a tool for managing ICU patients. The protocol was not modified for the study, nor was it changed during the study interval. The choice to initiate the furosemide infusion protocol was made by the physician on the basis of a patient’s clinical needs. The protocol was initiated after shock and capillary leak had subsided, as defined by stable blood pressure without the need for any vasopressor infusion or fluid resuscitation, but while the patient was still in the ICU. The protocol also provided guidance for replacement of electrolytes. Patients did not receive routine electrolyte replacement independent of the protocol. The ICU nurse could discontinue the furosemide infusion if hypotension developed or if there was concern about other adverse effects. The protocol does not include a bolus of furosemide except at the start of the protocol. Albumin and acetazolamide administration were not mandated by the protocol, but could be given at the discretion of the critical care physician.

Effectiveness

The effectiveness of furosemide infusion was evaluated by using measured fluid balance. All inputs, including tube feedings, flushes, intravenous fluids, and blood products, were recorded. For output, all urine and drain outputs were recorded. Stool was not counted unless liquid was obtained that could be subjected to a volume measurement. Measured fluid balance was the difference between the directly measured fluid input and output volumes. Daily weights were not assessed because of the inaccuracies inherent in weighing patients in ICU beds.

The mean daily fluid balance for each day of furosemide treatment was obtained by averaging all patients’ daily measured fluid balance values for that day. The fluid balances for full days of furosemide infusion (18 hours of infusion per day) were compared with those for partial days of furosemide infusion (1-17 hours of infusion per day). Individual cumulative fluid balance was calculated by adding together a given patient’s daily fluid balance values. The mean cumulative fluid balance was the average of the individual cumulative fluid balance values.

It was anticipated that patients’ unstable conditions would result in days on which no furosemide would be infused. It was expected that the furosemide infusion might be discontinued for acute hypotension,
volume depletion, recurrent sepsis, surgery, or high urine output. The furosemide infusion interval was defined as the time from the initial start to the final completion of the furosemide infusion, including the days on which furosemide had been temporarily discontinued. Within the furosemide infusion interval, fluid balance for days without furosemide infusion was reported separately from the fluid balance for days when there was some furosemide infusion, because it was not expected that furosemide would promote negative fluid balance on days when it was not administered.

### Safety Evaluation

All patients had continuous monitoring of heart rhythm during furosemide infusion. The safety of furosemide infusion was evaluated by using several measures. First, the episodes when the furosemide infusion was discontinued were evaluated. Physiological instabilities that required cessation of the furosemide infusion were categorized, and it was determined whether they resulted in temporary or permanent discontinuation of the furosemide infusion therapy.

Second, safety was evaluated by using measurements of MAP, which was measured automatically every 15 minutes in all patients in the respiratory ICU. The lowest MAP value for each patient each day was measured.

### Table 1

<table>
<thead>
<tr>
<th>Furosemide infusion protocol used at LDS Hospital*</th>
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### General information

- Intended for use when renal function is normal (creatinine clearance >50 mL/min per 1.73 m²)

### Monitoring

- Place patient on telemetry
- Chemistry panel, standing weights daily
- Check potassium and magnesium levels q6 hours
  - If potassium <3.2 mmol/L or infusion is >15 mmol/h, check potassium and magnesium levels q4 hours

### Diet/nutrition

- Change enteral feeding to RenalCal™ @.___ mL/h (suggested feeding rate is ideal body weight/2)
- Give amino acid liquid 40 mL via feeding tube q12 hours
  - Diet/nutrition should be ordered only if the gastrointestinal tract is functioning

### Medications – starting orders

- Start by giving furosemide 10 mg IV bolus
- Start furosemide infusion @ 0.5 mL/h, using undiluted furosemide (10 mg/mL)
- Units: 0.5 mL/h = 5 mg/h = 0.0833 mg/min = 120 mg/day
- Do not adjust infusion rate upward for at least 6 hours

### Adjusting furosemide infusion rate

- Urine output goal rate range is 150-250 mL/h (goal rate range may be modified)
- If urine output is less than goal after 6 hours of infusion, increase rate by 0.5 mL/h
  - Dose range: 0.1 to 6.0 mL/h = 0.0167 to 1 mg/min = 1 to 60 mg/h = 24 to 1440 mg/day
- Do not increase the rate more often than every 6 hours to avoid overshoot
- If urine output goal cannot be achieved with rates at or below 6 mL/h, contact physician
- If urine output for 3 hours is >3 times the upper urine output goal rate, decrease rate by 0.5 mL/h or by 1/2 the current rate, whichever is smaller
- Discontinue furosemide infusion if patient becomes hypotensive (systolic blood pressure <100 mm Hg) unless physician specifically orders it to continue

### Electrolyte management

- Discontinue all maintenance IV fluids and all sodium-containing IV and enteral products
  - EXCEPTION: pressure bags for monitoring catheters must use normal saline
- If sodium 146-150 mmol/L, give free water @ 25 mL/h (H₂O infusion via enteral tube or D5W IV).
- If sodium 151-154 mmol/L, give free water @ 50 mL/h (H₂O infusion via enteral tube or D5W IV)
- If sodium >154 mmol/L, give free water @ 100 mL/h (H₂O infusion via enteral tube or D5W IV)
- Maintain potassium >4.0 mmol/L by using potassium protocol
  - If creatinine level >2.0 mg/dL, keep potassium level >3.8 mmol/L
  - If potassium protocol and routine riders are not adequate to maintain potassium level >4.0 mmol/L, give potassium chloride via central catheter at up to 20 mmol/h
  - Use magnesium protocol to keep serum level of magnesium >2.0 mg/dL
  - If total CO₂ is >32 mmol/L, following physician approval, give acetazolamide 500 mg IV

Abbreviations: D5W, 5% dextrose in water; IV, intravenous or intravenously; q, every.

* Courtesy LDS Hospital, Salt Lake City, Utah.
recorded. In addition to recording lowest MAP values during the time the patients received the furosemide infusion, these values for the ICU days before the furosemide infusion was started and for the days after the furosemide infusion was concluded were recorded, to allow comparison of blood pressure values before, during, and after furosemide infusion therapy.

Third, safety was evaluated by using critical electrolyte values. Critical electrolyte values for our laboratory during the study were a magnesium level of 1.0 mmol/L or less or of 6.0 mmol/L or greater, a potassium level of 3.0 mmol/L or less or of 6.0 mmol/L or greater, and a sodium level of 120 mmol/L or less or of 155 mmol/L or greater.

Finally, safety was evaluated by assessing changes in renal function. The creatinine clearance was calculated by using the Cockcroft-Gault equation.4 The change in creatinine clearance was defined as the creatinine clearance on the last day of furosemide infusion therapy minus the creatinine clearance on the first day of furosemide infusion therapy. The changes in levels of creatinine and serum urea nitrogen were calculated in the same manner. Renal function was assessed for 3 days following the discontinuation of the furosemide infusion to determine whether there was delayed worsening in renal function after the furosemide infusion was discontinued.

As noted earlier, it was expected that furosemide infusions would be discontinued with development of new physiological instabilities. For the purposes of the safety analysis, all the data during the furosemide infusion interval were included, including the days when furosemide had been temporarily discontinued, to be sure that important safety problems that might be attributed to prior furosemide infusion were not missed. This is in contrast with the analysis of effectiveness, where fluid balance attributed to furosemide was calculated only for days in which furosemide was infused.

Statistics

Descriptive statistics were used for demographic and medical data including furosemide dose, daily fluid balance, cumulative fluid balance, electrolytes, serum level of urea nitrogen, creatinine level, creatinine clearance, and MAP. Data are presented as mean (SD), range, and percent.

Results

During the study period, the furosemide infusion protocol (Table 1) was used for all patients who received a furosemide infusion in the respiratory ICU. Forty-three patients met the study’s inclusion criteria, of whom 58% (n = 25) were men. Table 2 shows patients’ demographic and medical data. The most common primary diagnoses for our patients were pneumonia and sepsis.

Furosemide infusion was administered for a mean of 7.5 (SD, 4.4)
days (range, 2-25 days) per patient. The mean total dose of furosemide administered was 2240 (SD, 3340) mg (mean daily dose was 251 mg or approximately 10 mg/h). There was no correlation between total dose of furosemide and APACHE II scores \( (P = .28) \).

Acetazolamide was administered on 5% of the days during furosemide infusion. Albumin was administered on 22% of the days during furosemide infusion. The mean total dose of albumin was 201 g per patient. On days when albumin was administered, the mean daily dose was 74 g.

**Effectiveness**

The mean urine output achieved by the protocol was 150.4 mL/h. Furosemide infusion therapy was discontinued in 38 of 43 patients after improvement of edema (Table 3). The mean daily fluid balance for full days of furosemide infusion (218 hours of infusion) was -1908 (SD, 1607) mL. The mean daily fluid balance for partial days of furosemide infusion (1-17 hours of infusion) was -878 (SD, 2105) mL. The mean daily fluid balance for days within the furosemide infusion interval but without any furosemide infusion (see Table 3 for reasons that furosemide had been temporarily discontinued) was 907 (SD, 1876) mL.

Figure 1 shows cumulative fluid balance by day of therapy. The majority of negative fluid balance was achieved in the first 3 days of furosemide infusion therapy. The mean cumulative fluid balance for all days with furosemide infusion was -10600 (SD, 9100) mL. The mean cumulative fluid balance for days within the furosemide infusion interval but without any furosemide infusion (the days on which furosemide had been temporarily discontinued) was 7700 (SD, 13400) mL. Including all days of the furosemide infusion interval, regardless of whether furosemide infusion was administered on a given day or not, the mean cumulative fluid balance was -3776 (SD, 1752) mL.

**Safety**

Nine of the 43 study patients died during hospitalization, in all cases after the family and/or the

<table>
<thead>
<tr>
<th>Table 3 Reasons for discontinuing furosemide infusion in 43 patients</th>
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<tr>
<td><strong>Reason</strong></td>
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<tr>
<td>Permanent discontinuation (43 discontinuations in 43 patients)</td>
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<td>Improvement of edema</td>
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<td>Hypotension after recurrent sepsis</td>
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<tr>
<td>Worsening kidney function</td>
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<tr>
<td>Patient died (withdrawal of support at family’s request)</td>
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<tr>
<td>Temporary discontinuations (99 discontinuations in 43 patients)</td>
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<td>High urine output without hemodynamic instability</td>
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<td>Hypotension ( (n = 26) )</td>
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<tr>
<td>Furosemide given after recurrent sepsis</td>
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<td>New sepsis developing during furosemide infusion</td>
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<tr>
<td>Volume depletion</td>
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<td>Worsening kidney function</td>
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<tr>
<td>Electrolyte abnormalities (high sodium, low potassium)</td>
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<tr>
<td>Furosemide unavailable (interruption in pharmacy supply)</td>
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<td>Temporarily out of intensive care unit</td>
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<tr>
<td>Furosemide protocol started in error, then discontinued</td>
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<tr>
<td>Patient removed urinary catheter</td>
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<td>Lost intravenous access</td>
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<td>Unknown</td>
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patient requested withdrawal of active medical care. One patient died during furosemide therapy, whereas the other 8 patients died after completion of furosemide therapy. No deaths were attributed to furosemide therapy. For the 34 patients surviving hospitalization, the discharge dispositions were as follows: 9 discharged to home, 18 discharged to a skilled nursing facility, and 7 discharged to a rehabilitation facility.

Furosemide therapy was discontinued in 3 patients because of hypotension defined by physician discretion during recurrent sepsis, 1 patient because of worsening renal function, and 1 patient because of death due to withdrawal of medical support (Table 3). The other times that the furosemide infusion was discontinued were temporary, allowing resumption of the furosemide infusion once a transient condition had resolved (Table 3). The furosemide infusion was temporarily discontinued 13 times and permanently discontinued 1 time for worsening kidney function (Table 3).

Furosemide infusion was temporarily discontinued for hypotension 26 times. In 3 of these 26 episodes, hypotension was attributed to volume depletion, because the hypotension resolved with a fluid challenge. In 16 episodes in which patients recovered to normal blood pressure after recurrent sepsis, furosemide infusion was started but then discontinued when hypotension developed. In 7 episodes of hypotension, hypotension did not resolve with a volume challenge of 1 to 3 L of crystallloid. These 7 episodes were attributed to new sepsis because culture samples collected during the episodes subsequently showed growth of microorganisms.

Figure 2 shows the distribution of minimum daily potassium and magnesium values and maximum daily sodium values. Minimum daily potassium values occurred in the critical laboratory range 3.3% of the time (all critical minimum potassium values fell within the 2.2-3.0 mmol/L range). Maximum daily sodium values occurred in the critical laboratory range 0.2% of the time (a single value of 155 mmol/L). No magnesium values fell within the critical laboratory range.

On the day that the furosemide therapy was started, the patients’ mean serum level of urea nitrogen was 39 (SD, 20) mg/dL (range, 13-100 mg/dL; to convert to millimoles per liter, multiply by 0.357), and mean creatinine level was 1.4 (SD, 0.8) mg/dL (range, 0.4-4.5 mg/dL; to convert to micromoles per liter, multiply by 88.4). Figure 3 shows that the changes from beginning to end of furosemide infusion interval were 3 (SD, 22; range, -51 to +64) mg/dL for serum urea nitrogen, 0.2 (SD, 0.8; range, -2.4 to +2.8) mg/dL for creatinine, and -6 (SD, 16; range, -39 to +34) mL/min for creatinine clearance. Twenty-three percent of the patients had a decrease in creatinine clearance of more than 20 mL/min per 1.73 m² (to convert to mL/s per square meter, multiply by 0.0167). After completion of furosemide infusion therapy, the mean creatinine values decreased, so that by 3 days after the furosemide infusion, the mean creatinine level returned to baseline (mean [SD] for creatinine values after furosemide infusion: day 1, 1.6 [0.9] mg/dL; day 2, 1.5 [0.9] mg/dL; day 3, 1.4 [0.9] mg/dL).

Figure 4 shows the distribution of the lowest MAP values with respect to furosemide infusion.
to furosemide infusion interval. The mean lowest daily MAP values increased modestly over time. The lower ends of the distributions shown in Figure 4 might be more clinically important than the overall distributions. Considering the lowest minimum MAP values, the rate of the distributions with a minimum MAP less than 55 mm Hg were 17% before the furosemide infusion started, 12% during the furosemide infusion interval, and 9% after the furosemide infusion therapy was completed.

Discussion

Significant diuresis was achieved while patients were receiving the furosemide infusion. It is unclear why there was little additional negative fluid balance after 3 days of furosemide infusion therapy. Optimal fluid management strategies for critically ill patients appear to vary depending on the phase of a patient’s illness. During the early capillary leak phase, vigorous goal-directed fluid resuscitation results in improved mortality in patients with sepsis. However, after capillary leak has subsided in the postresuscitation phase, “excess fluid becomes an enemy when it is no longer physiologically needed.” In a retrospective analysis, Murphy et al suggest that both adequate initial fluid resuscitation and subsequent late conservative fluid management are necessary for optimal reduction of hospital mortality. A number of hypothesis-generating studies have suggested that a fluid-negative strategy might

![Figure 3](image-url) **Figure 3** Box and whisker plots of changes in renal function during furosemide infusion. Shown are the mean values (horizontal line within box), 25th and 75th percentiles (upper and lower edges of box), and 95th percentile (bars above and below box), and outliers (individual circles).

![Figure 4](image-url) **Figure 4** Minimum mean arterial pressure, before, during, and after furosemide. Shown are the mean values (horizontal line within box), 25th and 75th percentiles (upper and lower edges of box), and 95th percentile (bars above and below box), and outliers (individual circles).
be beneficial after fluid resuscitation in critically ill patients.\textsuperscript{18,47}

In the only large, controlled multicenter study of fluid balance in fluid-resuscitated patients with acute lung injury, the investigators found that a “conservative” fluid management strategy resulted in improved lung function and shortened duration of mechanical ventilation and ICU stay compared with a “liberal” fluid strategy, without any increase in nonpulmonary organ failure.\textsuperscript{2} A subset analysis of the surgical patients from the Acute Respiratory Distress Syndrome Clinical Trials Network study showed findings similar to the results of the whole-group analysis.\textsuperscript{18} However, these studies looked at patients with acute lung injury early in their illness, so these results may not apply to other groups of patients or to other times in the course of an ICU stay. Randomized clinical trials are needed to determine how best to treat edema in patients such as those in the respiratory ICU. The ideal fluid management strategy remains to be defined in patients with respiratory failure,\textsuperscript{19} and evidence is limited regarding the use of loop diuretics in ICU patients with acute kidney injury.\textsuperscript{20}

Furosemide infusion may come with adverse hemodynamic, electrolyte, and renal consequences. As Rivers\textsuperscript{6} also indicates, conservative fluid strategies, perhaps even with the use of diuretic provocation, along with appropriate caution to preserve organ perfusion and avoid metabolic derangement, are therapeutically sound in the postresuscitation phase. However, additional research is needed to determine how to accomplish these goals simultaneously and safely. Hemodynamically guided fluid management using cardiac index and pulmonary artery occlusion pressure does not improve survival rates or organ function compared with therapy guided by central venous pressure and was associated with more complications.\textsuperscript{21}

In our patients, hypotension was not more frequent with use of the furosemide infusion protocol. We are not aware of data that establish adequate MAP values, so we are not able to determine if our patients’ baseline values are adequate. Instead we evaluated whether there were furosemide-associated declines in MAP values compared with baseline MAP values (Figure 4).

Our results suggest that frequent temporary cessation of furosemide infusion because of instability of the patient’s condition may be necessary in management of edema in critically ill patients (Table 3). Sepsis was more frequently associated with discontinuation of furosemide infusion for hypotension than was volume depletion. Although electrolyte shifts were common, they seemed to be clinically manageable. Renal function trended worse with furosemide infusion, but returned to baseline within 3 days. Thus, although our data suggest an adequate safety profile, our nonrandomized data do not provide definitive conclusions about the safety of furosemide infusions in edematous ICU patients.

Our study does not compare furosemide administered by bolus with furosemide infusion therapy. In a study of 33 patients, Schuller et al\textsuperscript{22} concluded that continuous and bolus furosemide regimens are equally effective in achieving negative fluid balance. In a review of the literature, Martin et al\textsuperscript{23} found few well-designed studies of continuous infusion of loop diuretics, but they favored this approach on the basis of pharmacodynamic concepts. A controlled comparison of bolus versus continuous infusion furosemide is needed to determine if furosemide infusion is superior to bolus therapy.

Our study was not designed to evaluate the possible supplemental benefits of albumin therapy added to furosemide infusion, although some of our patients did receive albumin along with furosemide infusion. In a randomized controlled trial of 40 patients with acute lung injury, the 20 patients who received 25 g of 25% albumin every 8 hours for 3 days along with furosemide infusion had improved oxygenation, greater negative fluid balance, and better maintenance of hemodynamic stability than did the patients treated with furosemide infusion alone.\textsuperscript{24} Patients who received albumin had a greater negative 7-day cumulative negative fluid balance (approximately -4500 mL) than our patients had (-3900 mL), whereas the control patients had a less negative cumulative negative fluid balance (approximately -1500 mL). These results are similar to our results, when one takes into account that our patients received albumin on 22% of the furosemide infusion days, so that they might be expected to fall in between the control and albumin groups of Martin et al.\textsuperscript{24}

Physicians and nurses demonstrated considerable variability in decisions of when to discontinue the furosemide infusion. For example, some clinicians would discontinue...
the furosemide infusion for potassium values that were well above the critical minimum value of 3.0 mmol/L, whereas other clinicians would continue the furosemide infusion despite potassium values as low as 2.7 mmol/L. Therefore, our results are limited by the lack of predetermined end points specifying what degree of new abnormality should cause discontinuation of the furosemide infusion. Out of a total of 32 critical minimum daily potassium values and 1 critical maximum daily sodium value, furosemide infusion was discontinued only 6 times because of concerns about electrolyte values (Table 3). Physicians and nurses with more experience with the protocol seemed more confident that they could control electrolyte values while continuing the furosemide infusion. Our study is limited by lack of randomization. It was not our intent in this cohort study to assess outcome differences in patients undergoing diuresis compared with edematous patients who did not receive the furosemide infusion protocol, an issue that has been addressed by the Acute Respiratory Distress Syndrome Network study. Rather, we assessed outcomes of a clinical furosemide infusion protocol in edematous critically ill patients. Another limitation is that the furosemide infusion in our study was not directed by hemodynamic parameters.

Conclusion
Furosemide infusion therapy is associated with moderately negative cumulative fluid balances, electrolyte shifts, and mild transient worsening of renal function during therapy. Hypotension was not more frequent during furosemide infusion therapy, and most hypotension that resulted in discontinuation of furosemide was more often associated with recurrent sepsis than furosemide-induced volume depletion. Controlled studies are needed to determine optimal strategies for achievement of negative fluid balance in edematous ICU patients.

References

Clinical Outcomes of a Furosemide Infusion Protocol in Edematous Patients in the Intensive Care Unit

Facts
Furosemide infusions pose a challenge to critical care nurses who care for patients undergoing furosemide infusion therapy for volume overload. Many critically ill patients develop severe volume overload due to vigorous fluid resuscitation attempts. Clearance of edema fluid in the intensive care unit may be difficult, and optimal fluid management strategies to clear tissue edema are unclear. This study set out to assess outcomes of a clinical application of a furosemide infusion protocol in edematous critically ill patients.

- Forty-three patients met study inclusion criteria. The most common diagnoses for these patients were pneumonia and sepsis.
- Furosemide infusion was administered for a mean of 7.5 ± 4.4 days (range 2-25 days) per patient.
- The mean total dose of furosemide administered was 2240±3340 mg.
- Furosemide infusion therapy was discontinued in 38 of 43 patients after improvement of edema.
- The majority of negative fluid balance was achieved in the first 3 days of furosemide infusion therapy.
- Including all days of the furosemide infusion interval, regardless of whether furosemide infusion was administered on a given day or not, the mean cumulative fluid balance was -3776 ± 1752 mL.
- Nine of the 43 patients died during hospitalization, in all cases after family and/or patient requested withdrawal of active medical care. One patient died during furosemide therapy, while the other 8 patients died after completion of furosemide therapy. No deaths were attributed to furosemide therapy.
- Furosemide therapy was discontinued in 3 patients because of hypotension defined by physician discretion during recurrent sepsis, 1 patient because of worsening renal function, and 1 patient because of death due to withdrawal of medical support.
- Optimal fluid management strategies for critically ill patients appear to vary depending on the phase of a patient’s illness. During the early capillary leak phase, vigorous goal-directed volume resuscitation results in improved mortality in septic patients.
- After capillary leak has subsided in the postresuscitation phase, excess fluid becomes harmful when it is no longer physiologically needed.
- A retrospective analysis suggests that both adequate initial fluid resuscitation and subsequent late conservative fluid management are necessary for optimal reduction of hospital mortality. A number of hypothesis-generating studies have suggested that a fluid-negative strategy might be beneficial after fluid resuscitation in critically ill patients.
- Furosemide infusion may come with adverse hemodynamic, electrolyte, and renal consequences.
- Furosemide infusion therapy is associated with moderately negative cumulative fluid balances, electrolyte shifts, and mild transient worsening of renal function during therapy. Hypotension was not more frequent during furosemide infusion therapy, and most hypotension that resulted in discontinuation of furosemide was more often associated with recurrent sepsis than furosemide-induced volume depletion. Controlled studies are needed to determine optimal strategies for achievement of negative fluid balance in edematous intensive care unit patients.

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