Closed-Loop Resuscitation of Burn Shock

Stephen L. Hoskins, PhD, Geir Ivar Elgjo, MD, PhD,*
Jialung Lu, PhD,* Hao Ying, PhD,† James J. Grady, Dr PH,*
David N. Herndon, MD‡, George C. Kramer, PhD* 

Fluid therapy for burn shock is adjusted to establish a target level of urinary output. However, the means for adjusting infusion rate are not defined. Our objective was to compare the performance of automated computer-controlled resuscitation with manual control for burn resuscitation. Sheep with a 40% TBSA full-thickness burn, administered under halothane anesthesia, were resuscitated to restore and maintain normal sheep urinary outputs in a target range of 1 to 2 mL/kg per hour over the course of 48 hours using closed-loop resuscitation (n = 10) or manual hourly adjustment of infusion rate (n = 11). The automated closed-loop resuscitation system is based on a proportional—integral—derivative algorithm, which adjusted infusion rate based on continuous monitoring and changes in urinary output. Mean urinary outputs over the course of 48 hours were in target range and were virtually identical at 1.9 ± 0.5 mL/kg per hour for the closed-loop group and 2.0 ± 0.7 mL/kg per hour for the technician group. Mean infusion rates and infused volumes also were similar. The closed-loop group exhibited significantly lower hourly variation for both urinary output and infusion rate compared hourly control. Hourly targets were achieved in 41% of the measurements in technician group compared with 48% for the closed-loop group (P = .23). Hourly urinary output in the technician group was undertarget by 25% as opposed to 16% with the closed-loop group (P = .02). Automated closed-loop control of infusion rates after burn injury produced urinary outputs in target ranges with less variation and less under target values than manual hourly adjustments. Closed-loop resuscitation may provide an improvement over current resuscitation regimens. (J Burn Care Res 2006;27:377-385)

Optimal treatment of burn victims requires prompt initiation of fluid therapy and sustained care by specialized burn care experts. Advanced burn care experience and expertise are not common among clinicians, either military or civilian. A simpler and automated means for guide resuscitation could provide value to both burn centers and for the initial care givers whom do not have advanced burn care expertise. Furthermore, a systematic defined approach for adjusting infusion rate based on target endpoint(s) would provide a standardized resuscitation protocol for different burn centers, which would allow for comparison of other aspects of early burn care.

Recent clinical studies and reviews suggest that over-resuscitation of patients with burns and major surgery has become a common problem. The mortalities associated with fluid overload include pulmonary edema and impaired gas exchange; abdominal compartment and intestinal ischemia syndrome; delayed wound healing; increased incidents of infection and sepsis; and multiorgan failure. The Advanced Burn Care Life Support (ABLS) guidelines established by the American Burn Association recommend a range of total fluid volumes over the course of 24 hours of 2 to 4 mL/kg per % TBSA, with infusion rate adjusted to maintain a urinary output of 0.5 to 1.0 mL/kg/hr. A recent meta-analysis of published studies of burn resuscitation that used either the Brooke or Parkland formulas showed that both the total volume administered and mean urinary outputs were greater than ABLS guidelines. Actual resuscitation

From the *Resuscitation Research Laboratory, Department of Anesthesiology, University of Texas Medical Branch, Galveston, Texas; †Department of Electrical and Computer Engineering, Wayne State University, Detroit, Michigan; and ‡Shriners Burns Hospital, Galveston, Texas.

Address correspondence to George C. Kramer, PhD, Department of Anesthesiology, University of Texas Medical Branch, 301 University Boulevard, Galveston, Texas 77555-0891.

Supported by Shriners Burns Hospital Grants #8720 and #88450.

The research was conducted in UTMB's Investigational Intensive Care Unit.

Copyright © 2006 by the American Burn Association.

DOI: 10.1097/01.BCR.0000216512.30415.78

377
practices within a single institution often are quite individualized; despite over-resuscitation concerns, no clear guidelines are established for adjusting infusion rate to urinary output.

Closed-loop fluid resuscitation is automated adjustment of infusion rate based on a control algorithm that adjusts infusion rate to obtain a specific physiological endpoint. Clinically, closed-loop control has been used in nitropressure infusion of postsurgical cardiac patients. Experimentally, closed-loop fluid therapy has been used for treatment of hemorrhage using blood pressure and tissue oxygen as endpoints. Bowman and Westenskow described the design of closed-loop control for burn resuscitation using a proportional—integrative—derivative (PID) controller. We are unaware of any controlled study in which data on the performance of closed-loop resuscitation of burns has been reported.

A logical clinical application of closed-loop control of fluid therapy is burn resuscitation because one primary endpoint, urinary output, is clinically well established. Subsequently, we designed a PID controller and an automated closed-loop resuscitation system that used urinary output rate and short-term urinary output history as controller inputs for a feasibility study of the performance of closed-loop resuscitation system using a defined animal model of burn injury. We previously demonstrated that infusion rate could be adjusted using an hourly decision table based on urinary output and that this approach produced mean urinary outputs in the target range. The questions addressed in the present study: 1) Can a closed-loop system adequately control infusion rate? 2) How does closed-loop adjustment of infusion therapy compare with a decision table that defines hourly adjustment? The outcome variables were the mean and the variation of hourly urinary outputs, total infused volume and the percent of hourly measurements in which urinary output was above, in or below target range.

**MATERIALS AND METHODS**

The experimental protocol was reviewed and approved by the Institutional Animal Care and Use Committee of the University of Texas Medical Branch at Galveston, with adherence to National Institutes of Health guidelines for care and use of laboratory animals (NIHAR Publication, 1996 NRC ISBN 0-309-05577-3).

**Animal Preparation**

Adult, female Merino sheep (28–42 kg) were anesthetized with 1.5% halothane anesthesia and mechanically ventilated. They were then instrumented with indwelling vascular catheters in 1) the abdominal aorta for monitoring blood pressure and 2) the inferior vena cava for infusion of maintenance fluid during surgery and for infusion of resuscitation fluids after burn. A 7-French Swan Ganz catheter (Baxter Healthcare Corp, Irvine CA) was positioned in the pulmonary artery for measurement of cardiac output by thermodilution and to monitor hemodynamic stability throughout 48-hour time period of the study. The burn experiments were performed 5 to 7 days after surgery.

The **Closed-Loop Resuscitation System**

The closed-loop resuscitation system consisted of three components: a Wintel PC, a Baxter Flo-Gard model 620 IV pump (Baxter Healthcare, Deerfield, IL), and a Bard Criticare Urinary Output Monitor (C. R. Bard, Inc., Covington, GA). The Bard Urinary Output Monitor had a RS-232 output to provide data on urine volume, which was queried every 60 seconds. Another RS-232 output was connected to the Baxter Flo-Gard pump to provide digital control of infusion rate. Urinary output was averaged for running 5-minute blocks, and these data were used as the input signal for the controller. The controller, implemented in Visual Basic programming language, adjusted the infusion rate every minute.

PID is a common control approach used by engineers for machinery and electronic devices. It approaches control much as an expert physician intuitively analyzes clinical data. A burn expert evaluates the target levels compared with the patient's last urinary output (proportional), the last several measurements of urinary output (integral), and the rate of change of urinary output (derivative). The controller was designed as a positional PID controller. Infusion rate at time (t) is $I_t$ and is calculated from the previous infusion rate and an adjustment factor or $u(t)$ where

$$I_t = I_{t-1}[1 + u(t)]$$

and

$$u(t) = k_p e(t) + k_i \int e(t) dt + k_d \frac{de(t)}{dt}$$

where

$$e(t) = \text{target} - UO(t)$$

is the error signal. Here, $UO(t)$ is the measured urinary output and "target" is the desired urinary output. We used the discrete-time version of the controller. $K_p$, $K_i$, and $K_d$ are the proportional gain, integral gain, and derivative gain, respectively. In pilot experiments, we
tuned the controller and found that the most stable performance was achieved without the derivative control action (i.e., $K_p = 0$). As a result, the PID controller was reduced to a PI controller. Our tuning effort led to $K_p = 0.2857$ and $K_i = 0.6165$. These gains were then fixed for the remaining experiments. Due to the limitation of the animal number, we did not attempt to optimize the gains.

**Protocol.** The study length of 48 hours was chosen as being representative of the initial resuscitation period. The first 48-hour period after burn injury is critical for the resuscitation of burns greater than 40% TBSA and is aimed at supporting and stabilizing the patient in a burn-induced hypovolemic state. On the experiment day, sheep were anesthetized with halothane, weighed, and a urinary bladder catheter was placed and secured for measurement of urinary output. Sheep then received a 40% TBSA full-thickness flame burn while still under anesthesia. Sheep were then allowed to recover from the anesthesia. Buprenorphine, 0.3 mg intramuscularly, was administered before the burn injury and every 12 hours thereafter. Animals were denied water for the duration of the 48-hour experiment, but were allowed free access to dry food after 24 hours.

**Resuscitation.** One hour after burn injury, animals initially were resuscitated by starting the infusion with either the closed-loop system or by the technician who manually set the infusion rate on the intravenous pump. For both groups, the same initial rate was determined by using the Parkland formula, which is an initial rate of 10 ml/kg/hr for the 40% TBSA burn. No adjustments were made during the first hour of resuscitation for either group but, thereafter, the closed-loop system adjusted the infusion rate as determined by the controller and the technician began hourly adjustments using a decision table, Table 1. The minimum rate was set to 20 ml per hour and the maximum was set to 20 ml/kg/hr (800 ml/hr in a 40-kg sheep).

Both approaches were designed to adjust infusion rate to achieve and maintain sheep urinary outputs in a specific target range. In previous studies, we determined that a urinary output of 1.0 to 2.0 ml/kg/hr is the normal range of urinary output for sheep and equates to the standard of care target range in humans of 0.5 to 1.0 ml/kg/hr for fluid resuscitation of burns. When burn-injured sheep were resuscitated to this range of urinary output cardiac output was normalized and other measures of hemodynamics were indicative of adequate resuscitation. Specifically, for the technician-controlled resuscitation a decision table was used to adjust infusion rate when urinary output was out of normal or target range 1.0 to 2.0 ml/kg/hr (Table 1) as previously described. The closed-loop controller required a specific target value and was set for midtarget range or 1.5 ml/kg/hr. Resuscitation was continued through 48 hours, at which time the study ended and the animals were euthanized.

We assigned animals to receive either technician-controlled resuscitation or closed-loop control resuscitation. These experiments were performed during a period in which our laboratory was using both crystalloid and colloid (hetastarch and dextran) for initial resuscitation. In both groups approximately half the animals were resuscitated with crystalloid and half with colloids. We demonstrated in previous studies that our decision table could adequately control urinary output to a target range in burn-injured sheep using a variety of fluids. Fluid therapy was started at 1-hour after burn injury and sustained through 48 hours. The crystalloid animals were resuscitated exclusively with lactated Ringer’s (LR). The colloid animals had resuscitation started with either 6% Hetastarch (Hesperan, Baxter Healthcare), or 6% Dextran 70 (Gentran, Baxter Healthcare). After a 30 ml/kg dose of colloid, which typically lasted 6 to 8 hours, animals subsequently were resuscitated with LR until the study ended.

**Data Analysis.** For both groups, urinary output and infusion rate were recorded each hour. For the closed-loop control system, data also were captured electronically. Mean values and standard deviation as an index of variation were calculated for urinary output and infusion during the 48-hour resuscitation period. The means of hourly assessments for each animal were compared between groups using the Wilcoxon Mann–Whitney rank sum test. Total 48-hour cumulative urinary output, fluid infused, and net fluid (infused minus urinary output) were compared using a two-sample Student’s $t$-test. For com-

<table>
<thead>
<tr>
<th>Urinary Output table used for technician-controlled resuscitation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table 1. Decision table used for technician-controlled resuscitation</strong></td>
</tr>
<tr>
<td><strong>Urinary Output During</strong></td>
</tr>
<tr>
<td><strong>Previous Hour</strong></td>
</tr>
<tr>
<td>(ml/kg$^{-1}$.hr$^{-1}$)</td>
</tr>
<tr>
<td>&lt;0.5</td>
</tr>
<tr>
<td>0.5–0.75</td>
</tr>
<tr>
<td>0.75–1.0</td>
</tr>
<tr>
<td>1.0–2.0</td>
</tr>
<tr>
<td>2.0–3.0</td>
</tr>
<tr>
<td>3.0–4.0</td>
</tr>
<tr>
<td>&gt;4.0</td>
</tr>
</tbody>
</table>

paring the proportions of measurements when hourly urinary output measurers were "under-target," "on-target," or "over-target," a general linear model was fit using general estimating equations. Categories were combined to create binary outcomes assessed hourly (eg, "on target" vs "not on target"). The hourly measures from each animal were treated as a correlated cluster of data, with an assumed exchangeable correlation. Model estimates are reported as odds ratios and 95% confidence limits. Treatment effects were assessed at the 0.05 significance levels.

RESULTS

We performed 21 experiments, which were assigned randomly to either technician control (n = 11) or closed-loop control (n = 10). Of the 10 closed-loop control studies, 4 were with LR, 4 with dextran 70, and 2 were with hetastarch. Of the 11 technician control studies, 5 were with LR, 2 with dextran 70, and 4 with hetastarch. We monitored cardiac output, heart rate, right atrial and pulmonary pressures. Hemodynamics were normalized by resuscitation and were virtually identical in both treatment groups (closed-loop vs technical) and when compared for crystalloid or colloid. As in our present study and several published studies using this model full restoration and maintenance of hemodynamics are achieved with fluid therapy when normal urinary outputs are established.14,16,17 However, the focus of this study was not hemodynamics.

Mean urinary outputs of both groups are plotted as cumulative volume vs time (Figure 1). Results were identical for closed-loop group and the technician group. The total 48 hours of cumulative urinary outputs were 92.5 ± 5.4 ml/kg vs 94.5 ± 5.7 ml/kg for the closed-loop group and technician group, respectively. No differences in urinary output were apparent when animals were subgrouped for crystalloid or colloid treatment.

Figure 2 shows individual data of the cumulative urinary output in both groups. Despite the mean data being similar, a greater variation in the technician group was apparent vs the closed-loop group. These data are further examined in Figure 3 (upper graph), which shows hourly rate of urinary output (ml/kg/hr) plotted vs time with parallel dotted lines representing the low and high target levels. Mean hourly urinary outputs from both groups were near the upper limit of the target range. Over the course of 48 hours, the means ± SE for the rates of urinary output were similar 1.94 ± 0.52 ml/kg/hr for the closed-loop group and 1.97 ± 0.70 ml/kg/hr for the technician group. The highest and lowest mean hourly values, as well as higher peaks of urinary output, were

![Cumulative Urinary Output](image1)

**Figure 1.** Mean cumulative urinary output is plotted each hour during 48 hours of fluid therapy after a 40% TBSA full-thickness burn injury for technician control and for closed-loop control. Data shown are the mean values of 11 sheep resuscitated by technician control using a decision table (squares) and 10 sheep resuscitated by closed-loop control (circles).

![Cumulative Urinary Output](image2)

**Figure 2.** Individual sheep data shown in dashed lines for the cumulative urinary output of 11 sheep resuscitated with the technician control using a decision table (upper graph) and 10 sheep resuscitated by closed-loop control (lower graph). The single solid bold line on each graph represents the mean value of each group.
Figure 3. **Upper graph.** Mean urinary output for each hour of 48 hours of resuscitation is plotted for 11 sheep with infusion rate adjusted by technician control using a decision table (squares) and 10 sheep resuscitated by closed-loop control (circles). The parallel dotted lines represent the upper and lower targets for the normal urinary output of sheep. There was no significant treatment difference for rate of urinary output. **Lower graph.** The hourly standard deviation of urinary output is a measure of variation and is plotted for 48 hours of fluid therapy for 11 sheep resuscitated by technician control using a decision table (squares) and 10 sheep resuscitated by closed-loop control (circles). There was a significant treatment difference for variation of urinary output ($P = .027$).

Table 2. Hourly urinary outputs: on-target, over-target, and under-target with target range defined as 1.0 to 2.0 ml/hr target with performance statistically compared for both treatment groups

<table>
<thead>
<tr>
<th>Group</th>
<th>On Target</th>
<th>Over Target</th>
<th>Under Target</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technician control; 11 sheep, 508 measurements</td>
<td>198, 40%</td>
<td>175, 35%</td>
<td>122, 25%</td>
<td>495, 100%</td>
</tr>
<tr>
<td>Closed-loop control; 10 sheep, 475 measurements</td>
<td>214, 47%</td>
<td>173, 38%</td>
<td>73, 16%</td>
<td>460, 100%</td>
</tr>
</tbody>
</table>

Figure 3 (lower graph) is a plot of the variation (standard deviation) of the urinary output over the 48-hour period for each group. The variation is nearly superimposable for both groups during the first 12 hours but, thereafter, larger hourly variations were observed in the technician group, with noticeable peaks at postburn hours 18 and 30, and several peaks between postburn hours 40 to 46. The mean of the hourly variation over the course of 48 hours in the closed-loop group was significantly less, ie, 0.96 ± 0.08 ml/kg/hr, than in the technician group, ie, 1.38 ± 0.10 ml/kg/hr ($P = .027$).

Table 2 shows the number and percent of hourly occurrences for which urinary output was in, above, or below target range for both groups. Of the 495 urinary output measurements for the technician group, 40% were on target compared with 47% of the 460 measurements for the closed-loop group. The odds ratio for being on-target in the closed-loop group versus the technician group was 1.31 (95% confidence interval 0.85–2.0) but did not reach statistical significance ($p = .23$). The closed-loop group had urinary outputs that were undertargeted 16% of the time, which was significantly lower than the technician group in which 25% of the measurements were undertargeted, odds ratio equal to 0.58 (95% confidence interval: 0.38–0.89; $P = .02$). The overtarget incidence of urinary outputs were similar between groups, that is, 35% in the technician control and 38% with closed-loop control, with an odds ratio of 1.10 (95% confidence interval: 0.74–1.65; $P = .65$).

Mean infusion rate, Figure 4 (top graph), and total volume infused for the closed-loop group were both similar to that for the technician group measured over the course of 24 and 48 hours. The 24-hour infused volumes were virtually identical to Parkland rate in both groups, 3.1 ± 0.3 ml/kg/%TBSA and 3.2 ± 0.8 ml/kg/%TBSA in the closed-loop and technician groups, respectively. The choice of fluid did not influence the achievement of urinary output as examined from mean or individual animals. Figure 2 shows both the individual response of each animal and the apparent in the technician group at 10, 19, and 42 to 46 hours after burn injury.
mean group responses. When target urinary outputs were achieved, hemodynamics were normalized regardless of the fluid type in all animals. Further, the two treatment groups (closed-loop vs technician) were evenly matched with about half the animals resuscitated with crystalloid and half with colloid. There was no significant difference in the total volume of fluid infused between the technician group and closed-loop group when results were compared for fluid type. Table 3. Despite similar mean values for infusion rate, the variation (standard deviation) of hourly infusion rates, Figure 4 (bottom graph), were significantly higher in the technician group, 4.7 ± 0.4 mL/hr vs 3.6 ± 0.3 mL/hr for the closed-loop group (P = .032).

Table 3. Total 48-hour fluid requirements (mL/kg)

<table>
<thead>
<tr>
<th></th>
<th>Lactated Ringer’s</th>
<th>Colloid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technician</td>
<td>170 ± 6 (n = 5)</td>
<td>234 ± 21 (n = 6)</td>
</tr>
<tr>
<td>Closed-loop</td>
<td>147 ± 20 (n = 4)</td>
<td>197 ± 21 (n = 6)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

From the perspective of mean fluid in and mean urinary output, the performance of the closed-loop resuscitation system and the decision table were similar. Both treatments produced mean urinary outputs within the target range, but on the high side of the range. However, the variation was significantly lower for both urinary output and infusion rate in the closed loop group. Additionally, the percent of urinary output measurements in the under-target range were significantly less in the closed-loop group, which would suggest that closed-loop systems can provide tighter control and therefore are less likely to have instances of under-resuscitation occur when compared to hourly control. The overall goal of fluid resuscitation of burns is to continuously titrate the volume of fluid infused to prevent over- and under-resuscitation. The results of under-resuscitation and over-resuscitation can be deleterious and associated with increased incidence of morbidity and mortality.

In clinical settings, physicians may accept high urinary outputs without decreasing infusion rate and more diligently increase infusion rate when urinary output is low. This viewpoint appears to be confirmed by a meta-analysis of published burn resuscitation studies showing that mean urinary outputs and infused volumes were greater than ABLs guidelines.

Mean 24-hour urinary outputs were 1.2 ± 0.4 mL/hr/kg and mean fluid requirements were 5.0 ± 1.2 mL/kg/%TBSA as reported for 1340 patients in 23 studies. All studies reported mean volume requirements greater than the Brooke formula (2 mL/kg/%TBSA) and 88% reported mean values above the Parkland formula (4 mL/kg/%TBSA). These data suggest that most burn patients are being administered fluid in excess of guidelines. It is a reasonable hypothesis that burn patients could benefit by a systematic means for adjusting infusion rate, be it closed-loop control or the use of decision tables.

The clinical consequences of tighter control of fluid therapy after burn injury and other major trauma and the achievement of having urinary outputs within established guidelines with less hourly variation are not known. However, several recent reviews and studies suggest that over-resuscitation leads to significant pathology in burn patients and surgical patients.
in general. Pruitt suggested that "fluid creep" has occurred in modern burn care and that excessive resuscitation of burn injury has become more common. Such fluid excess can cause intra-abdominal compartment syndrome and pulmonary edema and may contribute to delayed wound healing and even the incidence of multiorgan failure.\textsuperscript{3,5,6,20} We suggest the defined systematic means for adjusting infusion rate using either a decision table or autonomous closed-loop control may improve outcomes in patients requiring large volume fluid therapy.

In 1981, Bowman and Westenskow were the first to suggest and build a PID controller for fluid resuscitation of burns.\textsuperscript{13} They built drop counters to monitor both infusion rate and urinary output. In an era before PCs were common, they built a specialized microprocessor for their controller. They used a PID algorithm based on a mathematical model, which was used to control resuscitation in a small number of dog experiments. They verified accurate monitoring of fluid in and urine out, but no performance trials were performed.

The present study demonstrates that in this model of burn resuscitation the application of a closed-loop control system vs manual hourly adjustments is feasible and may improve tighter control of urinary output than with a decision table, which is expected to be more the case after the controller gains are optimized. An extension of our findings is that an automated system may provide more accurate fluid resuscitation with fewer errors, especially in a multiprovider environment (two or three staff shifts per 24 hours) and scenarios in which a large number of patients with varying degrees of injury have to be resuscitated simultaneously. Scenarios in which mass casualties are generated can overextend first responders and burn unit resources. A closed-loop system's continuous and tight control over fluid delivery is a potential resource to save person-hours and optimize care. For automated, closed-loop fluid resuscitation to become reality, one of several necessary conditions must be met, the system itself must be stable, with built-in safety features and manual override. Ideally, all actions and results produced by the system must be easily viewed on a display.

Our closed-loop system performed well, but based on 48-hour means of total fluid in and mean urinary output, the results were essentially identical to the use of an hourly decision table. However, the lower variation in urinary output and infusion rate, along with the decreased incidence of undertarget urinary outputs, demonstrate a tighter control with closed-loop control. Both the technician control and closed-loop control regimens resulted in urinary outputs on the high side of the target range, which may reflect that changes in urinary output in response to changes in fluid infusion may not be symmetrical. It may be that some periods of high urinary outputs are a consequence of an inadequate resuscitation process. Increasing infusion in response to low urinary output may result in urinary outputs increasing more than a reduced infusion rate results in a decreased urinary output, which may explain why mean urinary outputs greater than target ranges are reported in most recent studies of burn resuscitation.\textsuperscript{3,8,21}

The greatest difference or effect of closed-loop control was the significant reduction in the hourly urinary output measurements undertarget. There was a larger number of on-target measurements with closed-loop control, but the difference was less and not significant. The current algorithm did not reduce the incidences of high urinary outputs. No control system for fluid therapy is likely to result in all hourly output measurements being on target, but it is hoped that better algorithms also can reduce the occurrences of high urinary output and further increase on-target values.

It is likely that better control algorithms can be designed for both the closed-loop system and the decision table. A decision table in which infusion rate was adjusted every 30 to 60 minutes is potentially as great an improvement as the potential for closed-loop therapy. Most burn centers perform 60-minute adjustments in infusion rate and, thus, 60 minutes was chosen for decision-assist and to compare with closed-loop control. A decision table for manual adjustment with scheduled adjustments for less than every 30 minutes is possible but not practical. Autonomous control would be labor saving and tirelessly diligent.

In this study, we chose to compare closed-loop control and decision table previously demonstrated to have successfully resuscitated sheep with a 40% TBSA. A clinical system of continuous urine monitoring and infusion rate adjusted by an automated controller might well produce a higher percentage of urinary outputs in the target range. A decision-table also could provide a better means to achieve and maintain target urinary outputs as compared to current approaches that vary between centers and even doctors at the same center. Decision-table or closed-loop algorithms improving outcomes is a reasonable hypothesis, but was not addressed in our study. Application of automated closed-loop control may have specific benefit for those medical personnel lacking in advanced burn care experience.

There are several limitations to our study. Sheep are not humans. Target ranges for urinary output for humans and sheep are different. All of our animals
were well resuscitated without the occurrences of complications that more severe clinical burns and concomitant injuries can cause. The study's design was to use a laboratory setting and an animal model to compare the closed-loop fluid therapy model and an experimental representation of what occurs in the clinical environment by using the technician adjusted therapy. Our closed-loop system and the decision assist table are both algorithm based designs in which adjustments in infusion rates are made based on calculated changes in urinary output. One might argue that either system could provide consistently and uniformly tighter control over fluid adjustments than what are observed in the current clinical setting where infusion adjustments are not standardized and staffing conditions may be strained. The closed-loop system does have a potential advantage over the decision table in that it continuously and accurately monitors urinary output, whereas clinically collected data is on the hour and can introduce human error. Under the busiest conditions, "hourly" measurement may be incorrect as readings are performed in a timely manner.

We resuscitated to a single well-defined endpoint, urine output, but it is appreciated that burn patients are resuscitated with a view to maintain additional endpoints such as hemodynamic stability and acid-base balance. An automated control system could be designed that uses multiple endpoints as its input signals. Nevertheless, it may be that even complex clinical cases are where tighter control of fluid therapy based on urinary output alone is most warranted and will provide a beneficial impact on outcomes.

A closed-loop resuscitation system will not replace medical expertise. Rather, we suggest that such a system can assist the burn care team to keep the fluid resuscitation on course. Automated fluid therapy could free up time that would allow devotion to other tasks. If an automated system can duplicate the infusion therapy of experienced physicians at an advanced burn center it can endow expertise to care givers with less experience. The clinical value of a closed-loop automated system for use in a burn center or an initial care unit awaits the development of optimized algorithms and their testing in controlled clinical trials.

CONCLUSIONS

We evaluated the performance of an automated closed-loop resuscitation system that measured urinary output and automatically adjusted fluid infusion rate based on urinary output. The automated system resulted in mean urinary outputs and infused volumes similar to hourly manual adjustments. Closed-loop resuscitation produced a lower incidence of urinary outputs under the target range and with less variation. Closed-loop resuscitation, as well as the application of decision tables, could provide an advance in burn care by standardizing and optimizing fluid therapy.

ACKNOWLEDGMENTS

We thank Mary Townsend for her preparation and editing efforts of the manuscript.

REFERENCES


