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USE OF MODERATELY HYPERTONIC SODIUM CHLORIDE IN THE
RESUSCITATION OF PATIENTS FROM INJURY(U) CALIFORNIA
UNIV DAVIS DEPT OF SURGERY J W HOLCROFT ET AL

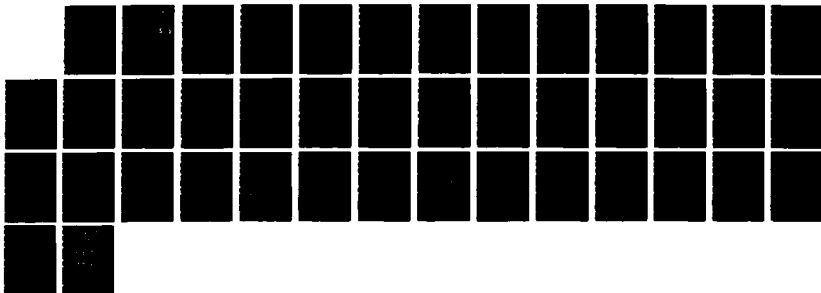
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ANNUAL REPORT

JAMES W. HOLCROFT, M.D.
MARY VASSAR, R.N.

AUGUST 8, 1986

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Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5012

Contract No. DAMD17-85-C-5096

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) The purpose of this contract was to test the hypothesis that 3% sodium chloride will 1) successfully resuscitate hemodynamically unstable patients who have been subjected to major trauma; and 2) will achieve this resuscitation with infusion of smaller volumes of solution than required by patients resuscitated with standard isotonic solutions. Based on the promising work with hypertonic solutions in animal models of shock, this study was begun as a means of obtaining clinical experience in patients undergoing operative repair of traumatic injuries. *Cont.		

20. (continued) Abstract

Over 2 hours, ten severely injured patients received 3% sodium chloride, 4 ml/kg/hr, in addition to isotonic fluids as needed to maintain urine output and blood pressure. Ten patients served as controls and received isotonic fluids only. At the end of 2 hours the cumulative fluid requirements in the 3% sodium chloride group were 39 ± 17 ml/kg versus 69 ± 35 ml/kg ($p < 0.03$) in the patients treated with standard isotonic solutions. The 3% sodium chloride patients had significant improvements in urine output and more rapid correction of acidosis. There were no adverse effects associated with the 3% sodium chloride treatment. The results from this trial are very promising and should now allow us to initiate trials evaluating the efficacy of more concentrated sodium chloride solutions earlier in the course of injury, where they are expected to be of the most benefit.

SUMMARY

One of the main causes of death following traumatic injury has been hemorrhagic shock. Based on numerous studies in animal models and in burn shock patients, there has been considerable interest in evaluating the efficacy of hypertonic sodium chloride solutions in the resuscitation for traumatic injury. The purpose of this contract was to initiate the clinical evaluation of a 3% sodium chloride (3% NaCl) solution versus resuscitation with standard isotonic solutions.

In brief, all patients had received at least 15 ml·kg⁻¹ of isotonic solutions in the hour before entry and all had received at least 6 liters of crystalloid and 2 units of blood since their injury. All studies were initiated within the first six hours after injury. Over two hours, 10 patients received 3% NaCl, 4 ml·kg⁻¹·hr⁻¹, in addition to isotonic fluids as needed to maintain urine output and blood pressure. Ten patients served as controls and received isotonic fluids only. At the end of two hours the patients in the 3% NaCl group required nearly one-half the volume of fluid required by the controls. In addition, there was significant improvement in urine output and more rapid correction of metabolic acidosis in the patients treated with 3% NaCl. These beneficial effects in the clinical setting support the experimental models which demonstrate superiorities of hypertonic solutions in resuscitation from shock.

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FOREWORD

For the protection of human subjects the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

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BODY OF REPORT

Background

Early adequate fluid resuscitation remains crucial to the ultimate survival of the hypovolemic injured soldier. The majority of deaths from trauma occur prior to or in the first few hours after reaching a treatment facility and are due to rapid hemorrhage or central nervous system trauma (1). Infusion of standard isotonic solutions frequently requires the administration of several liters of fluid in order to maintain hemodynamic stability. Hypertonic sodium chloride (NaCl) solutions have been used to resuscitate patients from burn shock (2,3,4). In this clinical setting, they have been shown to decrease the total water load required for adequate resuscitation, a factor which may prove valuable in the ultimate survival of the patient.

Shackford and colleagues studied the effects of infusing moderately hypertonic (514 mOsm) NaCl solution to 30 patients undergoing elective abdominal aortic reconstruction (5). Twenty-eight patients in the lactated Ringer's group received 10 liters of fluid for intra-operative maintenance of cardiovascular stability; the hypertonic group required 5 liters.

Extremely hypertonic solutions have been used to resuscitate dogs, sheep, rats, and pigs from hypovolemic shock (6,7,8,9,10,11). These solutions achieve excellent cardiovascular resuscitation and do so with infusion of very small quantities of fluid. In addition, in dogs and pigs (12), hypertonic solutions improve survival rates when compared to infusion of equivalent volumes of normal saline.

Resuscitation with small volumes of hypertonic NaCl offers many potential advantages for the care of injured soldiers and civilians. Besides the immediate improvements in hemodynamics and survival shown in the animal studies, a medic could potentially treat and stabilize a larger number of soldiers for transport to base hospitals. Hypertonic sodium may attenuate cerebral edema in those who have suffered head injuries (13). It may also reduce the incidence of shock associated organ dysfunction.

The purpose of this contract was to test the hypothesis that 3% sodium chloride (1028 mOsm) will: 1) successfully resuscitate hemodynamically unstable patients (as defined in methods) who have been subjected to major trauma; and 2) achieve this resuscitation with infusion of smaller volumes of solution than

required by patients resuscitated with standard isotonic solutions. Secondary objectives include the assessment of effect of 3% NaCl on organ function and mortality in trauma patients. It is expected that by obtaining in-hospital experience with the safety and efficacy of the 3% NaCl solution, that appropriate field trials may be initiated as well.

Methods

Criteria for Entry

Patients were entered into the study if they:

1. Were 13 years of age or older; and
2. Were subjected to major trauma in the previous 6 hours; and
3. Had evidence of hemodynamic instability:
 - a. Requiring at least 6 liters of crystalloid solution since the time of injury; and
 - b. Were known to have hypotension at any time with a mean systemic arterial pressure less than 70 mmHg.
4. Had received at least 2 units of blood replacement; and
5. Had received 15 ml·kg⁻¹ of crystalloid during the previous hour and were expected to continue receiving at least 15 ml/kg of fluid over the next hour (as indicated by the anesthesiologist or surgeon).

Patients were excluded if:

1. Their admission serum creatinine was greater than 2.0 mg/dl.
2. Their admission serum sodium concentration was greater than 147 mEq/L.
3. Their admission serum sodium concentration was less than 130 mEq/L.

4. Their admission serum chloride concentration was greater than 105 mEq/L.
5. Their admission serum potassium concentration was less than 3.5 mEq/L.
6. Their calculated serum osmolality was greater than 295 milliosmols/kg.
7. They had a history of a seizure disorder.
8. They had a history of cirrhosis.
9. They had a history of congestive heart failure.
10. If they were more than 6 hours from the time of injury.

Resuscitation Protocol

Patients were randomized into a 3% NaCl or lactated Ringer's treatment group according to who the attending trauma surgeon was at operation. Patients in the 3% NaCl group were given $4 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ of solution for up to 3 hours. Patients in the lactated Ringer's group received $12 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ of solution. Additional isotonic fluids were infused as needed at the discretion of the anesthesiologist or the surgeon using standard clinical judgement for maintenance of adequate urine output and blood pressure.

It should be mentioned that the volumes of the 3% NaCl and lactated Ringer's were selected largely out of clinical practicality. All patients were going to receive at least $15 \text{ ml} \cdot \text{kg} \cdot \text{hr}^{-1}$ of fluid at the time of entry. We believed that the most prudent protocol would be one which did not interfere with ongoing resuscitation efforts. Thus, to administer only $4 \text{ ml} \cdot \text{kg} \cdot \text{hr}^{-1}$ of 3% NaCl and $4 \text{ ml} \cdot \text{kg} \cdot \text{hr}^{-1}$ of lactated Ringer's would not have been practical. Thus, the $4 \text{ ml} \cdot \text{kg} \cdot \text{hr}^{-1}$ of 3% NaCl was essentially a supplement to the large volumes of isotonic fluid being administered at the time of entry.

Measurements

Serum samples were collected for measurement of chemistry panels, blood counts and blood gases, which were performed in the hospital laboratories. Vital signs, ventilator settings,

and strict measurements of fluid intake and output were collected by the clinical research nurse throughout the infusion protocol. Subsequent measurements were collected from the operating room, and nursing flow sheets. Injury severity scores were calculated, utilizing standard criteria (14,15).

The incidence of mortality and the presence or absence of organ failure at any time during the 30 days after entry into the study was evaluated. Severe organ failure was defined as follows:

Respiratory failure: requirement for mechanical ventilation with a ratio of systemic arterial partial pressure of oxygen to inspired oxygen concentration (P_{aO_2}/F_{iO_2}) less than 150 mmHg for a period of more than 24 hours after admission to the intensive care unit or the need for more than 3 days of mechanical ventilation. **Cardiac failure:** a cardiac index less than 3.0 liters·minute⁻¹·meter⁻² with a pulmonary arterial wedge pressure greater than 20 mmHg. **Hepatic failure:** one or more serum bilirubin concentrations greater than 5.0 mg/dl in the absence of hemolysis. **Renal failure:** one or more creatinine concentrations greater than 3.0 mg/dl. **Gastrointestinal failure:** any upper gastrointestinal hemorrhage requiring transfusion. **Intravascular coagulation:** a platelet count less than 50,000 cells/mcl with fibrin monomers and fibrin degradation products present in the serum on one or more occasions.

Statistics

The study was to be terminated if either 100 patients were entered or when a difference in net volume administered to the two groups was demonstrated at the 5% level or less. All data are reported as means $\pm$ 1 standard deviation. Closed circles in the figures represent the 3% NaCl patients. The lactated Ringer's treatment group is represented in the figures with open circles and labeled as isotonic. When measurements were not available in all patients, the number of patients in whom the measurement was made is indicated by the letter N. All probabilities were calculated using a two-tailed student's unpaired t-test. The Bonferroni Method was used to modify the t-test for multiple comparisons. Mortality was evaluated with Fisher's Exact Test.

Results

Characteristics of Patients at Time of Entry

Between July 1985 and April 1986, 1,156 patients were admitted to the trauma service. There were 579 operations and 131 deaths. Twenty severely injured patients were entered into

the study -- 10 in the 3% NaCl and 10 in the lactated Ringer's group. Approximately 35 patients were excluded: 10 had been stabilized by the time the research nurse had reached the operating room; 10 were more than 6 hours from their injury; 5 had electrolyte abnormalities; 10 lacked central venous catheters (which were initially required at the start of the study).

The mechanism of the injury for patients entered into the study is indicated in Tables I and II. Five patients in the 3% NaCl group and 4 patients in the lactated Ringer's group suffered blunt injuries. Five of the 3% NaCl patients and six of the lactated Ringer's patients suffered penetrating injury. Tables III and IV show that the baseline vital signs, laboratory values, urine output, fluid and blood replacement were similar for the two groups, with the exception of the P_{aO_2}/F_{iO_2} ratios and platelet counts. The patients in the 3% NaCl group had a mean P_{aO_2}/F_{iO_2} ratio of 240 ± 131 versus 380 ± 135 in the lactated Ringer's group ($p < 0.03$). The platelet counts for the 3% NaCl group were $231,000 \pm 17,000$ (cells/mcl) versus $149,000 \pm 77,000$ for the lactated Ringer's group ($p < 0.03$). The patients in the 3% NaCl group were entered into the study over a period ranging from 1.5 to 3 hours (mean = 2.1 ± 0.4 hours) from the time of injury; the time of entry for the lactated Ringer's patients ranged from 2 to 5 hours (3.5 ± 1.0 hours) ($p < 0.001$).

Response to Resuscitation Protocol

Data for the cumulative crystalloid replacement during the first 2 hours of the study and subsequent measurements carried out to 8 and 24 hours are shown in Figure 2. At the end of two hours, the volume of fluid required by the 3% NaCl group was 39 ± 17 ml·kg⁻¹. This was significantly less ($p < 0.03$) than the 69 ± 35 ml·kg⁻¹ of fluid required by the lactated Ringer's group to maintain hemodynamic stability.

At 8 hours, the cumulative volume of crystalloid administered was 103 ± 52 (ml·kg⁻¹) for the 3% NaCl group versus 187 ± 83 ($p < 0.04$) for the lactated Ringer's group. By 24 hours, the 3% NaCl group had received 189 ± 139 ml/kg of crystalloid versus 311 ± 107 ($p > 0.05$) in the lactated Ringer's group.

Figure 3 shows individual volumes (in milliliters) of 3% NaCl administered for the three hour study period. The volume of 3% NaCl administered at the end of 1 hour was 4.0 ± 0.0 ml·kg⁻¹. Two patients had the 3% NaCl infusion stopped at this time due to serum sodium concentrations above 155 mEq/L. The infusion was stopped in a third patient who no

longer required $15 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ of fluid. A fourth patient in the 3% NaCl group died during the first hour. All of the patients in the 3% NaCl group received supplemental isotonic solutions throughout the 3 hour study period. Only one lactated Ringer's patient was eliminated at the end of one hour, as he no longer required $15 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ of fluid.

At the end of two hours, five patients in the 3% NaCl group had the infusion stopped as they no longer required $15 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ of fluid. A sixth patient had the infusions stopped for a serum sodium concentration above 155 mEq/L , measured at the end of the first hour and reported one hour later. This resulted in the nine patients who were alive at the end of two hours receiving an average of $7.0 \pm 1.6 \text{ ml} \cdot \text{kg}^{-1}$ of the 3% NaCl solution. Three of the patients received the 3% NaCl solution for the full three hour period. This resulted in an average volume of $8.3 \pm 3.1 \text{ ml} \cdot \text{kg}^{-1}$ of 3% NaCl being administered over the 3 hour study period. In the lactated Ringer's group, one patient died at the end of two hours. The remaining lactated Ringer's patients continued to require at least $15 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{hr}$ of fluid at the end of the second and third hour evaluation periods.

During the course of the first two hours of the study, each group received equivalent amounts of sodium. This continued throughout the 24 hours evaluation period (Figure 4).

In conjunction with decreased fluid requirements, the cumulative urine output was $8.8 \pm 7.0 \text{ ml} \cdot \text{kg}^{-1}$ at the end of two hours in the 3% NaCl group versus $3.0 \pm 2.3 \text{ ml} \cdot \text{kg}^{-1}$ in the lactated Ringer's group ($p < 0.02$) (Figure 5). The 8 hour cumulative urine output in the 3% NaCl group was $21.6 \pm 10.4 \text{ (ml} \cdot \text{kg}^{-1})$ versus 10.2 ± 3.8 in the lactated Ringer's group ($p < 0.01$). The 24 hour values were 41.3 ± 20.0 for the 3% NaCl group versus 30.6 ± 11.6 ($p > 0.05$).

The volume of blood replaced, systolic blood pressures, and hematocrits were comparable throughout the 24 hour study period (Figures 6, 7, and 8). Serum sodium concentrations were found to be significantly increased in the 3% NaCl group at 1 hour -- 152 ± 6 versus 146 ± 2 ($p < 0.02$) (Figure 9). There were no further significant differences at 4, 8, and 24 hours. The maximum serum sodium concentration was 162 mEq/L in a patient who received 400 ml of 3% NaCl. In addition, he had received 10 ampules of sodium bicarbonate during the second hour of the study.

Serum chloride concentrations were elevated to 117 ± 6 at 1 hour in the 3% NaCl group versus 110 ± 5 ($p < 0.01$) in the lactated Ringer's group (Figure 10). The values were no longer different at 4, 8, and 24 hours. The maximum serum chloride was 130 mEq/L in the same patient mentioned above.

Serum osmolality in the 3% NaCl group was elevated to 313 ± 11 at 1 hour versus 299 ± 8 ($p < 0.02$) in the lactated Ringer's group. The 4 hour serum osmolality remained elevated at 311 ± 13 versus 302 ± 6 ($p < 0.04$) (Figure 11). These differences did not persist at 8 and 24 hours. The maximum serum osmolality was 370 mOsm/L in the same patient with the highest serum sodium and chloride levels.

These transient elevations in serum sodium, Cl and osmolality were not associated with any adverse effects. In addition, we evaluated the efficacy of infusion of the 3% NaCl solution via peripheral veins. There was no external evidence of inflammation at the catheter site.

All patients were mechanically ventilated on 100% oxygen at the time of entry into the study. The P_{aO_2}/F_{iO_2} ratios remained stable throughout the 24 hour study period in the 3% NaCl group (Figure 12). The P_{aO_2}/F_{iO_2} ratios in the lactated Ringer's group, which were better at the time of entry, deteriorated throughout the 24 hour period (Figure 12). At the end of 24 hours, the mean P_{aO_2}/F_{iO_2} ratio for the 3% NaCl group was 256 ± 108 versus 197 ± 94 ($p > 0.05$) in the lactated Ringer's. However, the difference between the baseline (380 ± 135) and 24 hour values (256 ± 108) for the patients in the lactated Ringer's group was significant ($p < 0.0003$). The baseline and 1 hour pH measurements were equivalent. At 4 hours, the pH in the 3% NaCl group had increased to 7.33 ± 0.07 versus 7.24 ± 0.07 ($p < 0.02$) in the lactated Ringer's group. At 8 hours, the mean pH for the 3% NaCl group had risen to 7.36 ± 0.07 versus 7.27 ± 0.08 ($p < 0.03$) in the lactated Ringer's group. By 24 hours the values for each group were similar (Figure 13).

Additional evaluations of fluid status, performed for up to 7 days after entry into the study did not show any differences between the two groups. Similar follow-up of pulmonary function did not show any differences for the first 7 days, nor at 14 and 30 days after entry into the study.

Post-Resuscitation Clinical Course

After operation, all patients required mechanical ventilation and were admitted to the intensive care unit. In the 3% NaCl group, two patients were extubated by the end of the

first 24 hours. Two more patients were extubated at 48 hours. One of these patients required re-intubation 5 days later. One patient died on day 6, a second patient died on day 8, and a third died 25 days after entry into the study. In the lactated Ringer's group, the first patient was extubated at 3 days. One patient died at 49 days, a second patient died 83 days after entry into the study. The 30 day mortality of 40% in the 3% NaCl group was not significantly different from the 10% mortality in the lactated Ringer's group. The final overall mortality in the lactated Ringer's group was 40%.

Details of the clinical outcomes are shown in Table V. The data for days of mechanical ventilation, days in the intensive care unit and days of hospitalization include the values for the non-survivors. Despite the initial stability of pulmonary function in the 3% NaCl group, seven patients developed respiratory failure, along with nine patients in the lactated Ringer's group. Only three patients in the 3% NaCl group remained free from postoperative complications of organ failure. All of the lactated Ringer's patients developed failure of one or more organs.

Conclusion

In summary, the short term results in this small number of patients were far better than we had anticipated, allowing us to terminate the study one year earlier than we predicted. In 20 patients, we found that the 3% NaCl solution achieved excellent resuscitation with less volume than was required by the lactated Ringer's group within two hours after entry into the study. All of the patients were seriously injured and these injuries seemed comparable, based on the injury severity scores and blood loss at time of entry and the subsequent 24 hour study period. The 3% NaCl solution provided a more rapid correction of metabolic acidosis and improved urine output while maintaining cardiovascular and pulmonary stability throughout the study. The 24 hour fluid intake was not statistically different, however, when corrections were made for multiple comparisons the marked deterioration in the P_{aO_2}/F_{iO_2} ratio in the lactated Ringer's group lends further support to the advantages of reducing water load by resuscitation with hypertonic solutions. The outcomes, in terms of development of organ failure were similar for the two groups. Despite the encouraging findings in the first 24 hours of the study, seven patients in the 3% NaCl group and ten of the patients in the lactated Ringer's group developed failure of one or more organs. Lastly, the early benefits of the 3% NaCl solution were not associated with any evidence of improved long-term survival.

Recommendations

The results of this first trial in a group of severely injured patients are promising. We have documented the safety and short-term efficacy of a 3% NaCl solution in moderate volumes. This should allow us to initiate more aggressive trials evaluating solutions with higher salt concentrations earlier in the course of resuscitation where they are expected to be of the most benefit to the injured soldier or civilian.

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TABLE I: MECHANISM OF INJURY FOR PATIENTS IN THE 3% NaCl GROUP

PATIENT	AGE/SEX	INJURY	OUTCOME
1	29/M	MCA; open femur fracture; partial, above knee amputation; Type III patellar and tibial plateau fractures; nephrectomy.	Survived
2	29/M	Multiple bilateral stab wounds to chest with hemothorax.	Died; 1 hour
3	26/F	MVA; pelvic, fibular head and ankle fractures; ruptured bladder.	Survived
4	29/M	Depressed frontal skull fracture; multiple stab wounds with bowel perforation, laceration of stomach and kidney.	Survived
5	24/M	MVA; bilateral pulmonary contusions with rib fractures; pelvic fracture, retroperitoneal hematoma, comminuted femur fracture; bilateral upper extremity fractures; splenic rupture; kidney fracture.	Died; day 6
6	20/M	MVA, flail chest; ruptured spleen, large retroperitoneal hematoma, acetabular fracture, fractured tibial shaft and radius.	Survived
7	49/M	Stab wounds to chest, colon, and small bowel enterotomies, hemothorax.	Survived
8	64/M	Stab wounds to chest, left ventricle and abdomen; hemopericardium.	Survived*
9	39/M	Stab wound to internal mammary artery, right hemidiaphragm and liver.	Died; day 25
10	39/M	Pelvic fracture with functional hemipelvectomy; transected sigmoid colon; avulsed ileum; ruptured bladder.	Died; day 8

*Remains in hospital at time of report.

TABLE II: MECHANISM OF INJURY FOR PATIENTS IN THE LACTATED RINGER'S GROUP

PATIENT	AGE/SEX	INJURY	OUTCOME
1	87/F	MVA; multiple rib fractures; pneumothorax; unstable pelvic fracture retroperitoneal hemorrhage.	Died; 2 hours
2	55/M	MVA; unstable pelvic fracture; bimalleolar ankle fracture; humerus fracture; brachial and popliteal artery injuries.	Died; day 74
3	28/M	MVA; pelvic fracture; open femur fracture; open tibia fracture.	Survived
4	19/M	Shotgun blast to right flank; multiple small bowel enterotomies, liver laceration, transection of transverse colon; multiple blast injuries to duodenum, head of pancreas, blow out of stomach and through-and-through splenic injuries.	Survived
5	29/M	Stab wound to epigastrium, with laceration to hepatic vein and left lobe of liver, multiple stab wounds to arm and forearm.	Survived
6	33/M	Multiple stab wounds to neck, head, bilateral chest, arm, and thigh; lacerated pulmonary artery and lacerated liver.	Died; day 87
7	33/M	Multiple gunshot wounds to shoulder, chest, flank, and abdomen; resulting in bilateral hemothoraces, multiple enterotomies; through-and-through wound to liver and axillary artery transection.	Survived
8	21/M	Stab wounds to colon; infrarenal abdominal aorta and infrarenal inferior vena cava.	Survived*
9	39/M	MVA; near amputation right foot; open Type III left talus fracture bilateral upper extremity fractures; bilateral rib fractures; transverse lumbar spine fracture; ruptured spleen.	Survived
10	26/M	Multiple gunshot wounds to axilla, arm, chest, abdomen, and thigh; resulting in hemothorax; multiple jejunoenterotomies; nephrectomy; femur fracture; popliteal artery transection.	Survived

TABLE III: CONDITION OF PATIENTS AT TIME OF ENTRY INTO STUDY

	<u>3% NaCl</u>		<u>Lactated Ringer's</u>
	Mean $\pm$ SD		Mean $\pm$ SD
AGE	36 $\pm$ 13		36 $\pm$ 21
GLASGOW COMA SCORE ¹	3 $\pm$ 0		3 $\pm$ 0
INJURY SEVERITY SCORE	34 $\pm$ 10		33 $\pm$ 8
SYSTOLIC BP (mmHg)	98 $\pm$ 41		105 $\pm$ 29
HR (beats/min)	107 $\pm$ 39		114 $\pm$ 13
P _a O ₂ /F _i O ₂ ²	240 $\pm$ 131	*	380 $\pm$ 135
pH	7.26 $\pm$ 0.08		7.22 $\pm$ 0.13
HCO ₃ (mEq/L)	18 $\pm$ 3		17 $\pm$ 5
SODIUM (mEq/L)	144 $\pm$ 3		145 $\pm$ 5
POTASSIUM (mEq/L)	3.8 $\pm$ 0.5		3.7 $\pm$ 0.3
CHLORIDE (mEq/L)	111 $\pm$ 7		109 $\pm$ 4
BUN (mEq/L)	11 $\pm$ 4		11 $\pm$ 4
CREATININE (mg/dl)	1.0 $\pm$ 0.2		0.9 $\pm$ 0.3
BILIRUBIN (mg/dl)	0.8 $\pm$ 0.4		0.8 $\pm$ 0.3
OSMOLALITY (mOsm/L)	308 $\pm$ 20		303 $\pm$ 10
HEMOGLOBIN (mg/dl)	9.1 $\pm$ 2.6		7.5 $\pm$ 2.6
HEMATOCRIT (%)	25.5 $\pm$ 7.6		22.7 $\pm$ 8.8
PLATELET COUNT (cells/mcl)	231,000 $\pm$ 17,000	*	149,000 $\pm$ 77,000

*Difference between groups (p<0.03).

¹Glasgow Coma Scores were 3 in all patients at time of entry due to anesthesia.

²P_aO₂/F_iO₂ = Ratio of partial pressure of oxygen in systemic arterial blood to fractional inspired oxygen concentration (Normal = approximately 450).

TABLE IV: FLUID STATUS AT TIME OF ENTRY INTO STUDY

	<u>3% NaCl</u>	<u>Lactated Ringer's</u>
	Mean $\pm$ SD	Mean $\pm$ SD
CRYSTALLOID Administered (ml/kg)	102 $\pm$ 20	120 $\pm$ 30
BLOOD REPLACEMENT (ml/kg)	23 $\pm$ 18	24 $\pm$ 17
SODIUM Administered (mEq/kg)	14 $\pm$ 3	17 $\pm$ 4
URINE OUTPUT (ml/kg)	3.4 $\pm$ 2.3	6.9 $\pm$ 6.6

TABLE V: OUTCOME

	3% NaCl	Lactated Ringer's
LENGTH OF OPERATION (Hours)	3.6 $\pm$ 2.0	5.7 $\pm$ 4.0
OVERALL SURVIVAL	6/10	7/10
DAYS OF MECHANICAL VENTILATION	14 $\pm$ 20	29 $\pm$ 26
DAYS IN INTENSIVE CARE UNIT	18 $\pm$ 27	38 $\pm$ 30
DAYS OF HOSPITALIZATION ¹	28 $\pm$ 36	49 $\pm$ 38
RESPIRATORY FAILURE	7/10	9/10
CARDIAC FAILURE	1/10	0/10
HEPATIC FAILURE	4/10	4/10
RENAL FAILURE	2/10	1/10
GASTROINTESTINAL FAILURE	0/10	0/10
COAGULATION FAILURE	1/10	2/10
NO ORGAN FAILURE	3/10	0/10
SINGLE ORGAN FAILURE	2/10	5/10
TWO OR MORE ORGAN FAILURES	5/10	5/10

¹One patient in each group remains hospitalized at time of report.

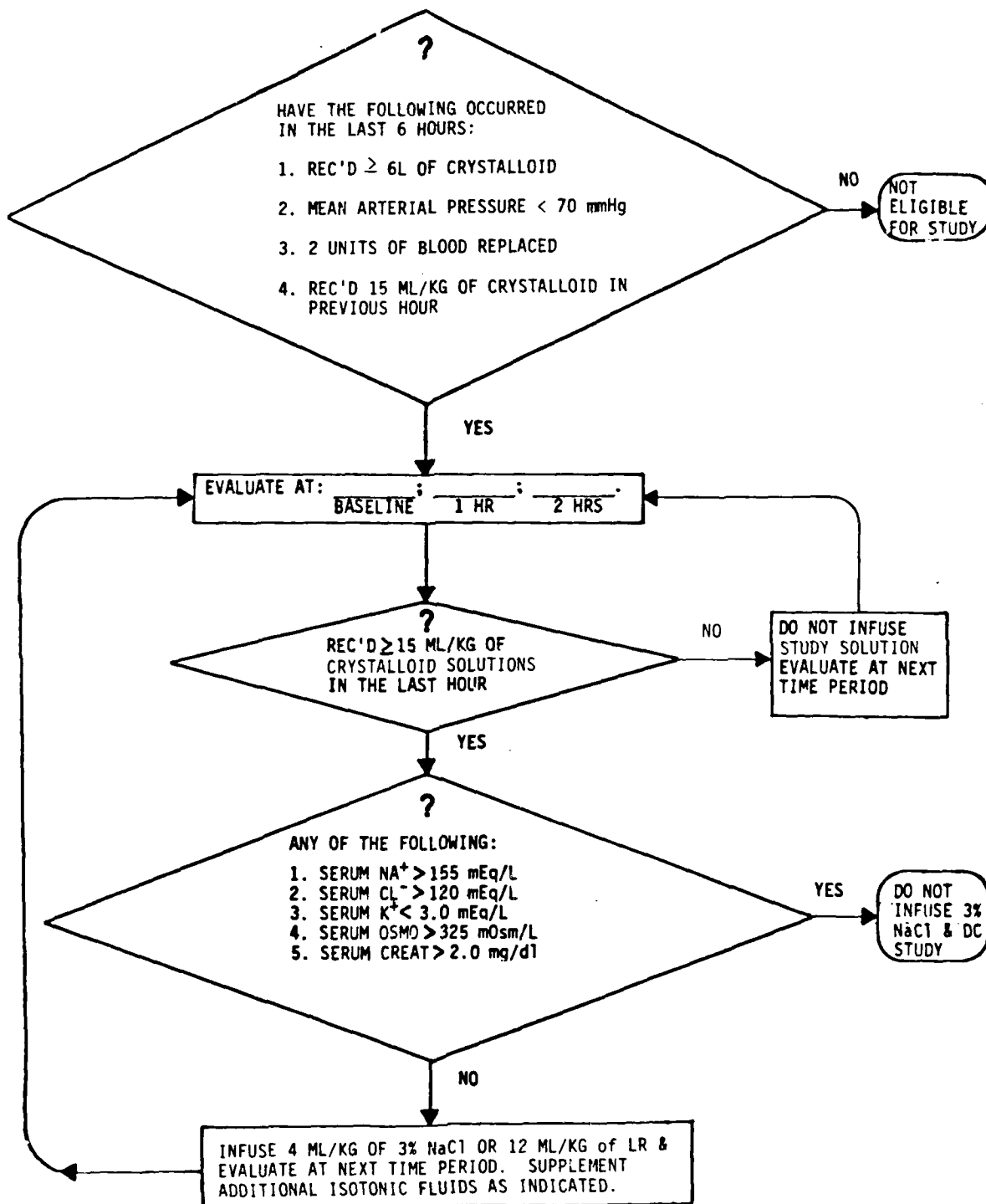


FIGURE 1: ALGORITHM FOR INFUSION OF 3% NaCl OR LR SOLUTION

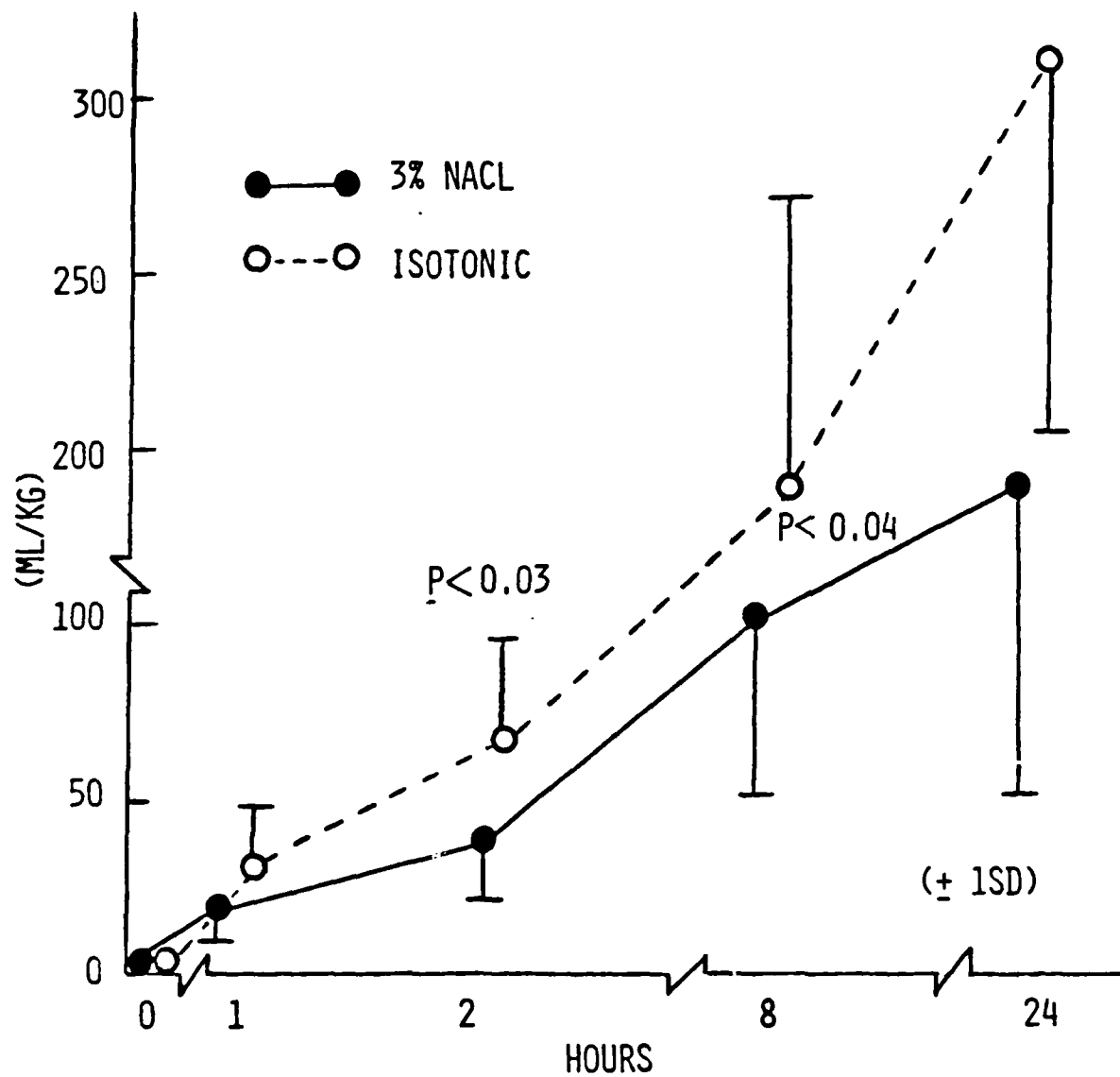
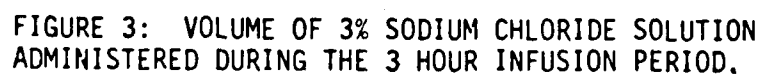


FIGURE 2: CUMULATIVE VOLUME OF CRYSTALLOID SOLUTIONS ADMINISTERED DURING STUDY.



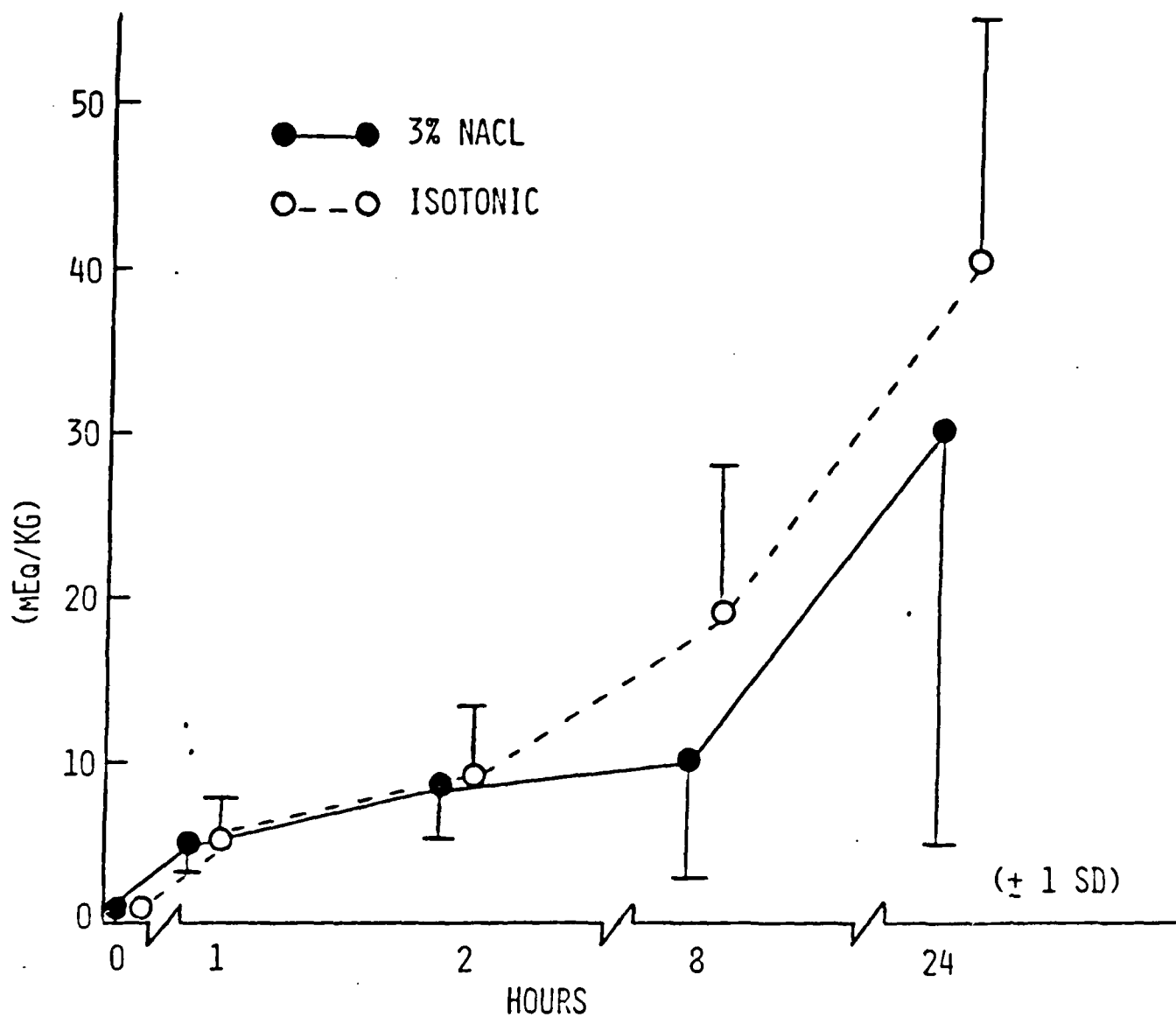


FIGURE 4: CUMULATIVE AMOUNT OF SODIUM ADMINISTERED.

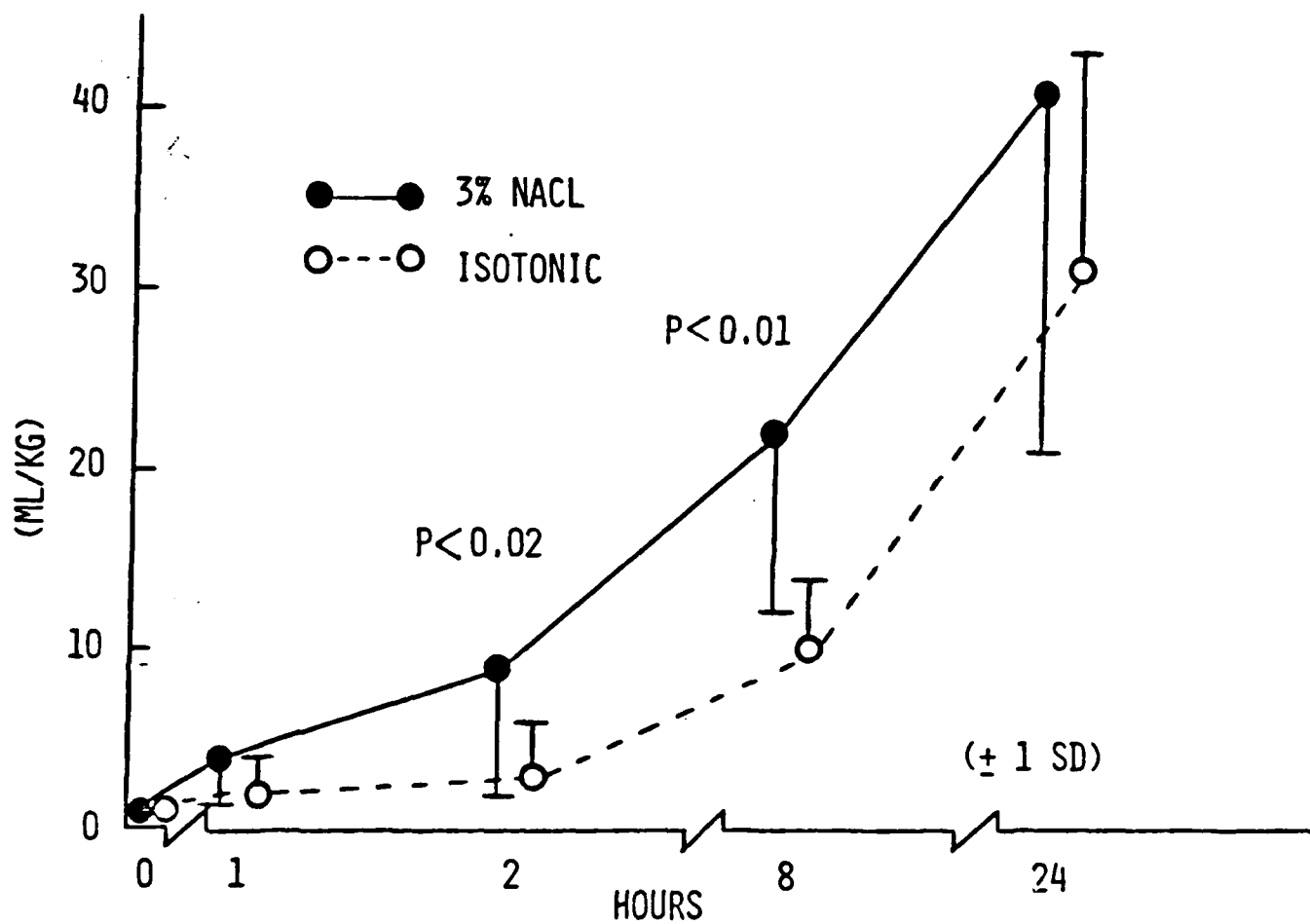


FIGURE 5: CUMULATIVE URINE OUTPUT.

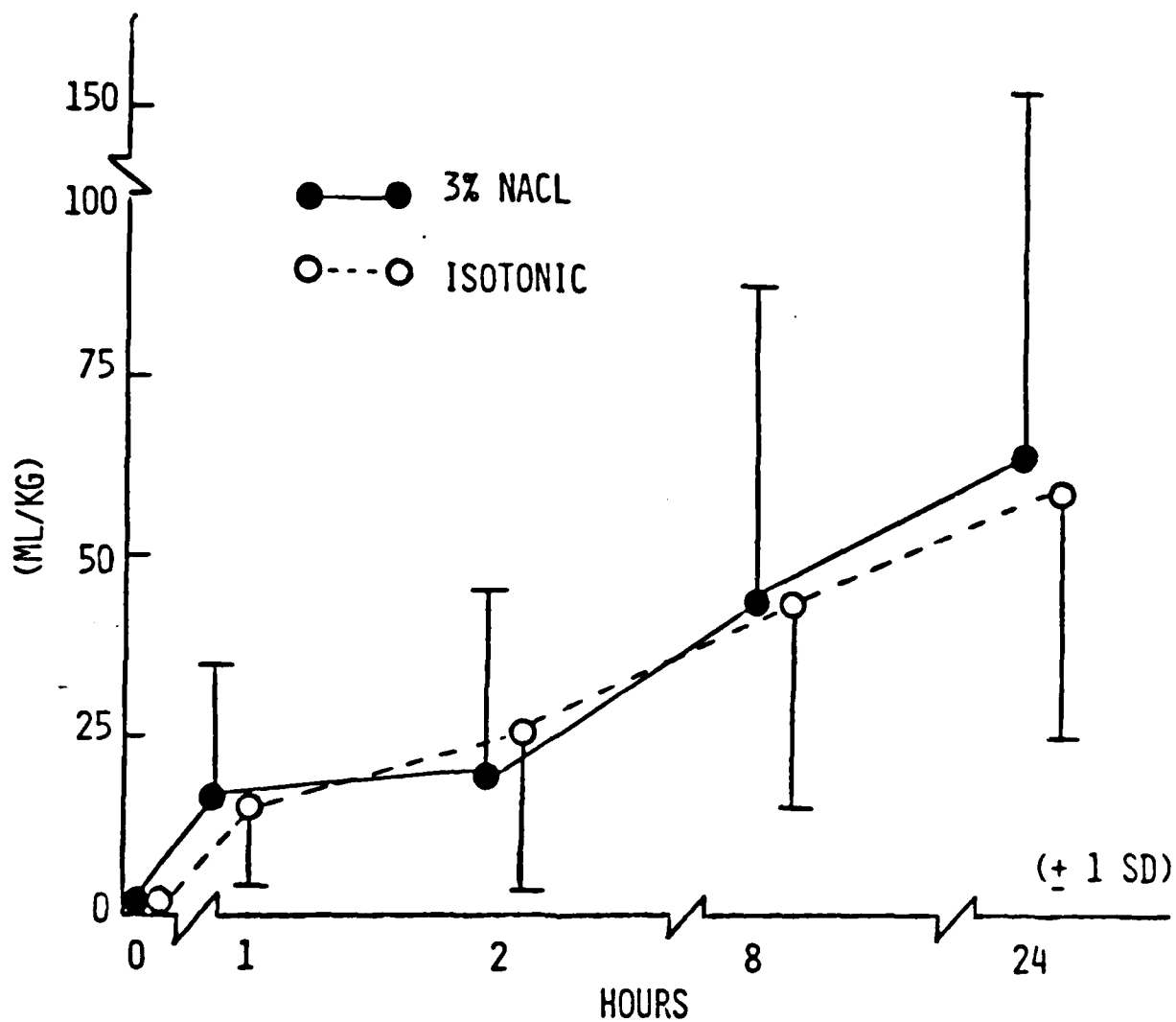


FIGURE 6: CUMULATIVE BLOOD REPLACEMENT.

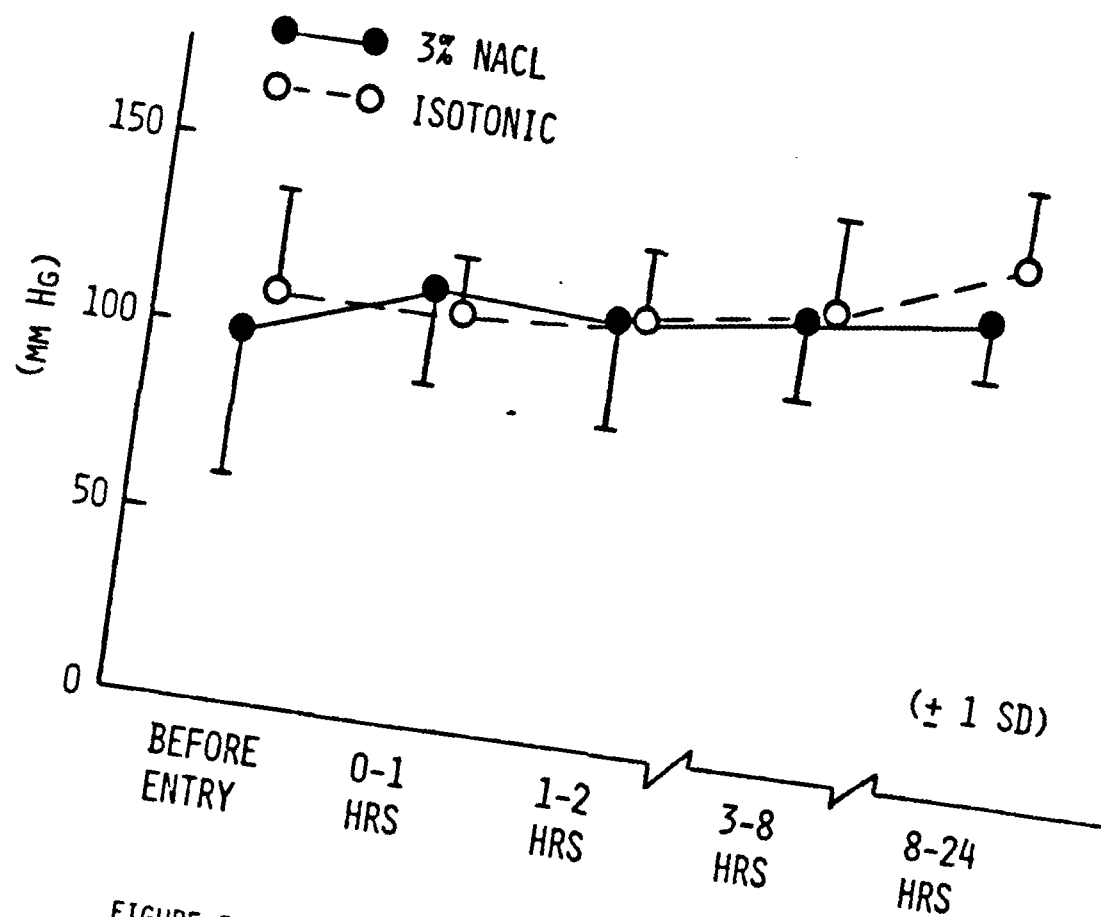


FIGURE 7: SYSTOLIC BLOOD PRESSURES.

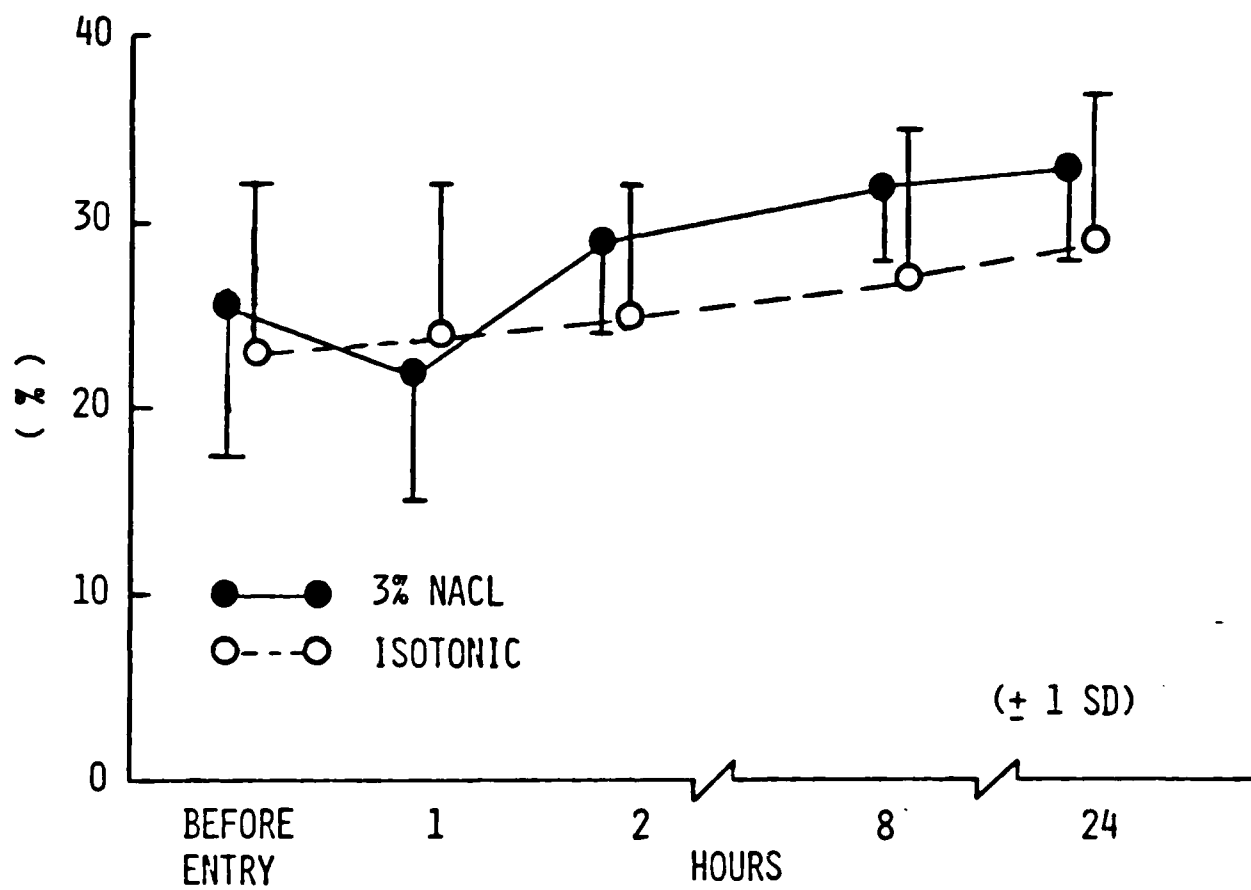


FIGURE 8: HEMATOCRITS.

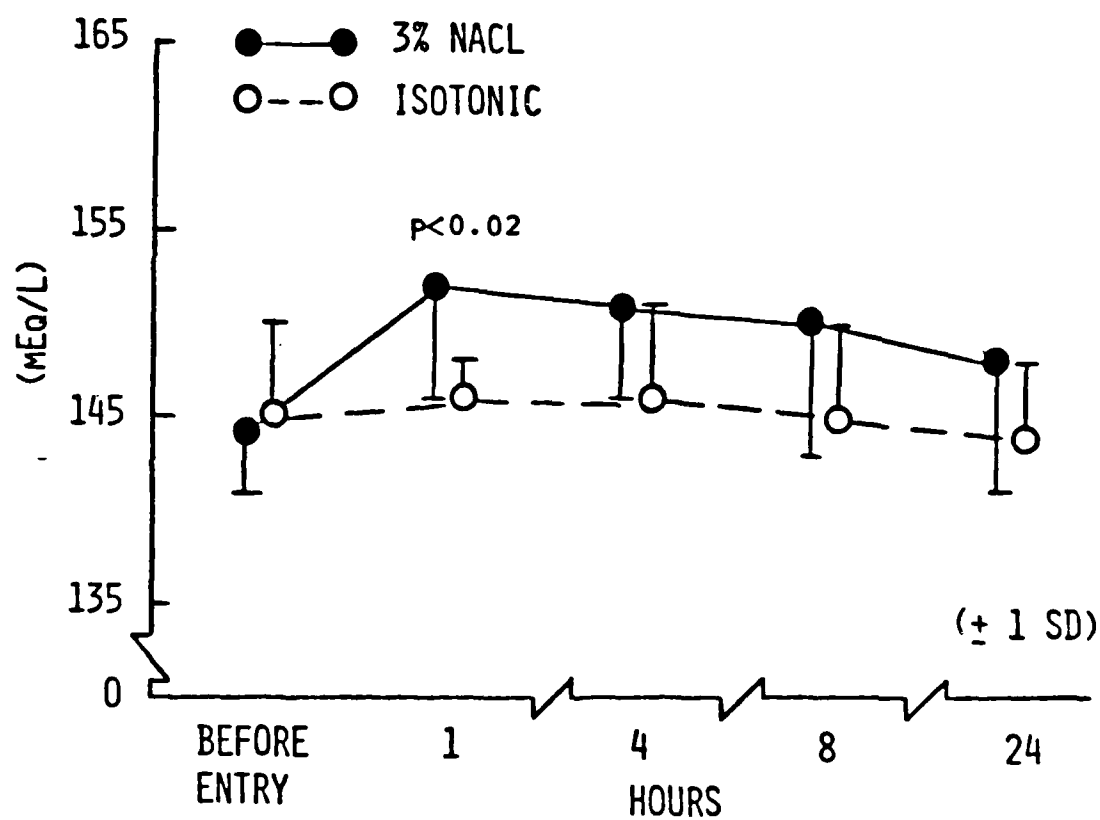


FIGURE 9: SERUM SODIUM CONCENTRATIONS.

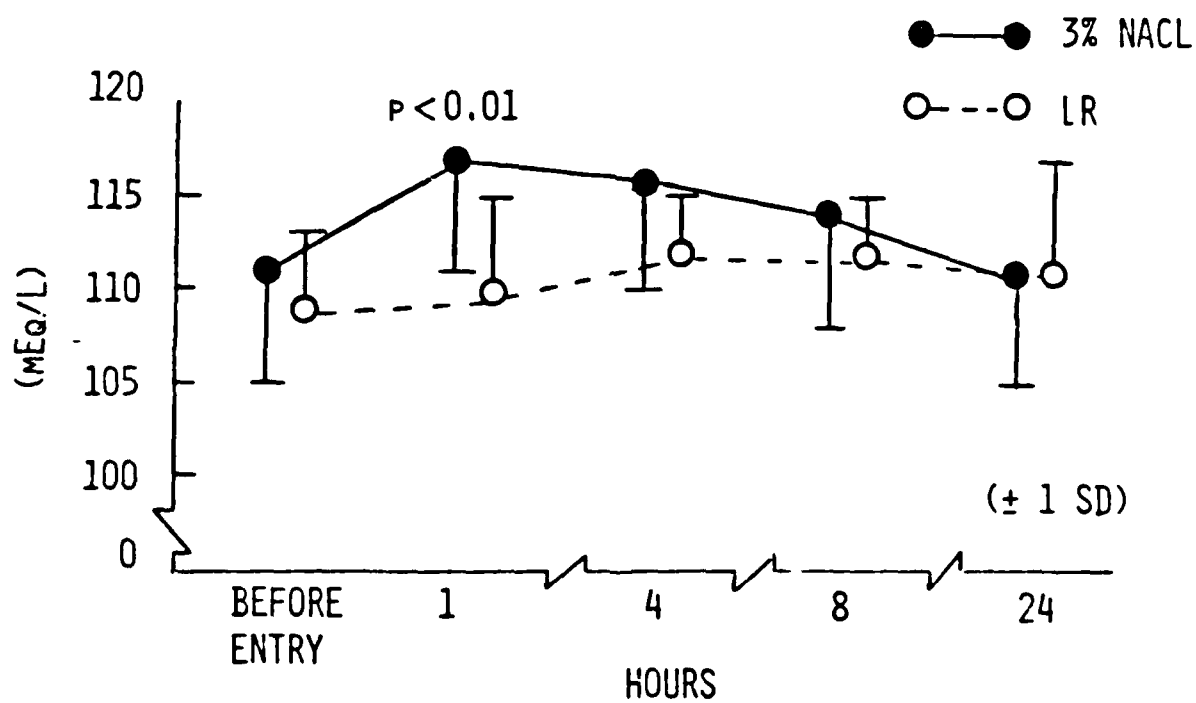


FIGURE 10: SERUM CHLORIDE CONCENTRATIONS.

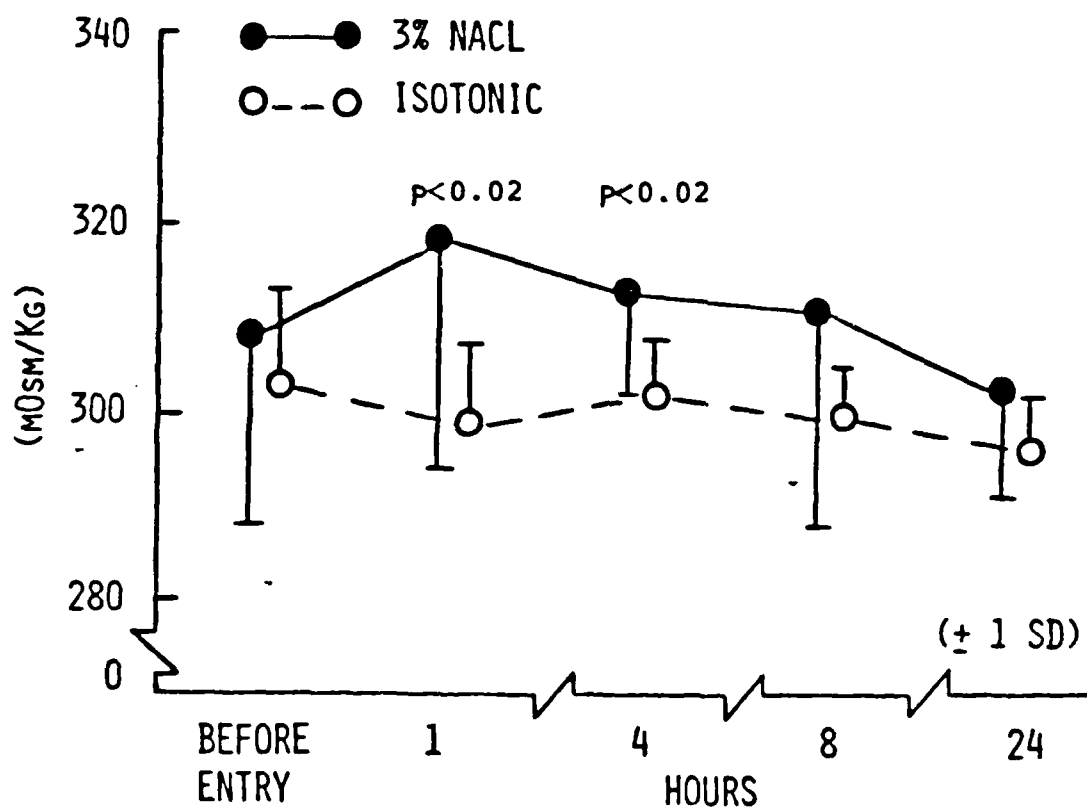


FIGURE 11: SERUM OSMOLALITY.

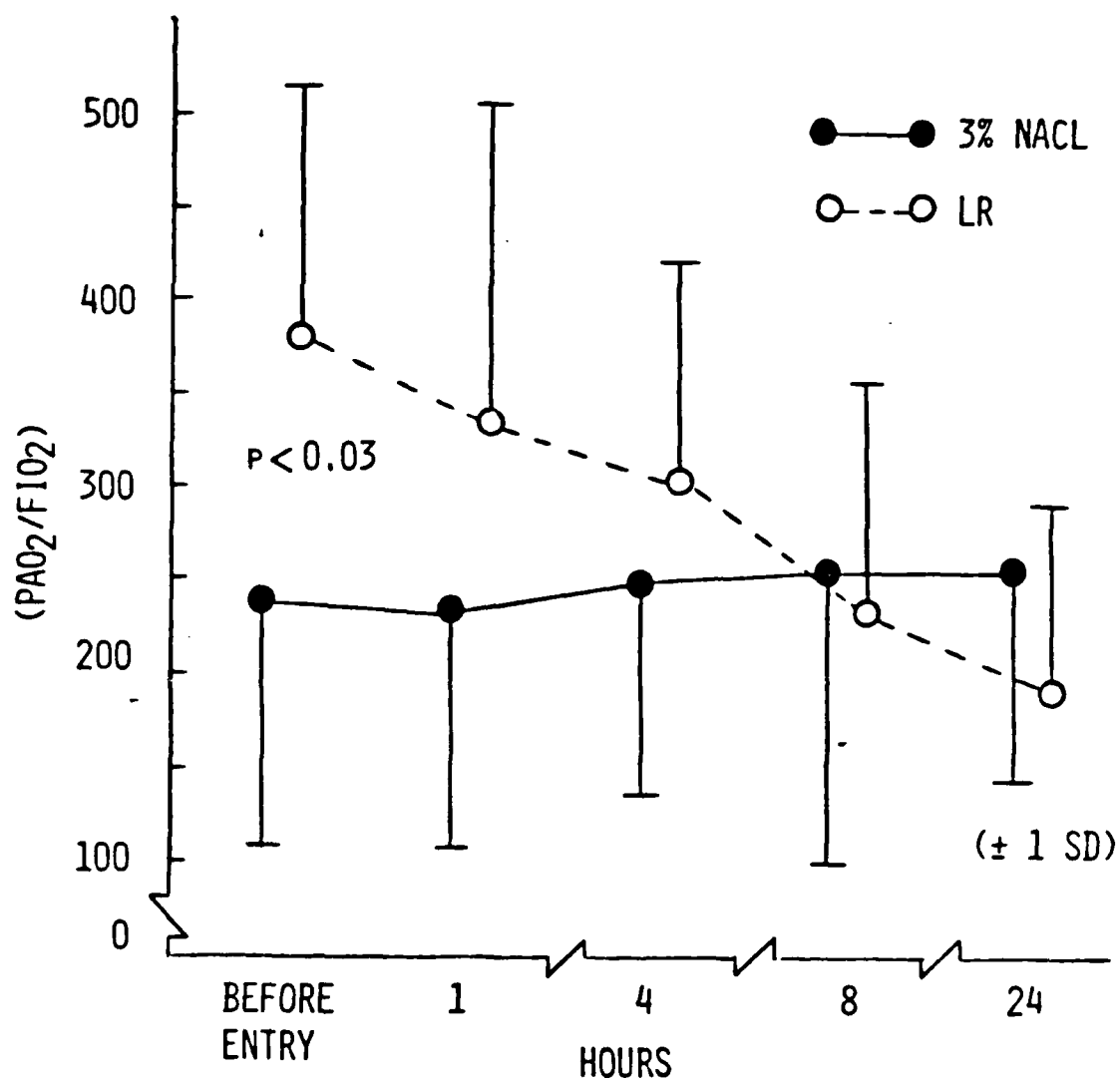


FIGURE 12: PAO₂/FIO₂ RATIOS. THE VALUES BEFORE ENTRY IN THE LR GROUP WERE SIGNIFICANTLY DIFFERENT FROM THE 24 HOUR VALUES ($P < 0.003$); THE VALUES FOR THE 3% NaCl GROUP REMAINED STABLE THROUGHOUT THE 24 HOUR PERIOD, DESPITE THE DIFFERENCES IN THE VALUES BEFORE ENTRY ($P < 0.03$).

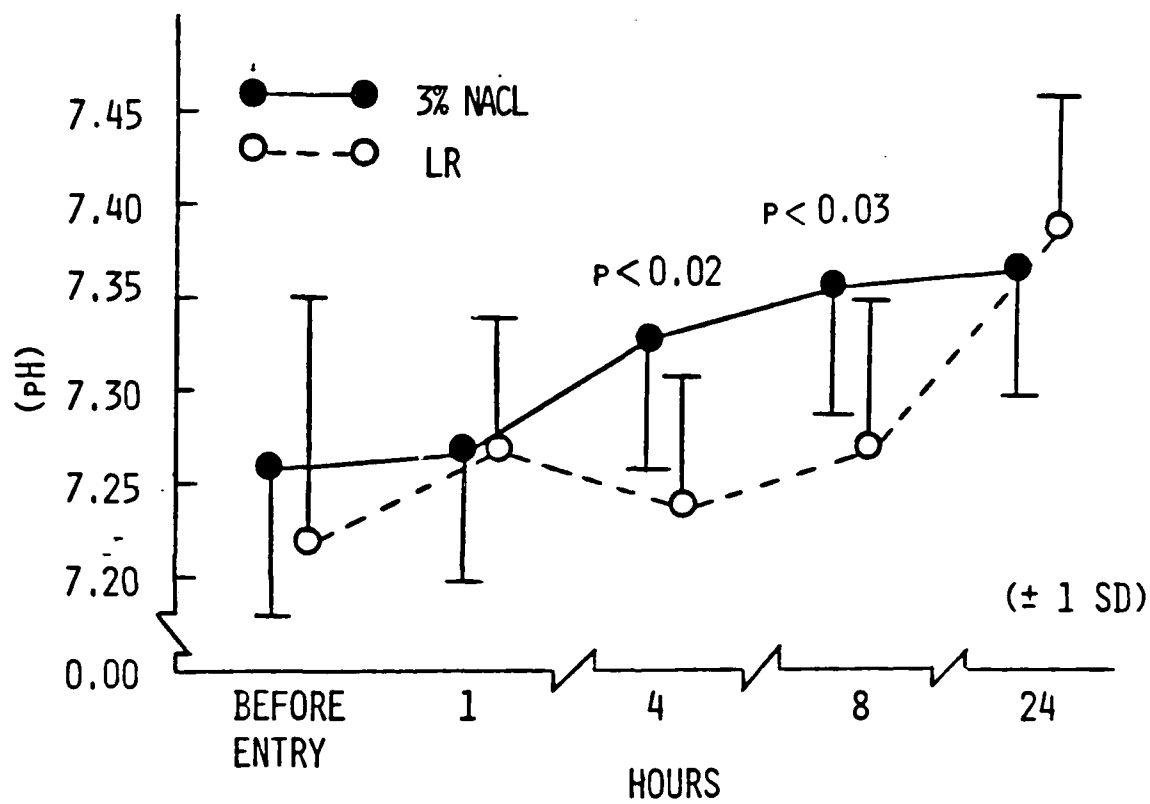


FIGURE 13: ARTERIAL pH MEASUREMENTS.

APPENDIX I

Abstract

USE OF A 3% NaCl SOLUTION TO RESUSCITATE SEVERELY INJURED PATIENTS
James W. Holcroft, M.D. and Mary J. Vassar, R.N.
Department of Surgery, University of California, Davis, CA

Twenty severely injured patients were entered into a prospective open-label study to evaluate a moderately hypertonic NaCl solution for resuscitation of shock. All patients had received at least 6 l of isotonic fluids for resuscitation before entry; all required at least 15 ml/kg during the hour before entry. Over two hours, ten patients received 3% NaCl, 4 ml/kg/hr, in addition to isotonic fluids as needed to maintain urine output and blood pressure. Ten served as controls and received isotonic fluids only. The hypertonic group received a total of 7.0 ± 1.6 (SD) ml of 3% NaCl over two hours.

		Total Na In (mEq/kg)	Total Blood In (ml/kg)	Total Fluid In (ml/kg)	Total Urine Out (ml/kg)	Systolic BP (mmHg)
Before	3%	14 $\pm$ 3	23 $\pm$ 18	102 $\pm$ 20	3 $\pm$ 2	100 $\pm$ 39
entry	Iso	17 $\pm$ 4	24 $\pm$ 17	120 $\pm$ 30	7 $\pm$ 7	112 $\pm$ 25
1 hr	3%	5 $\pm$ 2	15 $\pm$ 20	20 $\pm$ 10	4 $\pm$ 3	107 $\pm$ 41
	Iso	5 $\pm$ 3	14 $\pm$ 11	32 $\pm$ 16	2 $\pm$ 2	111 $\pm$ 15
2 hrs	3%	9 $\pm$ 3	19 $\pm$ 25	39 $\pm$ 17	9 $\pm$ 7	116 $\pm$ 29
	Iso	10 $\pm$ 4	26 $\pm$ 22	69 $\pm$ 35	3 $\pm$ 3	117 $\pm$ 18
				p<0.03	p<0.02	

Means $\pm$ 1 SD; p value by two-tailed t-test; intake and output cumulative during the study.

Discussion: 3% NaCl effectively maintained cardiovascular function in these severely injured patients and reduced fluid requirements by one-half. Hypertonic solutions may be particularly effective in the early resuscitation of injured patients, particularly in situations in which it is impossible to infuse large amounts of fluid.

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May 1986

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