Three Percent Saline Administration During Pediatric Critical Care Transport

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Objectives: The purpose of this study was to describe the administration of 3% saline (3%S) during pediatric critical care transport.

Methods: A retrospective study was performed on pediatric patients who underwent critical transport to Loma Linda University Children's Hospital from January 1, 2003, to June 30, 2007, and were given 3%S. Patients' demographics, admission diagnosis, route and amount of 3%S administration, serum electrolytes, vital signs, radiographic data, and Glasgow Coma Scale scores were collected and analyzed.

Results: A total of 101 children who received 3%S infusions during pediatric critical care transport were identified. Mean patient age was 5.9 years, and mean patient weight was 27.6 kg. The main indications for infusing 3%S were suspected cerebral edema (41%), intracranial bleed with edema (51%), and symptomatic hyponatremia (6%). The amount of 3%S bolus ranged from 1.2 to 24 mL/kg, with a mean of 5.4 mL/kg. Serum electrolytes before and after 3%S infusion demonstrated significant increases in sodium, chloride, and bicarbonate levels ($P < 0.05$). A significant reduction was also seen in serum urea nitrogen levels and anion gap. Radiographic imaging performed before 3%S infusion demonstrated findings consistent with concerns of increased intracranial pressure such as intracranial bleed and cerebral edema. The route of initial 3%S infusions was mainly through peripheral intravenous lines (96%). No complications related to the 3%S delivery such as local reactions, renal abnormalities, or central pontine myelinolysis were observed.

Conclusions: It seems 3%S may be administered safely during pediatric critical transport and administration routes can include peripheral lines. With the importance of initiating therapy early to improve patient outcomes, the use of 3%S may benefit transported children with brain injury and suspected intracranial hypertension.

Key Words: 3% saline, cerebral edema, intracranial pressure, peripheral intravenous, critical care transport

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The implementation of pediatric critical transport is an indispensable tool in the care of severely ill children. Numerous studies have demonstrated that early accomplishment of certain therapies can have a significant impact on patient mortality and morbidity. Brierley et al,[1] in the updated 2007 pediatric and neonatal septic shock guidelines, emphasized the early use of age-specific therapies to attain time-sensitive goals during the first hour of patient contact including aggressive fluid resuscitation and inotropic support through peripheral catheters until central access is obtained. The importance of quick intervention was further shown in a study by Han et al,[2] where aggressive fluid resuscitation in the pretertiary care hospital setting with the goal to reverse early pediatric shock increased the odds of survival by 9-fold. The timely administration of certain medical therapies can have a large impact on patient outcomes and, thus, should be initiated during pediatric critical care transport.

One of the most pressing medical emergencies during the course of pediatric critical care transport is suspected elevated intracranial pressures resulting from brain injury. A study by Pigula et al[3] demonstrated the importance of correcting hypotension and hypoxia with traumatic brain injury in pediatric patients with a near 4-fold decrease in survival in patients with initial hypotension and hypoxia. In this context, the use of hypertonic saline as osmolar therapy has gained wider acceptance for the treatment of cerebral edema. Clinical conditions for which hypertonic saline have been used include traumatic brain injury and subarachnoid hemorrhage.[4–7] We have previously described our experience with 3% saline (3%S) for altered mental status in patients with diabetic ketoacidosis (DKA).[8] In the most recent Pediatric Traumatic Brain Injury Guidelines, hypertonic saline is equally recommended with mannitol as osmolar treatment in pediatric head injury with associated intracranial hypertension.[9]

At Loma Linda University Children's Hospital (LLUCH), 3%S is the preferred osmotic treatment of brain injury with suspected intracranial hypertension during pediatric critical care transport. In this study, we present our experience with 3%S delivery during pediatric critical care transport and hypothesize that 3%S can be implemented safely for these children.

METHODS

Loma Linda University Medical Center's Institutional Review Board approval was obtained. The medical records for all LLUCH pediatric critical care team transports performed from January 1, 2003, to June 30, 2007, were reviewed.

Children were included in the study if they received 3%S during the course of their transport. Patient demographics collected included age, sex, and weight. In addition, the initial diagnosis at time of transport, mode of transport, and duration of transport were recorded. The duration of transport was defined as the time from initial patient contact at the referring hospital to the time of arrival of the patient to LLUCH. Radiographic imaging reports of the brain at the referring facility were compared with studies obtained within 72 hours of admission to LLUCH when available. Location of admission, days of hospitalization, incidence of mechanical ventilation, and final disposition were also analyzed. In addition, information was gathered on the route of administration of 3%S, the amount given, and whether a continuous infusion was started after the initial bolus during transport and after admission. The selected medical

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records were reviewed for laboratory results including electrolyte levels before and after the 3%S infusion. Patients' vitals of blood pressure and heart rate were examined just before and 30 minutes after completion of 3%S administration. The Glasgow Coma Scale (GCS) score was recorded from the documented physical examination findings for each child at the time of 3%S infusion and 1 hour after infusion unless given sedation or paralytic agents by either the referring facility or the transport team. Complications that may have resulted from 3%S infusion including extravasation at the infusion site, severe electrolyte alterations, and central pontine myelinolysis were also noted.

Electrolyte levels and vital signs were expressed as mean (SD). Differences among serum electrolyte levels, patient vitals, and GCS score before and after 3%S administration were assessed by paired t test analysis. Statistical significance was indicated by $P < 0.05$. All statistical analyses were performed using the SPSS software program version 12.0 (SPSS, Inc, Chicago, Ill).

RESULTS

During the study period, 3150 pediatric critical care transports were performed by the pediatric intensive care unit (PICU) transport team. A total of 101 children met inclusion criteria; all of whom were analyzed. Patients' age ranged from 2 months to 17 years, and patients' weight ranged from 4 to 92 kg (Table 1). All study children were initially admitted to the PICU and stayed in the unit with a range of 7 hours to 96 days. Admitting diagnoses are listed in Table 2. In the study group, 67% (68/101) of the patients were mechanically ventilated at the time of 3%S administration.

Transportation was performed by ground ambulance for 65% of the patients, and transport times ranged from 20 to 398 minutes (mean, 91 minutes). The major indications for 3%S were suspected cerebral edema (41%), intracranial bleed with edema (51%), and symptomatic hyponatremia (6%). These suspicions were based on clinical findings such as mental status depression, seizures, and radiographic imaging. The duration of initial infusion ranged from 9 to 180 minutes (mean, 47 minutes). The 3%S was given by the referring facility after transport request based on the recommendations of the attending physician at LLUCH in 3 patients, with the remainder being given by the transport team. The bolus amount ranged from 14 to 600 mL of 3%S (1.2–24 mL/kg; mean, 5.3 mL/kg). Four children received a second bolus during the transport. Eleven patients were administered mannitol, with 9 administered at the referring facilities and 2 administered by our pediatric critical care transport team. Dosages ranged from 0.05 to 1 g/kg (mean, 0.45 g/kg).

TABLE 1. Demographic Data

Baseline patient characteristics	
Mean age, y	5.9
No. males	69
No. females	32
Mean weight, kg	27.6
Mean length of PICU stay, d	10
Mean length of transport time, min	101
Mode of transport (no. patients)	
Ground	66
Helicopter	35

y indicates year; kg, kilograms; d, days; min, minutes.

TABLE 2. Admitting Diagnoses

Admitting Diagnoses	No. Patients
Traumatic brain injury	
Motor vehicle accident	23
Nonaccidental trauma	21
Nontraumatic brain injury	
DKA	16
Intracranial bleed	8
Hyponatremia	6
Near drowning	6
Brain mass/tumor	5
AVM	4
Seizures	3
Full arrest	3
VP shunt malfunction	3
Meningitis	2
Hypovolemia	2

AVM indicates arteriovenous malformation; VP, ventriculoperitoneal.

The route of initial 3%S infusion was through a variety of access routes. A peripheral line was used in most children (95%). A central line was used in 4 patients and an intraosseous line in 2 patients. There were no recorded infusion reactions locally or systemically. No other complications related to 3%S administration were identified.

A serum sodium level was obtained in 87 of the children before the 3%S infusion with a mean (SD) 135 (8) mM (range, 114–152 mM; Table 3). The mean (SD) level of serum sodium after infusion was 143 (8) mM (range, 127–183 mM), which was a statistically significant increase. Serum electrolyte levels were obtained from 1 minute to 10 hours (mean, 97 minutes) after 3%S infusion. The reasons for delays in acquiring postinfusion serum electrolyte levels included emergent surgery or radiographic imaging. Mean (SD) chloride level before infusion was 103 (8) mM and that after infusion was 115 (9) mM, which was a significant increase. A statistically significant decrease was noted for mean serum urea nitrogen (BUN) and anion gap level before and after infusion. There was also a statistically significant increase in bicarbonate and chloride levels before and after the 3%S administration. Patient vitals measured before and after 3%S infusions did not demonstrate a significant difference in heart rate and systolic and diastolic blood pressures (Table 4).

Head computed tomographic (CT) scans were available in 63 (62%) of 101 patients before 3%S infusion. The predominant findings on initial scans were intracranial bleed, cerebral edema with intracranial bleed, and isolated cerebral edema. The remainder of preinfusion imaging demonstrated hydrocephalus, normal results, and a posterior fossa mass. Radiographic imaging was obtained after infusion in 79 of 101 patients (74 head CT scans, 5 head magnetic resonance imaging [MRI] scans). Findings mirrored those noted on the initial scans. Of the 5 children who underwent head MRI, results were as follows: cerebellar mass and obstructive hydrocephalus, parietal occipital mass, cystic posterior mass with tonsillar herniation and hydrocephalus, and a parietal subdural hemorrhage. None of the head CT or MRI scans after 3%S infusion had evidence of central pontine myelinolysis.

The GCS score in 42 children who did not receive sedation or paralytic medications just before 3%S infusion was a mean (SD) of 9.3 (5.1). At 1 hour after infusion, mean (SD) GCS score

TABLE 3. Serum Electrolytes Before and After 3%S Administration

Serum Electrolytes	Number in Analysis	Before Infusion	After Infusion	*P* (2-Tailed)
Sodium, mM	87	135 (8)	143 (8)	<0.001
Potassium, mM	84	4.1 (1.0)	3.9 (0.9)	0.23
Chloride, mM	87	103 (8)	115 (9)	<0.001
CO_2	85	17 (7)	19 (5)	0.001
BUN	83	16.7 (15.5)	14.3 (15)	0.001
Creatinine	83	0.69 (0.59)	0.68 (0.47)	0.67
Anion gap	84	20.4 (7.5)	13.6 (5.7)	<0.001

Values are mean (SD).

was 9.4 (5.4), with no significant difference. Final patient outcome was discharge to home for 77 children (76%), transfer to another facility for 1 child (1%), and death in 23 children (23%).

DISCUSSION

This is the first large study detailing hypertonic saline use during pediatric critical care transport. The main clinical conditions for which 3%S was administered in our study mirrors the medical literature indications for 3%S use: cerebral edema, suspected intracranial hypertension, symptomatic hyponatremia, and DKA.[4–8,10] A study performed by Peterson et al[5] demonstrated that the early use of hypertonic saline effectively lowered intracranial pressure in head-injured pediatric patients with low complication rates of renal failure, pulmonary edema, or central pontine demyelination.

A major indication for 3%S use is to reduce intracranial pressure in patients with head trauma associated with cerebral edema. The effect of hypertonic saline on reducing brain volume was first recorded[11] in 1919. Further animal studies during the 1980s demonstrated that infusions of hypertonic saline could lower increased intracranial pressure and alleviate cerebral edema.[12–14] The use of 3%S to control and even lower intracranial pressure has been shown in recent reports in children.[4–6,15] The postulated mechanism of 3%S in the therapy for increased intracranial pressure is due to the creation of an osmotic gradient. This increased osmotic gradient can cause water to passively diffuse across the blood-brain barrier and into the intravascular space. The reduction of fluid within cerebral tissue decreases intracranial volume. The net effect is a decrease in cerebral edema and thus a reduction in intracranial pressure. Additional clinical uses of 3%S include its application in subarachnoid and other intracranial bleeding with demonstration of improved cerebral blood.[7,16]

The serum electrolyte analyses before and after 3%S infusion demonstrated expected changes. Sodium and chloride levels increased significantly after the initial bolus comparable to alterations reported in previous studies.[4,6,15] The analysis of the anion gap of the serum electrolytes interestingly revealed a significant decrease. It has been our experience, however, to see the development of hyperchloremic metabolic acidosis in some children with continued hospital use of 3%S administration. Our approach in these patients is to formulate the 3%S solution as a 3% sodium, 1.5% chloride, and 1.5% acetate mixture (510 mEq/L Na, 255 mEq/L Cl, and 255 mEq/L acetate) to minimize or correct this complication. It may also be difficult to differentiate between induced hypernatremia and diabetes insipidus because of pending cerebral herniation with prolonged 3%S therapy. The noted significant decrease in the initial anion gap and BUN levels could have possibly been due to an improvement in the patient's volume status.

TABLE 4. Measured Vitals Before and After 3%S Administration

Vitals Measured	Before Infusion	After Infusion	*P* (2-Tailed)
Heart rate, bpm	127 (34)	127 (29)	0.93
Systolic BP, mm Hg	114 (23)	114 (23)	0.92
Diastolic BP, mm Hg	67 (18)	68 (18)	0.65

Values are mean (SD).

BP indicates blood pressure; bpm, beats per minute.

Hypertonic saline seems to have additional benefits in fluid resuscitation by maintaining or improving blood pressure, cardiac output, and tissue oxygenation during hemorrhagic shock.[17–19] Our present study did examine possible hemodynamic alterations associated with hypertonic saline infusion. The vitals reviewed demonstrated no improvement or worsening of heart rate and systolic and diastolic blood pressures before and after 3%S infusions. A potential reason for not observing a significant change in patients' vitals could have been that only 1 bolus of 3%S was given during most transports. The infusion of more than one 3%S bolus may be needed to witness a significant effect in patients' hemodynamics. Nevertheless, hypertonic saline is the preferred osmotic therapy over mannitol in children with elevated intracranial pressure at our institution to maintain or improve intravascular volume. The concern of intravascular depletion is an issue with the use of mannitol because of its diuretic effects.[20,21] Mannitol can also precipitate electrolyte imbalances and possible rebound intracranial hypertension.[21–23]

There was no evidence of acute renal insufficiency or failure in our investigation that could be attributed to the 3%S infusion (no child required dialysis). There was no difference between initial and postinfusion serum creatinine levels. Serum urea nitrogen level decreased significantly, perhaps because of improved intravascular volume status hydration. Although the initial volume amounts varied somewhat among the patients, our usual method is to bolus with 5 mL/kg of 3%S and then continue a 1-mL/kg per hour infusion titrating to desired serum sodium measured every 4 to 6 hours. A recent study by Froelich et al[24] revealed no difference in the rate of renal failure, infection, or deep vein thrombosis in adult patients with neurocritical illness receiving either continuous hypertonic saline therapy or 0.9% saline.

In our study, most 3%S infusions were performed via a peripheral line. There has been concern that hypertonic saline may not be given through a peripheral catheter because of its

potential for extravasation and local tissue damage. Although we did not specifically document extravasation at an infusion site in our patients, no evidence of local reaction was found in any of the children. This is of obvious importance because, during the course of pediatric critical care transport, central venous access may not be available, thus delaying the implementation of a potentially beneficial treatment. In addition, the infusions through the central and intraosseous lines demonstrated no adverse site reactions. This study exhibits the possibility of safely infusing hypertonic saline through a variety of routes during pediatric critical care transport including peripheral venous access, allowing for early initiation of treatment to potentially maximize patient outcome. As is our practice, central line administration should be the preferred route of delivery if available and/or the 3%S infusion is to be continued.

There are further concerns and reservations regarding the use of 3%S in pediatric patients. These include central pontine myelinolysis, acute shrinkage of the brain leading to tearing of the bridging vessels, and additional possible local hemorrhages, systemic coagulopathies, and rebound intracranial hypertension.[25–27] In our study, children who had radiographic imaging after the 3%S demonstrated no evidence of central pontine myelinolysis. However, only 5 children underwent head MRI, which would have been the diagnostic test of choice. We also did not specifically measure any change in initial intracranial bleed that could have been a result of 3%S infusion, although none were grossly evident. Rebound hypertension was difficult to ascertain because of the lack of direct intracranial pressure monitoring in patients during the transport. Autopsy and microscopic evaluation of brain tissues of all study patients who died would also have been of interest. One child with DKA who died demonstrated diffuse cerebral edema, tonsillar and uncal herniation, and hemorrhagic necrosis of the pituitary on brain examination. This patient had a physical examination that revealed fixed and dilated pupils before pediatric critical transport and infusion of 3%S. Two other neuropathology autopsy examinations in a child who died of nonaccidental brain trauma and a child who drowned in an irrigation ditch also did not show evidence of central pontine myelinolysis. Care should always be taken in not allowing induced situations of hypernatremia to be corrected too rapidly in an effort to minimize these potential complications.

Our study has the limitations associated with a retrospective review and the lack of controls. The absence of direct intracranial pressure monitoring during transport also questions actual correction of intracranial hypertension in these patients. Furthermore, no information can be obtained regarding the direct effects of 3%S use in children with intracranial bleeding and cerebral edema and whether neurologic outcome improves in the long term.

CONCLUSIONS

It seems that 3%S may be administered safely during pediatric critical transport, and initial administration routes can include peripheral lines. With the importance of starting therapy early to improve patient outcomes, the use of hypertonic saline may benefit transported children with brain injury and suspected intracranial hypertension as well as hyponatremia. Further studies are needed to investigate the effects of hypertonic saline on hemodynamics, hospital stay, and neurologic outcomes.

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