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Ringer’s Lactate vs. Normal Saline in the pre-hospital protocols. Isotonic, hypertonic, hypotonic fluids, when, why, and where are they primarily used?

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Ringer's Lactate, Normal Saline, Isotonic, Hypertonic, Hypotonic Fluids.

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Abstract

Normal Saline (NS) (0.9% Sodium Chloride Solution) and Ringer's Lactate (RL) also known as lactated Ringers (LR) (Propanoic acid, 2-hydroxy-, calcium potassium sodium salt, hydrochloride (1:1:1:2:4)) (ChemSpider, 2015) are the two primary fluids used in resuscitation in the pre-hospital environment. In generally established protocols, these two rarely exist together in the same protocol for use by EMS personnel. In theory, NS is the primary fluid used in much of the Eastern United States (US), while Ringer's Lactate is generally relied upon in the Western United States. The primary goal of this study is to examine resuscitative fluids as well as the others discussed in our course textbook. Three questions are to be addressed: When are these fluids used, why is one Isotonic Crystalloid Solution better than another for a given resuscitative purpose? Why is there a difference not only in our text, but also in the common usage for these fluids? Where are these fluids commonly used within the US, (i.e. where based on prehospital protocol guidance are these used)? Other Isotonic, Hypotonic, Hypertonic, Colloidal, and Electrolytic fluids will be examined under similar context. Peer Reviewed Authoritative Studies, if possible, interview with Medical Directors and EMS Council representatives setting locality based Protocols, and cursory web survey/review of available online EMS protocols will be used to answer these questions.

Due to uncontrollable circumstances, interviews were not possible. Electrolyte administration discussed in Guy is a special condition of hypertonic solutions. Electrolytes will not be specifically discussed in this paper. This study found many study authors acknowledge the long time debate along the same lines, which is best, NS or RL. Based on the research, this author would lean toward use of Ringer's Lactate except in the case of pediatric patients where Ringer's Acetate might be a better fluid. Which ever the fluid, the paramedic is advised based on this study to become educated in the various types of fluids, when and where they are to be used, their protocols, and most importantly study the acid-base balance impact of the various types of fluid.

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Introduction

Pre-hospital fluid resuscitation administration education includes numerous options for the provider. The range of fluids available is generally oriented to usage based on the region of the United States, hospital, agency, and even within the department of the hospital. Resuscitative fluids are categorized in numerous ways. These fluids are first categorized as crystalloid or colloid solutions. Then tonicity is provides further categorization. Tonicity relative to the homeostatic balance of sodium determines the isotonic, hypertonic, and hypotonic categorization. A third categorization included in Caroline but not in Guy determines the best way to restore the body’s homeostatic fluids however they are not yet available in most pre-hospital agencies: oxygen carrying solutions or blood or blood substitutes. This third category will not be further discussed in this paper.

While studying, and in discussion with peers, nursing staff, and doctors during clinical practice, the question of “Why normal saline (NS) versus Ringer’s Lactate (RL)?” occurred frequently. Answers were typically: “its geographical, in the Eastern US, practice uses NS, in the Western US, NS is seldom found but Ringer’s Lactate is typically used”. (Citation based on mixed conversation and inquiry) During Mary Washington Hospital (MWH) Labor and Delivery Department (L&D) clinical rotation, I was asked to administer a replacement 250ml bag of Ringers Lactate. I asked why RL. The nurse preceptor informed me, ‘RL is typically used within L&D’ (verbal, E. Smith). This was especially curious as the patient had severe a case of nephrolithiasis having already had five stints placed into her ureters, and based on my understanding of the higher levels of calcium and potassium in RL than NS. (One paper studied specifically countered this “myth”.)

This paper will extend the question of NS vs RL further, our text (Guy, 2011) provided instruction on numerous other resuscitative fluids to be administered via IV/IO route for fluid expansion and how the type of fluid migrated within the proportions of body fluids. Examining local protocol from REMS, many of these are not provided nor discussed even at the Paramedic level .

Problem Statement

Based on the RCC advanced pharmacology course, numerous pre-hospital resuscitative fluids have been discussed. Many of these are not found in our local protocols. What are these fluids? Why is there a difference not only in our text, but also in the common usage of these fluids? When are these fluids used, (i.e. what makes one Isotonic Crystalloid Solution better than another for a given resuscitative purpose)? Why is there a perceived difference across the US as to usage of Normal Saline (NS) (0.9% Sodium Chloride Solution) and Ringer’s Lactate (Propanoic acid, 2-hydroxy-, calcium potassium sodium salt, hydrochloride (1:1:1:2:4)) (ChemSpider, 2015) in pre-hospital protocols. Where are these fluids used and for what therapeutic value? Is there a pattern of practice with respect to the locations? Do other first world countries share in our variety of usage (are there recognized examples)? Is it true, in general established protocols, these are rarely together in the same protocol or issue to EMS agencies? The hypothesis exists stating NS is the primary fluid used in much of the Eastern United States (US), while Ringer’s Lactate is generally relied upon in the Western United States. Can this be verified and to what level of finding. The other Isotonic, Hypotonic, Hypertonic, Colloidal, and Electrolytic fluids discussed in our text (Guy, 2011) will be examined under similar context.

Methodology

Six peer reviewed authoritative studies, two paramedic textbooks, three informational (medical and research oriented) web sites, and a cursory web survey/review of available online EMS protocols was used in this research. Approximately 15 other peer reviewed studies were read in preparation but as they were specific to certain disorders were not included in this study.

Resuscitative Fluids

After establishing ABCs in our prehospital patient, our priority along with assessment of the patient is then to begin treatment. In almost all cases ensuring proper tissue perfusion and hemorrhage control becomes our goals. Increasing vascular volume (and consequently the blood pressure) becomes the priority. The EMS system provides IV or IO fluids in order to perform expansion of the vascular system. The EMS professional must have a knowledge of fluid distribution within the body for selection of the necessary resuscitation fluid. Total body water is roughly 60% of body weight. Intracellular and extracellular fluid is separated by the cell membrane a semi- permeable passage for water and some electrolytes. The movement is controlled by ionic concentration. The volume is maintained by the sodium-potassium ATPase pump. The capillary membrane separates the interstitial and plasma fluids. These fluids are similar in concentration except the plasma contains more proteins due to the membrane being highly permeable except for large proteins. The osmotic pressure across the capillary membrane has its own designation – oncotic pressure. A healthy patient has an oncotic pressure of 28mmHg. Total osmotic pressure is approximately 5400mmHg. A table in this cited reference is helpful for understanding the distribution of pressures. Therefore, the molecular size of the resuscitative fluid components need to be taken into consideration in order to target the intravascular space. (Protheroe & Nolan, 2001)

Historic Reference

Normal Saline was first established in 1883 by a Dutch Physiological Chemist Hartog Hamburger (1859-1924), Ringer’s lactate was developed by Sidney Ringer (1834-1910) an Australian physician introducing a NaCl solution with potassium and calcium promoting isolated heart contractions leading to Alexis Hartmann (1898-1964), an American pediatrician, adding a non-Cl anion lactate to prevent metabolic acidosis. This solution was called Ringer’s lactate or Hartmann’s solution. Figure 1 in this cited reference provides a graphical comparison of the composition of these and modern balanced crystalloids. (Santi, et al., 2015)

Pediatric Sidebar

Pediatric IV fluids have their own set of goals. The ideal resuscitative fluid would have no tissue storage, no adverse electrolyte impacts, no acid-base balance challenges, no hematologic or immunomodulating effects. It would be compatible with all pediatric medications, have a long shelf life, low cost, and no special storage requirements. We know such a fluid doesn’t really exist.

Studies with low sodium fluids lead to 0.9% solutions, concerns over hyponatremic encephalopathy as well as the induced risk of hyponatremia lead to use of maintenance NS as an exception for pediatric patients. Acid-base balance is impacted by use of NS, NS being a Chloride ion rich fluid not containing a buffering ion or an ion metabolized into HCO3- generally increases Cl-, decreases HCO3- ions creating hyperchloremic metabolic acidosis, often referred to as dilution acidosis. This acidosis has a short life unless the patient is suffering from kidney disease or injury. (Not compared but the article stated intensive care patients fair better with hyperchloremic acidosis than patients with non-hyperchloremic or lactic metabolic acidosis.) It went on further to state the high Cl- content of saline may contribute to kidney injury resulting in sodium retention. While describing other negative impacts of NS, one potential severe impact is the possibility of misinterpreting fluid losses due to sepsis, shock, and gastrointestinal tract, thus increasing dilution acidosis leading to administration of even more fluids due to a perception of the patient being hypovolemic.

RL did not seem to be a complete answer as it's sodium level is lower than extracellular fluid. In the pediatric patient this potentially decreases circulating sodium levels, possibly leading to hyponatremic encephalopathy. This encephalopathy and increase in brain water content is important due to the brain to skull ratio and reduced infantile sodium pump activity. The authors recommended use of acetate based Ringers vice lactate based in order to prevent the lactate glucogenesis and possible misinterpretation of lactate as a marker for tissue oxygenation in children. Acetate stabilizes pH quicker and is metabolized in the tissues vice the lactate metabolism in the liver, never the perfect compromise, acetate in pediatric patients is attributed with some cardiodepressent and vasodilator effects.

The authors remind us IV fluids should be treated as a medicine in the same fashion as insulin, antibiotics, chemotherapy. Restricted use may be a superior strategy for the patient, ending with a call for development of better fluids in order to end the "great fluid debate". (Santi, et al., 2015)

"Water"

D5W (5% dextrose in water) is considered being free of particles distributes to the various compartments of the body in proportion to each compartment's percentage of total body water (TBW). D5W therefore will distribute proportionally into both Intracellular Fluid (ICF) and Extracellular Fluid (ECF). Within the ECF, likewise the distribution will be proportional into both the intravascular fluid and the interstitial fluid. (Guy, 2011) D5W is considered isotonic in the bag but due to the dextrose metabolism, becomes hypotonic upon administration. D5W is used in the prehospital environment for medication infusions of dopamine or amiodarone. (Caroline & Pollak, MD, FAAOS, 2012)

Crystalloid Solutions

Crystalloid solutions contain crystals of salts or sugars dissolved in water. These solutions are based on the ability of the fluid to cross cellular membranes altering fluid levels or provide fluid expansion. Crystalloids are used to replace fluids, most importantly blood, lost in trauma. In prehospital care, in order to provide expansion supporting the restoration of blood pressure, a three to one (3 to 1) rule should be followed due to two thirds of the infused fluid being either absorbed into interstitial space or excreted.

Crystalloid solutions are given as a 20mL/kg bolus for adults, protocol specific levels for pediatrics, and in other situations to maintain perfusion, not raise to the blood pressure to normal levels. Crystalloid solutions decrease the proportion of hemoglobin potentially interfering with hemostasis. (Caroline & Pollak, MD, FAAOS, 2012) In one citation, depending on the saline concentration and the ability to pass through the microvascular membrane, distribution is even across the extracellular compartment requiring (differing whether normal or hypovolemic) four to one ratio for intravenous replacement of blood loss. (Protheroe & Nolan, 2001)

Colloid Solutions

Colloid Solutions, generally considered hypertonic contain large molecules remaining in the vascular compartment of the ICF. Most colloid solutions have a high osmolality drawing fluid from both the interstitial and intracellular compartments, expanding the vascular compartment, effectively reducing edema especially in pulmonary and cerebral physiology. Potentially causing dramatic fluid shifts if not used in a controlled environment, colloid solutions are rarely used in prehospital except for transport agencies. (Caroline & Pollak, MD, FAAOS, 2012). Two colloid solutions were discussed in Guy: Albumin and Hetastarch. Other colloid examples include dextran and Plasmanate. (Caroline & Pollak, MD, FAAOS, 2012)

Dextran is a polysaccharide synthesized by bacteria *Leuconostoc Mesenteroides* and are colloids in the blood. Anaphylaxis is greater with dextran than with other colloids. Dextran does have a long half-life (2-5 hours), and is used for microcirculatory flow and prevention of thromboembolisms. (Hahn, 2012) Dextrans reduces viscosity and platelet adhesiveness as well as enhancing fibrinolysis with the side effect of increased bleeding. Older versions of Dextrans interfered with blood matching occasionally contributing to anaphylaxis leading to its falling out of favor as a resuscitative fluid. (Protheroe & Nolan, 2001) None of these solutions are available in area's protocols.

Albumin causes approximately 80% of the fluid administered to shift to the intravascular space vice the 25% of NS or RL. Albumin is often used for burn therapy as well as nephritis, its side effects include allergy and coagulation problems. (Hahn, 2012) Albumin has free radical scavenging and anticoagulant properties, helps preserve integrity of the microvasculature but correlates poorly with colloid oncotic pressures. It is considered expensive and there are studies questioning its efficacy with respect to outcome. Due to better lab controls, most albumin is now sourced from the USA. (Protheroe & Nolan, 2001)

Hetastarch causes 100% of the fluid administered to move into the intravascular space with a third of the volume remaining long after administration. This provides great advantage in the military or extremely rural EMS systems where transport time to hospital/trauma center is long. (Guy, 2011) Hetastarchs can exhibit an increased allergic response as well as hemorrhage complications. Studies found molecules remaining for years. (Hahn, 2012)

Tonicity

Tonicity discussion is normally based on sodium concentration. Isotonic solutions are the same as a cell, not flowing across the cellular membrane nor impacting the shape of the cell and therefore have the same osmotic pressure. Hypertonic solutions have a higher solution (more sodium ions dissolved in the solute than isotonic), exerting a greater osmotic pressure drawing fluid out of the ICF into the ECF, shrinking or dehydrating the cell, similar to that of a grape into a raisin. Hypotonic solutions have a lower solution (less sodium ions dissolved in the solute vice an isotonic) leading to water being drawn into the ICF from the ECF. Cells exposed to a hypotonic solution can expand and possibly burst due to the increased osmotic pressures.

Fluid movement within the human body are controlled through osmotic pressures, water moving from the area of lowest particle concentration to the area of highest concentration until homeostasis is achieved. The two primary particles establishing osmotic pressure are sodium and serum proteins such as albumin. (Guy, 2011)

Isotonic

Isotonic crystalloid fluids consist primarily of normal saline (NS), 0.9% sodium chloride (NaCl) and Ringer's lactate (RL) (Propanoic acid, 2-hydroxy-, calcium potassium sodium salt, hydrochloride (1:1:1:2:4)) (ChemSpider, 2015).

Normal Saline

NS essentially inert in prehospital fluid administration affects the acid-base balance. The 0.9% NaCl contains 33% more chloride than ECF causing the kidneys to respond by excreting bicarbonate ions in order to maintain homeostasis for the chloride levels potentially dropping pH. Therefore, while we can use NS to treat mild metabolic alkalosis, metabolic acidosis can result. (Dennison, RN, CS, MSN & Blevins, RN, CS, MSN, 1992) One article felt NS should be abandoned due to the tendency toward metabolic acidosis and decreased glomerular filtration rate effects. NS can cause increased breathing rates in conscious patients, and takes longer than RL to eliminate. Pediatric have a greater propensity for postoperative hyponatremia, RL would be of greater benefit. (Hahn, 2012)

One articles, based in Virginia, discussed both the isotonicity, and the euvolumic (maintaining the homeostatic fluid volume) characteristics of NS. RL was not addressed except in a table comparing the electrolyte content of IV solutions, per liter. The nutritional values of sodium as well as the water requirements for patients were examined. While in the prehospital environment we are advised to provide 1-2 liters of IV NS (in this region) as fluid replacement, and potentially much more in the hospital environment. One citation demonstrated an elderly patient taken to the hospital due to dehydration had an average daily sodium intake less than 100mEq daily (roughly 2300 mg – well within the Food and Drug Administration (FDA) Recommended Daily Allowance (RDA) of 47-147 mEq/day. Over a 72-hour period from prehospital through discontinuation of IV fluids, the patient had taken in over 9.6 liters of water, and 1478 mEq of sodium (roughly 34 grams or 10 days of her normal intake over 3 days). Use of hypotonic solutions and dilution of NS by alternating with D5W were discussed as a means of reducing the sodium intake. (Corbett, Jr., Brodie, Brodie, & Parrish, 2007) This article would be excellent for inclusion into the pharmacology and pathophysiology courses for the paramedic.

Ringer's Lactate

RL consists of sterile water with added electrolytes, lactate, or acetate. RL doesn't contain buffering bicarbonate ions but is metabolized to bicarbonate. The acetate variety is more rapidly metabolized to bicarbonate. The half-life for distribution from the plasma to the interstitial fluid is approximately 8 minutes. Four half-lives (32 minutes) are required in order for RL to achieve the typical 25-30% infused volume. RL is eliminated by normal body voiding in

15-25 minutes in healthy conscious volunteers. If the patient is dehydrated, hypovolemic, pregnant, or under general anesthesia, the elimination half-life is extended to greater than 40 minutes. RL has no allergic potential but can increase coagulant effect at up to 20-30% hemo-dilution levels but when levels of dilution are higher, there is a slight anticoagulant effect because of increased concentration of plasma proteins. (Hahn, 2012)

RL is generally used prehospital for patients with high volume blood loss. Containing lactate and metabolized in the liver as well as forming bicarbonate, the key buffer in preventing acidosis, RL should not be administered to patients with liver problems. RL contains calcium capable of binding to anti-coagulants during blood transfusion can possibly cause blood clots. RL is also contraindicated for use with nitroglycerin, nitroprusside, norepinephrine, propranolol, and methylprednisone infusions. (Caroline & Pollak, MD, FAAOS, 2012) A common myth exists stating RL is safe for all patients, it is very close to serum but if a patient has liver disease, lactic acidosis can develop when the liver fails to break down the lactate. Also, should the patient have a serum pH greater than 7.5, bicarbonate will form as the lactate breaks down causing alkalosis. (Dennison, RN, CS, MSN & Blevins, RN, CS, MSN, 1992) The American College of Surgeons' Committee on Trauma (ATLS, 1997) recommends lactated Ringers because large volumes of saline can induce hyperchloremic acidosis. The same cited studies indicated large volumes of RL contributing to cerebral edema. These two fluids each having their negative attributes almost lead to use of a different isotonic fluid known as Plasmalyte 148 for trauma patient resuscitation. (Protheroe & Nolan, 2001)

Myth-busting?

There exists a myth about LR not existing for NS, the myth is LR should be avoided in the resuscitation of patients with hyperkalemia (excess of potassium). Three sets of evidence counter this myth. First, while LR has a higher concentration of potassium (4mEq/L) than NS (0), the myth says this additional potassium would exacerbate the problem. Rules of solutions and osmotic pressures would rule the opposite, a patient with hyperkalemia would have higher than 4mEq/L thus osmotic pressure would draw the patients levels down to that of LR. Second, this cited study does the math, showing LR containing a considerably large amount of potassium would be needed at a concentration of 8mEq/L or higher to increase the patient's levels serum levels. The body stores roughly 98% of its potassium within the cells at a value of approximately 140mEq/L. A third set of evidence relates to shifting potassium between the cells and the extracellular fluid. Based on the extracellular fluid containing less than 2% of the bodies potassium this may be more of a problem with NS than LR.

NS causes a non-anion gap metabolic acidosis, shifting the potassium out of the cells where LR containing 28mEq/L equivalence of bicarbonate provides some alkalinizing effects. Three studies were reviewed by the myth-busters, each with 50+ patients undergoing renal transplants. Roughly half of the patients received LR, the other half NS during surgery, per these three studies, those on NS increased serum potassium by roughly +0.5mEq/L, while those on LR decreased by 0.5mEq/L - a demonstrated decrease. An added benefit cited was lower pH levels.

The article questioned Plasmalyte and Normosol as well, finding their levels of potassium and alkalinizing capabilities better than LR. The study concluded by stating the myth was "BUSTED", as LR typically lowered levels of potassium. "Understanding the effect that a crystalloid will have on serum potassium concentrations involves considering effects on acid-base physiology and intracellular potassium shifts, which are more important than the amount of potassium in the plastic bag." (Farkas, 2014)

Hypertonic

Hypertonic Saline Solutions, such as 3%, 5%, or 7% saline are used in similar fashion as the colloid solutions discussed previously. In traumatic brain injury (TBI) cases, such as motor vehicle accident (MVA) and falls, swelling or edema can occur surrounding the brain. Hypertonic solutions are then used to pull the fluid out of the ECF into the ICF for circulation and elimination through the normal bodily efforts to reestablish homeostasis. (Guy, 2011) Hypertonic solutions increase vascular volume many times the volume infused. Hypertonic saline can cause increased chronotropic and inotropic effects, while reducing peripheral vascular resistance and endothelial edema. The addition of a colloid (dextran-70 6%) extends the half-life of the fluid in the vascular system. This combination is being further studied (Protheroe & Nolan, 2001) Often "hypertonic" refers to fluids containing high proportion proteins as well. For any hypertonic solution, monitoring is necessary especially with impaired heart or kidney function, diabetic ketoacidosis or risk of cellular dehydration. (Caroline & Pollak, MD, FAAOS, 2012) Concentrations of 3 and 7.5% are used to treat hyponatremia and brain edema due to head trauma as well as prehospital plasma volume expansion. The study found minimal benefit from use of 7.5% NaCl. (Hahn, 2012)

Hypotonic

Hypotonic saline solutions such as the combination of NS and the same volume of water creating 0.45% saline are used to hydrate the cells. This solution is used when a patient is dehydrated and needs additional fluid with higher proportions in the ECF but also requiring fluid replacement in the ICF. The water portion flows into the ICF proportionately, however the normal saline does not move into the ICF. (Guy, 2011) Hypotonic solutions are often administered during diuretic therapy to prevent cellular dehydration in dialysis and diabetic ketoacidosis where the high serum glucose levels are drawing fluid out of the cells. D5W over an extended period of time can cause increased intracranial pressure (ICP). Additional special cautions with hypotonic solutions are due to possible "third spacing" – an abnormal fluid shift into the serous linings for burn, trauma, malnutrition, and liver disease patients. (Caroline & Pollak, MD, FAAOS, 2012)

Volume Replacement

Impact and reasoning for use of resuscitative fluids, indicates typical prehospital calls are based on illness, where dehydration, loss of fluid in the intravascular space due to emesis or diarrhea are risks. The vascular system is losing fluids to the ECF, concentrating the blood components. Perfusion restoration becomes critical; in order to restore perfusion, fluids are administered to raise blood pressure with increased ICF volume. A fluid leading to maximal expansion within the ICF is necessary. Isotonic fluids such as NS or RL provide the greatest expansion. (Guy, 2011) Our goal is titration of blood pressure to 90 mmHg systolic. (Caroline & Pollak, MD, FAAOS, 2012) Per discussions with long experienced RCC instructors, prior trauma fluid replacement protocols expected infusion of two to three liters of NS or RL prior to hospital arrival. Guy, 2011 discusses ICF replacement due to blood loss requires three times the blood loss quantity of NS or RL to provide the necessary expansion in the medical scenario.

Within a short time of extreme blood loss due to trauma, the body responds by auto-resuscitation to draw fluids from the ECF into the ICF. This exchange of fluid locations becomes critical within the pre-hospital environment to establish fluid replenishment in order to protect vital organs preventing organ dehydration and subsequent failure. The above noted excessive use of resuscitative fluids was removed due to potential edema and pulmonary complications. (Guy, 2011)- (Dennison, RN, CS, MSN & Blevins, RN, CS, MSN, 1992)

Protocol Examination

Using the website www.emsprotocols.org, a site oriented to assisting protocol writers create common protocols, the following areas were reviewed:

Rappahannock EMS Council - Virginia
Peninsulas EMS Council - Virginia
LA County - California
Northwest Regional EMS – Washington (state)

Other Protocols were available through this web site. However, only LA County addressed RL, and only as an option. Both Virginia protocol sets and the Washington state only referenced NS for usage. This seems to "bust" the geographic usage of RL.

Conclusion

The debate of crystalloid versus colloid has evidently been ongoing for over 50 years (as cited in a 1997 study) due to lack of randomized controlled trials. One study concluded initial fluid should be crystalloid, as current protocols state, then a combination both crystalloid and colloid for the best outcomes. Plasmalyte 148 shows better outcomes than either NS or RL and use of Hetastarch is the preferred colloid. (Protheroe & Nolan, 2001)

The debate over RL vs NS will not be solved here, the prehospital paramedic or EMS provider must both follow good practice and their local protocols. This examination reminds us "All things are poison, and nothing is without poison; only the dose permits something not to be poisonous." (Santi, et al., 2015). Reading this study and the cited papers would lead to the conclusion we are using the wrong resuscitative fluid. NS while simple, long lasting, causes short term acidosis, solves the hypovolemic issues, and helps ensure the patient gets to the hospital with the best treatment we are able to provide. RL should be contraindicated for pediatric use due to possibly increasing the brain water content, and being contraindicated with nitroglycerin, and other cardiac medications commonly used.

Overall, the study provided detailed study into an often-frustrating debate of one medication over another, and why a study survey doesn't provide the answers. It did seem to answer one area by researching a topic of personal question. We are also reminded asking peers and even more advanced professionals in one area may not yield the best answer.

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