Clinical Pearl 84
NJ EMS Fellowship

"Normal" Saline vs Balanced Solutions for Fluid Replacement Therapy

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On a daily basis in the emergency care setting, we see patients that require fluid replacement. From sepsis, diabetic ketoacidosis, dehydration, etc., we obtain intravenous access and give a few boluses (along with the cocktail of antibiotics, insulin, or vasopressors that is appropriate for the clinical scenario). However, disagreement exists as to which type of fluid is best to use for replacement. This pearl aims to summarize the current evidence comparing the most common crystalloid fluids - Normal Saline and Lactated Ringers.

Intravenous fluids were first used in 1832 when Robert Lewens administered an alkalized salt solution to patients with Cholera in an effort to replace lost serum.[1] He noted that the amount of fluids that patients needed appeared to be proportional to the amount of fluids lost.[1] In 1885, Alexis Hartman started giving a modified salt solution to children with gastroenteritis.[1] In 1941, Human Albumin was used as a resuscitative fluid for patients burned during the Pearl Harbor attack.[1] Since then, there have been multiple types of fluids created in an attempt to replicate human plasma.

The ideal replacement fluid has a composition close to extracellular fluid, is metabolized and excreted without accumulation, has no adverse effects and is cost effective.[1] Of course, this fluid does not exist. The two categories of fluids created to best meet the aforementioned requirements are colloids and crystalloids.

Colloids are suspensions of molecules that do not cross a healthy capillary membrane.[1] Popular examples include Albumin and Hyperoncotic Startch.[1] These fluids are not widely used as they have not shown a clear benefit over crystalloids, are expensive and can be harmful.[1,2,3,4,5,6] For these reasons the rest of the discussion will focus on crystalloids.

Crystalloids are the most frequently used fluids in resuscitation. They are made of freely permeable ions, such as sodium and chloride, that determine tonicity.[1,7] The two most common types are 0.9% Normal Saline (NS) and Lactated Ringers (LR). These two types of fluids in particular have been the subject of debate over many years.

Despite the name "normal", 0.9% Normal Saline has a 10% higher sodium concentration and 50% higher chloride concentration compared to human serum.[7] It was originally described by Jacob Hamburber, who carried out red blood cell lysis studies in the early 1880s to determine that it was close to physiologic fluid.[1,7] Today, we continue to call 0.9% NS "normal" based on in vitro studies from the 1880's. The main argument against normal saline is the adverse effect of a hyperchloremic metabolic acidosis.[1,7] This can result in organ dysfunction, and in particular, renal dysfunction.[7]

A proposed solution to the problems associated with 0.9% NS were the "Balanced" or "Physiologic" crystalloid solutions, Lactacted Ringers (LR) or PlasmaLyte. These are meant to have an electrolyte composition similar to that of human plasma.[1,8] Lactated Ringers are hypotonic to human plasma and also contain potassium, calcium and lactate.[1]

PlasmaLyte is also hypotonic and contains magnesium, acetate, gluconate without the addition of lactate.[1] For this discussion we will focus on LR, since it is commonly used in the latest research.

Proponents of LR claim that it will help avoid the metabolic acidosis and renal injury seen during large volumes of crystalloid infusion.[8] However, large volumes of LR can cause a metabolic alkalosis and hypotonicity.[8] A common argument against the use of LR is the theoretical risk of increasing the potassium level in a hyperkalemic patient. Studies have shown this to not only be false, but in fact it is normal saline that has a greater risk of causing hyperkalemia due to pH shifts.[7,9,10] Furthermore, the lactate in LR has also been shown to be beneficial. Research has shown that lactate is one of the preferred substrates used by the body in energy crisis conditions, such as septic shock and acute heart failure.[8,11]

Until 2018, the best study comparing 0.9% Normal Saline and Balanced Solutions was the SPLIT trial. Published in 2015, it was a prospective, blinded, cluster randomized, crossover study performed in four New Zealand Intensive Care Units.[12] Their primary outcome was the proportion of patients with AKI.[12] There were 2278 patients enrolled and assigned to either buffered crystalloid or normal saline.[12] This trial did not find any significant difference in outcome between the two fluids. However, most patients were admitted from surgery with only 316 of the patients coming from the Emergency Department. Furthermore, on average, the study patients only received approximately 2 liters of crystalloid. [12]

This year, 2018, delivered two articles that looked at balanced crystalloid versus saline in critical and non-critical patients. The Isotonic Fluids and Major Adverse Renal Events Trial (SMART) and the Saline Against Lactated Ringers or PlasmaLyte in the Emergency Department (SALT-ED) are both large, single center, randomized trials looking at the two types of fluids.[13,14] The SMART trial studied a primary outcome of major adverse kidney events within 30 days.[13] Out of the more than 15,000 patients, there was a statistically significant difference in these events, 14.3% vs 15.4% (Balanced Solution to Normal Saline, respectively).[13] The SALT-ED trial enrolled over 13,000 patients with a primary outcome of hospital free days (which was not statistically significant) but did have a secondary outcome of Major Adverse Kidney Events within 30 days, which was 4.7% vs 5.6% in favor of balanced solutions.[14] It should be noted that the Major Adverse Kidney Events within 30 days is a composite outcome. A composite outcome combines multiple endpoints (in this case: death, initiation of Renal Replacement Therapy and persistent renal dysfunction) and uses them as a primary outcome. This type of statistical analysis does add some ambiguity to the results. Both trials do have some methodological flaws (non blinded, single center, most patients receiving LR rather than Plasma-Lyte); however, it is some of the highest quality of data we have at this point.

Based on the current data, it seems unlikely that the choice of NS vs. LR will have a major effect on mortality. The data does seem to lean towards LR when it comes to outcomes like acute kidney injury. LR will not cause a metabolic acidosis, has less chance of renal injury, does not cause hyperkalemia and may have a benefit by way of the included lactate. The difference in cost between the two is negligible and both are usually well stocked. Therefore, this author would suggest that LR is likely the better choice for fluid resuscitation, especially when using large volumes.

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