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Brief Report

DOES INTRAVENOUS LACTATED RINGER'S SOLUTION RAISE SERUM LACTATE?

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□ **Abstract—Background: Serum lactate increases in states of severe sepsis and shock, but its interpretation may be subject to confounders. Lactated Ringer's solution (LR) is used in the resuscitation of septic patients and contains 28 mmol/L of sodium lactate. Objectives: We sought to determine if a bolus of 30 mL/kg of LR increases serum lactate levels. Methods: In this double-blind, randomized controlled trial, 30 volunteers were assigned to receive either 30 mL/kg of intravenous LR or normal saline (NS). Serum lactate was measured before and after the fluid bolus. The primary outcome was the difference in the change in lactate between the LR and NS groups. Secondarily, we assessed the change in pH, bicarbonate, sodium, and chloride in each group. Results: After 30 mL/kg of intravenous LR, the mean serum lactate level increased by 0.93 mmol/L (95% confidence interval 0.42–1.44 mmol/L). However, there was also a small increase in the mean serum lactate level in the NS group of 0.37 mmol/L (95% confidence interval −0.26 mmol/L to 1.00 mmol/L), such that there was not a statistically significant difference in the change in lactate when comparing the LR group to the NS group (p = 0.2). The NS group saw larger declines in pH and bicarbonate and greater increases in chloride compared with the LR group. Conclusion: In healthy individuals, a modest but significant rise in mean serum lactate was seen after a 30 cc/kg LR bolus. There was no difference in mean serum lactate when comparing a 30 mL/kg bolus of NS to LR.** © 2018 Elsevier Inc. All rights reserved.

□ **Keywords—isotonic fluids; lactate; lactated Ringer's; resuscitation; sepsis**

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INTRODUCTION

Since "early goal-directed therapy," early recognition of septic shock using the serum lactate has become standard of care (1–4). Indeed, the central place of lactate in sepsis care has been promoted by the Surviving Sepsis campaign, and it is now backed by financial incentives for hospitals with its adoption as a Centers for Medicare and Medicaid Services Core Measure (5).

In this context, it is important to elucidate all possible causes of hyperlactatemia. Previous studies have shown that serum lactate increases in all shock states, not just septic shock (6). In addition, lactate has also been shown to increase from albuterol, antiretroviral medications, metformin, propofol, and alcohols (7,8).

According to Surviving Sepsis Guidelines, patients diagnosed with septic shock should receive 30 mL/kg of crystalloid solution within 3 h (9). One commonly used crystalloid, lactated Ringer's solution (LR), contains 28 mmol/L of racemic lactate in the form of sodium lactate. While lactate is rapidly metabolized by the liver and kidney, aggressive fluid resuscitation with LR may transiently raise serum lactate, potentially confounding the interpretation of this test.

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There has only been one trial looking at the question of whether administration of LR raises serum lactate. That study did not show a difference in lactate levels in those receiving LR versus those receiving alternative crystalloid solutions. However, that study used only 1 L of LR delivered over 1 h (10). As mentioned above, patients in septic shock are mandated to receive 30 mL/kg of crystalloid solution, and the fluids are typically given at a rate faster than 1 L per hour. Therefore, when LR is given at a volume and rate more similar to what is done for septic shock patients, LR may have an effect on serum lactate level that was not identified in the previous study.

We performed a double-blind, randomized controlled trial to investigate whether the administration of intravenous LR at 30 mL/kg increases levels of serum lactate. As our study was comparing the effect of normal saline (NS) and LR, it lent itself easily to secondarily investigating changes in sodium (Na), chloride (Cl), and pH in the NS group compared to the LR group.

MATERIALS AND METHODS

Study Design and Setting

This was a double-blind, randomized controlled trial performed on a group of healthy volunteers made up primarily of family, friends, and colleagues of the investigators. The study was approved by our local institutional review board (UMC-2017-54). It was registered prospectively with clinicaltrials.gov (NCT02950753).

All subjects were healthy volunteers ≥18 years of age. Healthy volunteers were defined as subjects with no acute symptoms who met none of the following exclusion criteria: pregnant, breastfeeding, prisoners, history of conditions associated with fluid overload (congestive heart, renal, or hepatic failure), baseline serum lactate level >2.2 mmol/L, and baseline creatinine >1.5 mg/dL.

All volunteers filled out a short data collection form assessing their age, weight, gender, and medical history. All volunteers signed a written consent, approved by the institutional review board.

A random-number generator was used to assign each subject to either LR or NS. After assignment, a pharmacist with no role in data collection prepared the fluids in a locked room. The pharmacist used an opaque black bag to obscure the fluids. The subjects then received 30 mL/kg rounded to the nearest 100 mL of the solution to which they were randomized.

An investigator placed an 18-gauge IV in 1 upper extremity, and an initial serum lactate and electrolyte panel were drawn, measured using the i-STAT 1 analyzer (Abbott Point of Care, Princeton, NJ). Fluids were administered as a rapid bolus via pressure bag. Posttreatment blood was drawn from the contralateral upper extremity 5 min after the conclusion of the IV fluid administration.

Outcomes

The primary outcome was the difference in change in serum lactate levels between the LR and NS groups. Secondarily, we compared the change in lactate within each group (before and after treatment), and we

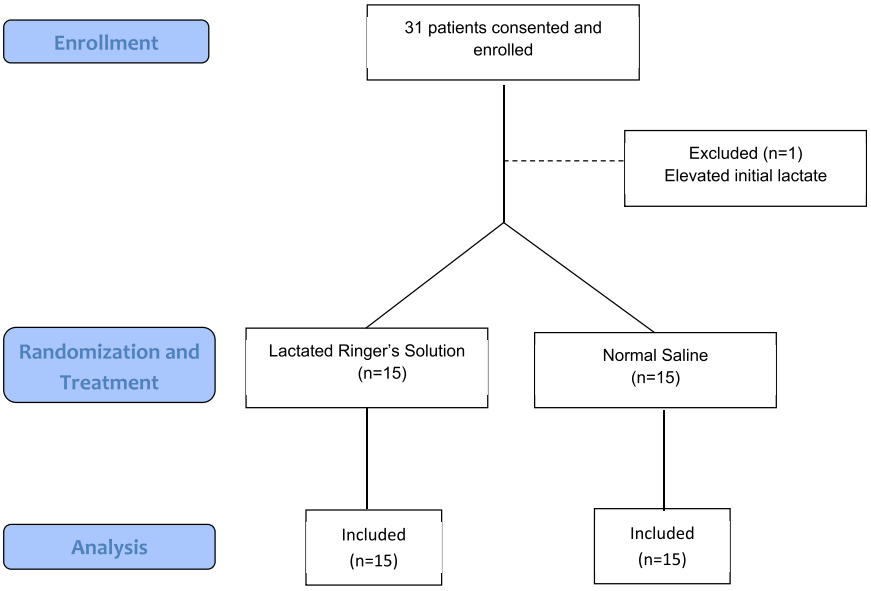

Figure 1. CONSORT diagram demonstrating the flow of subjects.