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Acid-Base and Electrolyte Teaching Case

Intravenous Solutions in the Care of Patients With Volume Depletion and Electrolyte Abnormalities

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Infusion fluids are often given to restore blood pressure (volume resuscitation), but may also be administered to replace ongoing losses, match insensible losses, correct electrolyte or acid-base disorders, or provide glucose. The development of new infusion fluids has provided clinicians with a wide range of products. Although the choice for a certain infusion fluid is often driven more by habit than by careful consideration, we believe it is useful to approach infusion fluids as drugs and consider their pharmacokinetic and pharmacodynamic characteristics. This approach not only explains why infusion fluids may cause electrolyte and acid-base disturbances, but also why they may compromise kidney function or coagulation. In this teaching case, we present a 19-year-old patient in whom severe hypernatremia developed as a result of normal saline solution infusion and explore the pharmacokinetic and pharmacodynamic effects of frequently used infusion fluids. We review clinical evidence to guide the selection of the optimal infusion fluid.
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INDEX WORDS: Chloride; crystalloids; normal saline; hypernatremia; hyponatremia; acute kidney injury (AKI); volume resuscitation; infusion fluid; intravenous solution; solute diuresis.

Note from Feature Editor Jeffrey A. Kraut, MD: This article is part of a series of invited case discussions highlighting the diagnosis and treatment of acid-base and electrolyte disorders. Advisory Board member Nicolaos E. Madias, MD, served as the Consulting Editor for this case.

INTRODUCTION

Volume resuscitation has become the therapeutic mainstay for critically ill patients after its humble and tentative beginnings in an era when cholera caused fluid losses of epidemic proportions.[1] Besides volume resuscitation, infusion fluids may be administered to replace ongoing losses, match insensible losses, correct electrolyte or acid-base disorders, or provide glucose.[2] Despite an increase in the options for infusion fluids to choose from in recent decades, choices are often driven by habit and are not always based on physiologic principles. This teaching case highlights frequently overlooked side effects of infusion therapy and provides guidance in rationally selecting the optimal type of infusion fluid. We argue that balanced salt solutions should be considered the primary infusion fluid for volume resuscitation, whereas other fluids should be reserved for indications for which their specific effects are required.

CASE REPORT

Clinical History and Initial Laboratory Data

A 19-year-old woman was evaluated for progressive hypernatremia 6 days after admission to the neurosurgical ward. The patient had a history of cerebral palsy, epilepsy, and intellectual disability. After hemorrhagic hydrocephalus, a ventriculo-atrial drain was placed. Unfortunately, this drain became infected, resulting in recurring Gram-positive bacteremia, and she was referred for a surgical drain exchange. On admission, she was receiving vancomycin, acetaminophen, and valproic acid. During the following week, her serum sodium level increased from 139 to 165 mEq/L, while serum creatinine level increased from 1.19 mg/dL (estimated glomerular filtration rate [eGFR], 66 mL/min/1.73 m^2 as calculated by the CKD-EPI [Chronic Kidney Disease Epidemiology Collaboration] equation[3]) to 1.32 mg/dL (eGFR, 59 mL/min/1.73 m^2; Table 1). Serum creatinine level prior to admission was 0.43 mg/dL (eGFR, 148 mL/min/1.73 m^2).

On physical examination, the patient had a short stature (3.9 feet) and low body weight (79 lb) and appeared ill and agitated. Her vital signs were unchanged from those at admission (blood pressure, 132/83 mm Hg; heart rate, 109 beats/min; no fever; Glasgow Coma Scale, E4M5V2), except for Kussmaul breathing. Since admission, she had received 0.9% sodium chloride solution (1 L/d) as "maintenance fluid." Nasogastric tube feeding had been discontinued 1 day earlier because of vomiting. She did not have diarrhea. Urine output was not recorded. Laboratory data revealed hypernatremia, reduced GFR, high anion gap metabolic acidosis, and supratherapeutic vancomycin levels (Table 1). She had relatively low urine osmolality that did not increase after a trial of 1 μg of intravenous desmopressin.

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Table 1. Laboratory Data

Parameter	Value (reference range)
Serum chemistry	
Sodium (mEq/L)	165 (135-145)
Potassium (mEq/L)	3.6 (3.5-5.0)
Chloride (mEq/L)	129 (97-107)
Bicarbonate (mEq/L)	5.7 (21-27)
Glucose (mg/dL)	108 (55-135)
Osmolality (mOsm/kg)	339 (275-300)
Creatinine (mg/dL)	1.32 (0.6-1.0)
eGFR (mL/min/1.73 m^2)[a]	59
Anion gap (mEq/L)	30.3 (10-14)
Lactate (mg/dL)	12.6 (<15.3)
Trough vancomycin concentration (mg/L)	45.2 (15-20)
Urine chemistry	
Creatinine (mg/dL)	12.4
Sodium (mEq/L)	133
Chloride (mEq/L)	117
Potassium (mEq/L)	6
Urea (mg/dL)	98
Glucose	Undetectable
Ketones	Undetectable
Osmolality (mOsm/kg)	314
Urine volume (mL/24 h)	2,700

Note: Conversion factors for units: serum creatinine in mg/dL to μmol/L, ×88.4; lactate in mg/dL to mmol/L, ×0.111; glucose in mg/dL to mmol/L, ×0.05551; urea in mg/dL to mmol/L, ×0.357.

Abbreviation: eGFR, estimated glomerular filtration rate.

[a]eGFR calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.

Additional Investigations

Although it was not possible to calculate tonicity balance, a closer look at the patient's urine revealed relatively high solute excretion with respect to her body weight (urine osmolality × volume = 314 mOsm/kg × 2.7 L/d = 847.8 mOsm/d), which mostly comprised sodium and chloride ([133 mEq/L + 117 mEq/L] × 2.7 L/d = 675 mEq/d). Electrolyte-free water clearance was 425 mL/d (volume × [1 − (urine sodium + urine potassium)/serum sodium]) = 2.7 L/d × (1 − (133 mEq/L + 6 mEq/L)/165 mEq/L), explaining the progressive hypernatremia.

Diagnosis

Hypernatremia due to normal saline solution infusion in a patient with solute diuresis and acute kidney injury.

Clinical Follow-up

Normal saline solution infusion in combination with severe kidney injury was central to the various electrolyte and acid-base disorders in the patient. The degree of GFR loss had been underappreciated because of her low muscle mass, which is not taken into account in the CKD-EPI equation. Kidney injury was likely caused by vancomycin toxicity resulting in the urinary concentrating defect (hypernatremia failing to cause a maximal urine osmolality; Table 1). Because she had a solute (mostly electrolyte) diuresis and not a water diuresis, hypernatremia must have been caused by the infusion of isotonic saline solution in combination with her inability to access water. The relatively high electrolyte excretion is consistent with a sodium-overloaded state. The combination of antibiotics, antiepileptic drugs, and acetaminophen suggests that the high anion gap metabolic acidosis was due to accumulation of 5-oxoproline (pyroglutamic acid),[4] although this was not measured. Kidney failure likely contributed to the metabolic acidosis. This is apparent from the positive urine anion gap (urine sodium + urine potassium − urine chloride = 133 mEq/L + 6 mEq/L − 117 mEq/L = 22 mEq/L) and the small urine osmolal gap (urine osmolality − [2 × [urine sodium + urine potassium] + urea/2.8] = 314 mOsm/kg − [2 × [133 mEq/L + 6 mEq/L] + 98 mg/dL/2.8] = 1 mOsm), which indicates low urinary ammonium excretion.

The aims of fluid therapy in this case would be to gradually correct hypernatremia, not to aggravate acidosis and kidney failure, and to prevent fluid overload. Accordingly, water administration (as intravenous dextrose because the enteral route was not available) and withdrawal of all drugs and other fluids were advised. We also recommended against actively correcting metabolic acidosis before potassium had been supplemented to prevent severe hypokalemia during correction of acidosis. However, because of the patient's neurologic condition and frequent hospitalizations, her parents and neurosurgeons decided to refrain from further treatment. The patient died 3 days later.

DISCUSSION

With the range of choices for types of intravenous fluids, it is important to approach intravenous fluids as drugs with consideration for both their dynamic and kinetic aspects.[5] Unfortunately, the most commonly used infusion fluids have not been subjected to the rigorous kinetic and dynamic profiling that is now required for drug registration.

Apart from volume, 3 aspects define an infusion fluid: its oncotic properties, its ionic composition, and thereby its osmotic characteristics. The gradient in hydrostatic force across the capillary wall is countered by differences in colloid osmotic pressures. Although the capillary wall is permeable to small solutes, movement of proteins and other anionic macromolecules is restricted. This means that these molecules contribute to the generation of osmotic pressure: the colloid osmotic pressure (or, in case of proteins, oncotic pressure). The endothelial glycocalyx layer, a dense network of proteoglycans in association with assorted negatively charged glycosaminoglycans, appears to be the main barrier to protein filtration. Because the subglycocalyx space is virtually free of protein, water movement across the vascular wall is mainly restricted by the colloid osmotic pressure gradient across the endothelial glycocalyx layer, with smaller contributions from the endothelial basement membrane and extracellular matrix.[6] It follows that if this barrier is degraded, as may occur during inflammation[7-9] or hypervolemia,[10] permeability of the endothelial glycocalyx layer to polyanionic macromolecules is impaired, allowing water to move into the interstitium. Because concentrations of specific ions directly affect a wide range of biological processes, it seems intuitive to choose a fluid with a composition that closely resembles the ionic makeup of the aqueous fraction of blood plasma and is able to sustain a plasma pH of 7.35 to 7.45. Acidemia is