Medication Diluent Impact on Cumulative Chloride Load in Critically Ill Septic Patients

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BACKGROUND

Chloride is the most abundant anion in extracellular fluid and there has been an increase in the use of chloride-rich solutions such as 0.9% Sodium Chloride leading to increased adverse events.[1] Medication diluents account for a significant portion of unintended chloride and total volume administered to intensive care unit (ICU) patients.[1,2] Increasing chloride burden can lead to hyperchloremia, electrolyte disturbances, acute kidney injury (AKI), metabolic acidosis, and the need for renal replacement therapy (RRT).[1,2] A single center, prospective study was conducted in intensive care patients comparing the use of 0.9% Sodium Chloride with Dextrose 5%, which found an increase in the incidence of hyperchloremia and acute kidney injury in the 0.9% Sodium Chloride group.[2] Despite the known risks associated with increased 0.9% Sodium Chloride use and elevated chloride loads, there is a lack of robust clinical literature demonstrating the fluid burden and adverse events related to medication diluents.

PURPOSE

The purpose of this study is to quantify the total diluent chloride and non-diluent chloride loads for septic patients in the intensive care unit.

METHODS

This is a single center, retrospective chart review of adult patients with a primary diagnosis of sepsis admitted to the ICU from May 1, 2019 to June 30, 2019. This study was approved by the Institutional Review Board (IRB).

Inclusion Criteria: Patients ≥ 18 years old with a primary diagnosis of sepsis admitted to the ICU were evaluated

Exclusion Criteria: Pregnant, breastfeeding, and/or did not receive intravenous fluids or medications in the ICU

Patient demographics, electrolytes, serum creatinine, fluid type and quantity were obtained from the electronic medical record

Evaluated quantity of chloride loads, incidence of hyperchloremia, AKI, and RRT

Statistical Analysis: Descriptive statistics, Mann-Whitney U, and Spearman's Rho Correlation were performed

Definitions

Diluent chloride	• Chloride from continuous and intermittent medications
Non-diluent chloride	• Chloride from maintenance and resuscitation fluids
AKI	• Increase in serum creatinine (Scr) of ≥ 0.3 mg/dL within 48 hours • Scr ≥ 1.5 times baseline within the prior 7 days • Urine volume < 0.5 mL/kg/h for 6 hours[3]
Hyperchloremia	• Chloride ≥ 110 mEq/L
RRT	• Identified through dialysis orders or review of physician notes

OUTCOMES

The primary objective is to quantify the total diluent and non-diluent chloride loads that patients received during their ICU stay. Secondary outcomes include hospital and ICU length of stay (LOS), correlation of chloride loads with the incidence of hyperchloremia, AKI, and/or need for RRT.

RESULTS

Table 1: Baseline Characteristics

Baseline Characteristic	Result (N = 41)
Age in years, mean ± STD	66.5 ± 14.7
Female, no. (%)	22 (53.7%)
ICU LOS in days, mean ± STD	4.6 ± 3.4
Hospital LOS in days, mean ± STD	10.8 ± 9.9
Medical Intensive Care, patients (%)	27 (65.9%)
Surgical Intensive Care, patients (%)	13 (31.7%)
Cardiac Intensive Care, patients (%)	1 (2.4%)
Hyperchloremia, patients (%)	22 (53.7%)
Acute Kidney Injury (AKI), patients (%)	24 (58.5%)
Need for Renal Replacement Therapy (RRT), patients (%)	7 (17.1%)

Table 2: Spearman's Rho Correlation for hyperchloremia, AKI and RRT

	Diluent Chloride Load Correlation Coefficient	Non-Diluent Chloride Load Correlation Coefficient
Hyperchloremia	ρ = 0.238	ρ = 0.488
AKI	ρ = 0.25	ρ = 0.218
Need for RRT	ρ = 0.167	ρ = 0.230

Table 3: Chloride load and development of hyperchloremia

	Hyperchlorermia (N = 22)	No Hyperchloremia (N = 19)	P-value
Diluent Chloride Load (mEq/L), median (IQR)	218.4 (110.3-639.3)	135.9 (38.0-266.4)	0.133
Non-Diluent Chloride Load (mEq/L), median (IQR)	1265.3 (939.4-2000.3)	462.0 (314.3-1155.8)	0.002
Total Chloride Load (mEq/L), median (IQR)	1483.7 (1272.1-2485.9)	597.9 (484.9-1439.9)	0.0159

RESULTS

Table 4: Chloride load and development of AKI

	AKI (N = 24)	No AKI (N = 17)	P-value
Diluent Chloride Load (mEq/L), median (IQR)	164.6 (74.7-552.3)	189.9 (52.7-277.1)	0.874
Non-Diluent Chloride Load (mEq/L), median (IQR)	1141.9 (803.7-1472.5)	700.7 (365.2-1374.8)	0.169
Total Chloride Load (mEq/L), median (IQR)	1306.2 (957.6-2203.3)	890.6 (484.7-2196.8)	0.384

Table 5: Chloride load and need for RRT

	RRT (N = 7)	No RRT (N = 34)	P-value
Diluent Chloride Load (mEq/L), median (IQR)	541.6 (154.0-681.3)	157.2 (55.1-320.7)	0.298
Non-Diluent Chloride Load (mEq/L), median (IQR)	440.4 (298.0-1174.4)	1141.9 (685.8-1460.9)	0.154
Total Chloride Load (mEq/L), median (IQR)	982.0 (657.3-2326.0)	1299.1 (807.9-2118.3)	0.944

CONCLUSION

Diluent chloride load accounted for a smaller proportion of total chloride and volume compared to other studies. Non-diluent chloride was moderately correlated with the development of hyperchloremia. Diluent chloride load was similar among patients who developed hyperchloremia, acute kidney injury and/or the need for renal replacement therapy compared to those who did not. Larger, prospective studies investigating the impact of medication diluents and alternatives on chloride load are required. Limitations of this study include sample size, retrospective review, and that total chloride loads were dependent on appropriate nurse documentation. Future direction includes the development and implementation of a fluid guideline or protocol to limit or reduce the total chloride load in critically ill patients.

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