Title:

Efficacy and Safety of Citrate Anticoagulation in CRRT for Patients with Liver Failure/DysfuncTION, the CAUTION trial! A retrospective study on etiology of liver failure and their complications.

Background

Continuous renal replacement therapy (CRRT) is a crucial intervention for managing acute kidney injury (AKI) in critically ill patients. Citrate anticoagulation has become a preferred method in CRRT due to its effect in longer filter longevity and less bleeding compared to unfractionated heparin[1]. However, its use in specific patient populations, such as those with liver failure or severe shock, necessitates careful evaluation.

Citrate acts as an anticoagulant by chelating calcium, an essential cofactor in the coagulation cascade, thus preventing clot formation within the extracorporeal circuit[2]. The citrate-calcium complex is then metabolized mainly in the liver, where citrate is converted into bicarbonate, and calcium is released back into the bloodstream. This mechanism provides dual benefits: effective anticoagulation and metabolic alkalization.

Patients with liver failure present unique challenges for citrate anticoagulation. Impaired liver function can lead to the accumulation of citrate, resulting in high anion gap metabolic acidosis and hypocalcemia[3]. These risks underscore the need for vigilant monitoring and potential adjustment of citrate dosing in this population. The aim of the present study is to explore whether the etiology of liver failure, which can range from alcoholic liver disease to drug-induced liver injury or shock liver, influences the incidence and severity of citrate-related complications.

Methods

Study design

A retrospective cohort study will be conducted to compare the efficacy and safety of citrate anticoagulation in CRRT among patients with liver failure/dysfunction and severe shock.

Objectives

1. **Primary Objective**: To determine if the etiology of liver failure impacts the incidence of citrate-related complications in patients undergoing CRRT.
2. **Secondary Objectives**: To compare the efficacy of citrate anticoagulation in terms of renal recovery, filter lifespan, and patient survival between those with liver failure/dysfunction and severe shock.

Participants

- **Inclusion Criteria:**
    - Critically ill patients diagnosed with AKI requiring CRRT.

- Documented liver failure or significant liver dysfunction (e.g., elevated liver enzymes, bilirubin levels, or clinical diagnosis of liver failure) and clincal diagnosis of shock (NE of 0.25 µg/kg/min and or association of second vasopressor).
- Age ≥ 18 years.

Data Collection and Analysis

- Data will be collected retrospectively from medical records and CRRT logs.
- Statistical analysis will include descriptive statistics for baseline characteristics and outcomes.
- Comparisons will be made between patients with liver failure/dysfunction of various etiology using appropriate statistical tests (e.g., chi-square test, t-test, Kaplan-Meier analysis for filter lifespan).
- **Baseline Assessment:**
  - Collection of demographic data, medical history, and liver function tests (LFTs).
  - Baseline renal function tests and relevant clinical parameters.
- **Safety Assessment:**
  - **Primary Safety Endpoint:** Incidence of citrate-related metabolic complications (e.g., citrate accumulation).
  - **Secondary Safety Endpoints:**
    - Incidence of electrolyte imbalances (e.g., hypocalcemia).
    - Incidence of adverse events related to anticoagulation.
- **Efficacy Assessment:**
  - **Primary Efficacy Endpoint:** Filter lifespan (time until filter clotting).
  - **Secondary Efficacy Endpoints:**
    - Renal function recovery markers (e.g., free from renal replacement therapy).
    - Mortality

References

1. Jacobs R, Verbrugghe W, Dams K, Roelant E, Couttenye MM, Devroey D, Jorens P. Regional Citrate Anticoagulation in Continuous Renal Replacement Therapy: Is Metabolic Fear the Enemy of Logic? A Systematic Review and Meta-Analysis of Randomised Controlled Trials. Life (Basel). 2023 May 17;13(5):1198.
2. Mehta RL, McDonald BR, Aguilar MM, Ward DM. Regional citrate anticoagulation for continuous arteriovenous hemodialysis in critically ill patients. Kidney Int. 1990 Nov;38(5):976-81.
3. Kramer L, Bauer E, Joukhadar C, Strobl W, Gendo A, Madl C, Gangl A. Citrate pharmacokinetics and metabolism in cirrhotic and noncirrhotic critically ill patients. Crit Care Med. 2003 Oct;31(10):2450-5.