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Continuous renal placement therapy and potential impact on serum lipase and amylase concentrations

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Keypoints

1. Continuous renal replacement therapy (CRRT) has been used to manage patients with severe pancreatitis and acute renal failure to decrease cytokines and inflammatory molecules, remove excess fluid, and correct electrolyte imbalances.
2. The clearance by CRRT of a solute or serum marker such as amylase or lipase is determined by the effluent (dialysate) flow rate and solute concentration in the dialysate. The latter is determined by the concentration in the blood and sieving coefficient (S) of the solute. A solute with an S of 1 can pass freely through a filter. The amount of solute that diffuses through the membrane (S) is dependent on the solute molecular size and protein binding as well as the characteristic of the CRRT circuit (membrane thickness, surface area, and pore size).
3. With an S that approached 1 for both amylase and lipase (serum concentration equal to the CRRT effluent concentration) combined with high effluent flow rates, a significant amount of amylase and lipase may be cleared thereby impacting the serum concentration and its diagnostic accuracy.

Abstract

Continuous renal replacement therapy (CRRT) has been used to manage patients with severe pancreatitis and acute renal failure, as well as for those without renal failure, to remove cytokines and other inflammatory molecules. It is also commonly used in patients with septic shock and acute renal failure to remove excess fluid and correct electrolyte imbalances. We present a young adult who received CRRT as part of this therapy during care for a critical illness in the Pediatric ICU. During his stay, pancreatitis was diagnosed based on clinical findings and confirmed by plasma values of amylase and lipase. The concentration of amylase and lipase in the ultrafiltrate from CRRT was relatively equal to those noted in the serum. We hypothesize that high CRRT clearance of these laboratory parameters may impact their diagnostic utility in pancreatitis. Previous reports of CRRT clearance of other diagnostic laboratory values is presented and the impact of this therapy on the diagnostic values of these values is discussed.

Keywords

lipase, pancreatitis, continuous renal replacement therapy

Introduction

On an annual basis, acute pancreatitis (AP) accounts for approximately 6.5 hospital admissions per 100,000 children in the United States [1]. Its severity ranges from mild to severe, with mild cases comprising 90% of cases. Mild cases are characterized by the absence of organ failure, local or systemic complications. Moderate cases involve transient organ failure and systemic complications, while severe cases are marked by persistent organ failure lasting more than 48 hours [1,2]. The diagnosis of AP requires meeting at least two of the following three criteria: characteristic acute abdominal pain in the epigastrium, often radiating to the back; amylase or lipase levels more than three times the normal upper limit; and characteristic imaging findings on ultrasound, contrast-enhanced CT, or MRI [3]. AP can result from both primary and secondary causes. Primary causes include biliary pancreatitis due to gallstones, alcohol-induced pancreatitis, hypertriglyceridemia, hypercalcemia, medication-induced pancreatitis, non-gallstone pancreatic duct obstruction, infections, autoimmune disorders, trauma, and post-endoscopic retrograde cholangiopancreatography (ERCP). Secondary causes are typically associated with systemic diseases, such as sepsis, shock, hypoperfusion states, systemic lupus erythematosus, and vasculitis [4,5]. We present a young adult who received CRRT as part of this therapy during care for a critical illness in the Pediatric ICU. During his stay, pancreatitis was diagnosed based on clinical findings and confirmed by plasma values of amylase and lipase. We noted that the concentration of amylase and lipase in the ultrafiltrate from CRRT was relatively equal to those noted in the serum. We postulate that high CRRT clearance of these laboratory parameters may impact their diagnostic utility in pancreatitis.

Case report

Review of this case and presentation in this format followed by guidelines of the IRB of Nationwide Children's Hospital. A 21-year-old male with Pallister syndrome, short bowel syndrome (50% distal small bowel and right colon remaining after a volvulus three years ago), and multiple comorbidities who presented with facial and extremity edema and fever. His history included dependence on gastro-jejunal (GJ) feeds, hypertension, minimal change nephrotic syndrome on chronic steroids, Nissen fundoplication for severe GERD, chronic urinary tract infections, intractable epilepsy, and severe developmental delay. During a telehealth visit with nephrology for worsening edema and fever (up to 101°F), "gurgling" breathing sounds with increased work of breathing were noted, prompting a call to EMS. He was transferred to the ED, where he appeared ill, with tachycardia, respiratory distress, and delayed capillary refill. He was hypotensive, hypoxemic, and febrile (101.1°F, RR 18). In the ED, he was placed on a 100% oxygen non-rebreather mask. Intraosseous access was established, and he received fluid resuscitation with normal saline, stress-dose hydrocortisone, a rescue dose of epinephrine, and an epinephrine infusion. Endotracheal intubation was performed due to poor oxygenation. Broad-spectrum antibiotics (vancomycin, piperacillin-tazobactam, and amikacin) were initiated for septic shock. Initial pertinent labs showed potassium 2.9 mmol/L (3.5–5), carbon dioxide 41 mmol/L (22–26), BUN 67 mg/dL (5–18), creatinine 0.78 mg/dL (0.5–1.2), glucose 709 mg/dL, albumin 1.7 g/dL (3.4–5.2), ALT 38 U/L (<40), AST 28 U/L (15–50), lactate 5.6 mmol/L (0.5–2.2), lipase 687 U/L (<202), and urine protein 100 mg/dL. WBC was 2.9 × 10^3/μL (4.5–11), hemoglobin 4.2 g/dL (13.5–17.5), platelet count 343 × 10^3/μL (150–450), PT 16.6 seconds (12.4–14.7), APTT 23 seconds (24–36). Chest radiograph revealed bilateral pleural effusions, bowel distention, low lung volumes, and left lower lobe opacification. The patient was admitted to the PICU, epinephrine was administered by continuous infusion to support blood pressure, and packed red blood cells were transfused to treat anemia. On hospital day 1, persistent abdominal distention and imaging showing dilated bowel loops prompted a diagnostic laparoscopy, which revealed clear ascites and small bowel adhesions without

perforation. Ascitic fluid was sent for culture. During hospital day 2, the epinephrine infusion was continued, and fluconazole was added due to presumed immunosuppression in the context of nephrotic syndrome. Lipase increased to 1,542 U/L. Due to concerns for sepsis-induced pancreatitis, an abdominal ultrasound was ordered for further stratification and evaluation. The ultrasound revealed bilateral pleural effusions and moderate ascites, though the pancreas was not visualized. On hospital day 3, given that the abdominal ultrasound was inconclusive and there was concern that third-spacing and multiorgan dysfunction could be secondary to pancreatitis, a CT angiography was performed for further assessment and staging. The imaging showed normal pancreatic enhancement, pneumoperitoneum likely from the laparoscopy, bowel wall thinning, and no evidence of perforation. An echocardiogram was also performed as part of the workup for fluid overload and revealed moderate right ventricular dysfunction. On hospital day 4, due to persistent fluid overload, diuretic therapy was advanced to continuous furosemide and chlorothiazide infusion. On hospital days 5 and 6, hypotension and poor urine output continued, necessitating the placement of a central dialysis catheter and initiation of CRRT. Given concerns that lipase levels may be cleared by the CRRT circuit, a sample from the circuit ultrafiltrate was sent, revealing a lipase level of 237 U/L (serum 245 U/L) and amylase of 112 U/L (148 U/L). During hospital days 7-10, CRRT was continued, and the patient tolerated a net negative fluid balance of -100 mL/h a few hours after initiation, with approximately 8 liters removed. Stress-dose hydrocortisone was weaned and discontinued. The patient's patient trachea was extubated, antibiotics were completed, CRRT was stopped, and the patient was subsequently transferred to the inpatient ward. The remainder of his hospital course was uneventful.

Discussion

The use of continuous renal replacement therapy (CRRT) has been proposed for managing patients with severe pancreatitis with or without acute renal failure to remove cytokines and other inflammatory molecules [6,7]. CRRT is also commonly used to remove excess fluid and correct electrolyte imbalances [8]. In addition to clearing fluid and other potentially harmful mediators, therapeutic agents and laboratory markers may also be cleared. As noted in our patient, the concentrations of amylase and lipase from the CRRT ultrafiltrate (effluent) paralleled those in the serum. As such, with high flow rates of fluid/dialysate from CRRT, it is feasible that serum concentrations of these markers may decrease significantly.

Several factors influence the clearance of different molecules during CRRT. Highly protein-bound drugs and solutes are less likely to be removed, as only the unbound fraction is available for filtration. Molecular size also plays a role, larger molecules have more difficulty passing through the dialysis membrane, resulting in lower clearance compared to smaller ones [9]. Additionally, drugs with a large volume of distribution are widely dispersed into tissues, reducing their concentration in the plasma and making them less available for removal by CRRT [10].

The general clearance (K) equation quantitatively measures how efficiently CRRT removes solutes from the blood based on the effluent flow rate and solute concentration gradient between the effluent and the blood [11]. This can be represented by QE x CE/CB. K is the clearance or the rate at which solutes are removed from the blood by the CRRT process, measured in milliliters per minute. QE is the effluent flow rate from the CRRT filter, which is the rate at which the dialyzed or filtrate fluid flows during CRRT (milliliters per minute). QE can be adjusted by the dialysate flow rate through the filter. CE is the concentration of the solute in the effluent while CB is the concentration of the solute (mg/dL) in the patient's blood after passing through the CRRT circuit. CE and CB are measured in concentration units (milligrams

per deciliter). CE/CB is also referred to as the sieving coefficient (S). A solute with an S of 1 can pass freely through a filter. If S is 0, the solute cannot pass through the filter. The amount of solute that diffuses through the membrane and hence its S is dependent on the solute molecular size and protein binding as well as the characteristic of the CRRT circuit (membrane thickness, surface area, and pore size). In this case, the S approached 1 for both amylase and lipase. As approximately 8 liters of ultrafiltrate were removed from the patient, which likely reduced the concentration of amylase and lipase in the serum, potentially complicating the diagnosis.

The biomarkers lipase and amylase may increase without being related to pancreatic injury in patients with renal dysfunction due to impaired clearance [12]. However, no previous reports have evaluated the clearance of diagnostic biomarkers in patients undergoing CRRT. Given that lipase and amylase have a molecular weight of 45,000 Da, a low volume of distribution, and low protein binding capacity, they can be expected to be readily filtered by CRRT [13,14]. In our case, we confirmed the presence of lipase and amylase in the ultrafiltrate, in concentrations that paralleled those in the serum. As such, based on the flow rate of CRRT, enough lipase and amylase may be filtered thereby decreasing or even normalizing their values, potentially masking the diagnosis of pancreatitis.

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