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CLINICAL VIGNETTE

Personalized Treatment of Hypertriglyceridemia Induced Pancreatitis in a Patient with End Stage Renal Disease (ESRD)

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Introduction

Severe hypertriglyceridemia is a well-known cause of acute pancreatitis. Standard treatment usually involves intravenous (IV) fluids and insulin infusion and plasmapheresis is reserved for cases with worrisome features. We present a patient with end stage renal disease on hemodialysis with hypertriglyceridemia-induced acute pancreatitis and the complexities related to management.

Case Report

A 59-year-old male presented to the Emergency Department with chronic epigastric abdominal pain, nausea, and vomiting which had worsened over the past few months. He has End Stage Renal Disease (ESRD) on hemodialysis for the past 8 months. He also has Type 2 Diabetes on insulin and chronic pancreatitis. One week prior to admission, the patient reported dietary changes, and consuming a higher quantity of processed foods and higher fat meals. He denied any alcohol use. He had multiple prior admissions for acute on chronic pancreatitis. No chronic medications were associated with hypertriglyceridemia or pancreatitis.

Vital signs on presentation were temperature 96.8F, blood pressure 135/86 mm Hg, pulse 73/min, and respiratory rate 15/min, saturating at 94% on room air. On exam, patient was alert, oriented, in mild distress. Abdomen was diffusely tender in all four quadrants. He had no cutaneous xanthomas or lipemia retinalis. Labs included lipase 228 U/L (13-69 U/L), amylase 135 U/L (31-124 U/L), lactate dehydrogenase 352 (125-256 U/L), triglycerides 2,127 mg/dL, and calcium 7.6 mg/dL. Serum glucose was 132 mg/dL and Hemoglobin A1c was 6.5%. Hepatic function panel was normal.

He received 500 mL of normal saline and IV hydromorphone for pain in the emergency department. Due to risk of hypervolemia, the patient was treated with plasmapheresis instead of IV insulin drip with dextrose fluids. A very low fat and low carbohydrates diet was ordered. After his first plasmapheresis session, triglycerides decreased to 568 mg/dL. Triglycerides decreased to 345 mg/dL after a second plasmapheresis. His abdominal pain resolved and he was discharged after 5 days. Icosapent ethyl 2g twice daily with meals was added.

Discussion

Hypertriglyceridemia induced acute pancreatitis (HTGAP) is a rare complication of hypertriglyceridemia and is important to treat effectively to reduce complications including necrotizing pancreatitis, organ failure, death.[1,2] Personalized treatment is needed for patients with underlying kidney disease and hypertriglyceridemia (HTG) as they will encounter barriers with traditional treatments for HTG. Patients with HTG and ESRD have increased risk of polypharmacy and a higher risk of medication side effects.[3] To optimize health outcomes in patients with HTGAP and chronic kidney disease (CKD), it is important to understand HTG in CKD, risks of developing pancreatitis, and available treatments.

The prevalence of dyslipidemia in CKD is higher than in the general population, reported in 45-50% of hemodialysis patients.[4] The characteristic lipid pattern in patients with CKD stage 3 or higher consists of hypertriglyceridemia, low levels of HDL cholesterol and variable levels of LDL cholesterol and total cholesterol.[5] HTG levels tend to be moderately elevated with 46% reported with triglyceride levels greater than 200 mg/dL.[4,6] Severe HTG typically occurs in patients with underlying primary dyslipidemia and secondary conditions such as renal disease, excess alcohol intake, obesity, poorly controlled diabetes, and the use of certain medications.[2,6]

The association of HTG leading to acute pancreatitis (AP) may not be recognized given rarity of cases. Marked elevation of TG level appears to be causally linked to AP and is found in 12% to 38% of patients presenting with AP.[7] Very Severe HTG (>2000 mg/dL) levels are associated with lipemic serum and increased risk of pancreatitis, described as chylomicronemia syndrome. In patients with severe (>1000 mg/dL) or very severe TG levels, the LpL removal system is saturated and leading to reduced catabolism of dietary triglyceride incorporated into chylomicrons. There is concern that even triglyceride levels above 1000 mg/dl can rapidly increase after a fat rich meal leading to risk of pancreatitis.[6] Havel et al further proposed that HTG causes pancreatitis due to capillary plugging leading to ischemia and acidosis.[8] In the acidic environment, free fatty acids cause activation of trypsinogen and initiate AP. Interestingly, pancreatitis itself can cause HTG leading to an endless cycle of pancreatitis and HTG.[6]

The initial management of HTGAP is focused on the treatment of AP and reducing triglyceride levels in hope of preventing pancreatitis related complications. Standard management of AP is supportive care including pancreatic rest, pain control, and fluid resuscitation.[9] In HTGAP, reducing triglyceride levels below 500 mg/dl may expedite clinical improvement. A subset of patients with HTGAP are treated with insulin infusions as first line given efficacy and safety profile. However, in select patients, plasmapheresis may be used as adjuvant therapy.[1,9] Reported side effects associated with plasmapheresis include hypotension, arrhythmias, sensations of cold associated with paresthesias, temporarily elevated temperatures, and shock. Additional caution is needed in older adults as may come with the risk of additional risk of numerous adverse effects including clotting, access difficulty, and allergic reactions.[9] Thus, plasmapheresis is typically reserved for sicker patients unresponsive to conservative management due to its noninferiority and safety profile compared to insulin therapy. Our patient was unique in that he was unable to receive insulin drip therapy due to volume overload and improved triglyceride levels with only plasmapheresis treatment.

For long term treatment of hypertriglyceridemia in adults with CKD, the Kidney Disease Improving Global Outcome (KDIGO) guidelines recommend therapeutic lifestyle changes for adults with hypertriglyceridemia (>500 mg/dL) and CKD including those treated with chronic dialysis or kidney transplantation. Dietary changes that may reduce serum TGs include low-fat diet (<15% total calories), reduction of monosaccharide and disaccharide intake, reduction of the total dietary carbohydrates, and use of fish oils to replace some long-chain TGs. Other therapeutic lifestyle changes include weight reduction, increased physical activity, reduction in alcohol intake, and treatment of diabetes if present.[3]

For adults with severe and very severe HTG (>1000 mg/dL), the Endocrine Society clinical practice guidelines recommend combining drug treatment and reduction of dietary fat and simple carb intake to reduce the risk of pancreatitis. The Endocrine Society recommends that a fibrate be used as a first-line agent for reduction of triglycerides in patients at risk for triglyceride-induced pancreatitis.[6] Pharmacologic treatment is more complex in the subset of patients with HTG and CKD due to lack of reliable information. There are no published randomized trials that targeted patients with HTG and CKD and too few participants with CKD were included in previous trials. Fibric acid derivatives can be considered to prevent pancreatitis from severe HTG (>1000 mg/dL) although the safety and efficacy is extremely weak especially in patients with CKD. If fibric acid derivatives are prescribed, they must be dose-adjusted for kidney function. In the setting of ESRD, fibric acid derivatives are not FDA approved. Caution is needed prescribing fibric acid derivatives in the elderly. There is an association between new prescriptions for fibric acid derivatives and increased SCr levels, as well as a small increase in the risk of hospitalization and nephrologist consultation.[3]

For adults with moderate to severe triglyceride levels, standard treatment can include three drug classes (fibrates, niacin, n-3 fatty acids) alone or in combination with statins.[6] The use of both a fibric acid derivative and a statin is not recommended in patients with CKD due to the potential for toxicity.[3] Pharmacological doses (2–4g per day) of omega-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid) reduce triglyceride levels by up to 45% in a dose dependent manner in patients with CKD or ESRD.[5] The benefit of statins in patients with CKD and ESRD has been studied. In normal or mildly elevated TGs, statins appear to prevent pancreatitis.[10] Other agents such as Niacin and the cholesteryl ester transfer protein inhibitor anacetrapib are currently being investigated in clinical trials in the general population and await investigation in CKD patients.[3]

In conclusion, our case highlights the use of plasmapheresis in ESRD patients with severe HTGAP who may not tolerate insulin infusion with fluid resuscitation due to risk of hypervolemia. For long-term treatment of his severe hypertriglyceridemia, we encouraged the patient to optimize his diet along with other therapeutic lifestyle choices. Fish oil was started on discharge. Future plans include consideration for adding a statin if triglycerides remain above 1000 mg/dL. We did not start a fibric acid derivative as it is not FDA approved in setting of ESRD. Further research is needed to determine the best approach for acute treatment of HTGAP in patients who also have ESRD as well as the efficacy of treatment of severe HTG in patients with ESRD to reduce their risk of pancreatitis.

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