CLINICAL VIGNETTE

Hypertriglyceridemia Induced Pancreatitis – What Happens after Hospitalization

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Introduction

Hypertriglyceridemia (HTG) is a well-established but less common etiology of acute pancreatitis. While there is some uncertainty on the most effective strategy in acutely controlling triglyceride levels there is also a limited consensus on preventing recurrence while balancing the side effects.

Case Report

A 25-year-old obese, East Asian male with Type II Diabetes on insulin presented to the ER with intractable abdominal pain radiating to the flank. The patient had recently been drinking heavily the day prior to symptom onset, but normally rarely consumes alcohol. He also stopped using insulin for the past month. Physical exam was unremarkable, including normal bowl sounds, and abdominal tenderness and negative Murphy sign. Labs were remarkable for elevated Lipase 1256 u/L, Aspartate aminotransferase (AST) 44 u/L, Alanine aminotransferase (ALT) 71 u/L. Lipids included Triglyceride 3104 mg/dL, HDL 14, with "very lipemic" specimen. CT abdomen confirmed presence of acute pancreatitis and fatty liver. Urine analysis showed +2 ketones and elevated glucose, blood glucose was 329 mg/dL, however VBG was unremarkable, ruling out concurrent diabetic ketoacidosis. HgbA1c 10.1 mmol/ml. The patient was readmitted and restarted on insulin, as well as IV fluids. He was also given Fenofibrate 160 mg and Atorvastatin 80 mg. Symptoms improved without complications and labs one day later showed Lipase 162 u/L and Triglyceride 304 mg/dL. Patient continued on high-dose atorvastatin and fibrate until primary care follow-up one month later. At that time lipid panel showed improved Triglyceride and HDL, with LDL in normal limits. However, repeat LFTs showed elevated AST and ALT considered likely a possible consequence of statin and fibrate use.

Discussion

The relationship between elevated triglycerides and pancreatitis is well-known accounting for roughly 10% of cases. It only occurs when triglycerides levels are greater than 1,000 mg/dL.[1] The exact pathophysiology of this type of pancreatitis is unclear with two plausible mechanisms. Hydrolysis of triglycerides causing high concentration of free fatty acids that then damage acinar cells and microvascular membranes. Another mechanism posits elevated concentrations of chylomicrons could increase blood viscosity resulting in vascular obstruction in the pancreas thus causing ischemia and necrosis. However, why this obstructtion only occurs in the pancreas remains unclear.[2]

Acute management lacks standard guidelines with strategies varying greatly ranging from plasmapheresis to heparin infusion, although there is consensus on the importance of controlling triglyceride levels which is an independent prognostic indicator.[3] They also include triglyceride fibrates <500mg/dL after the first 24 hours.[4] Generally approaches bowel rest, fluid resuscitation, and pain control.

Once stabilized prevention of recurrence becomes important. The rate of recurrence is unclear with some studies citing rates as high as 44% and as low as 5%. Many of these studies are small with varying comorbidities[1,4] Prevention requires identification of inciting factors. Rarely is HTG the primary etiology with 5% due to genetic causes.[5] More often it is secondary to diabetes, obesity, pregnancy, excess carbohydrate intake, hypothyroidism, alcohol, hepatitis, sepsis, renal failure, and drugs like estrogen, glucocorticoids, thiazides, bile acid binding resins, tamoxifen, and isotretinoin. It has also be shown that young age and diabetes are independent risk factors specific to the development of HTG acute pancreatitis and not just elevated fatty acids alone.[6]

In our patient, the HTG was due to a multitude of factors including young age, poorly-controlled diabetes, recent alcohol intake, and obesity. Approaches to prevention must be multifaceted including lifestyle modifications to target weight loss, limiting fat and sugar intake as well as abstinence from alcohol. Control of diabetes and hyperlipidemia, should be prioritized and often require use of lipid lowering medications.[1] One study of 41,210 patients with severe hypertriglyceridemia, were started on lipid lowering medications with triglyceride goals of <500 mg/dL. The group able to remain <500 mg/dL had decreased risk of pancreatitis episodes, cardiovascular events, renal disease, and lower hospital costs over three years.[1]

In regards to medications, fibrates remain the mainstay of controlling HTG.[1] HMG-coA reductase inhibitors (i.e. statins) are generally used only in combination with fibrates as they have a weak triglyceride lowering effect and should be avoided as monotherapy. In severe cases of hypertriglyceridemia, combination therapy with fibrates and statins have been effective, but should be weighed with the increased risk of myopathy.[1] Myopathy is generally attributed to earlier fibrates,

specifically gemofibrozil as it interferes with statin glucuronidation. Thus, fenofibrate is generally recommended and patients should be on the lowest tolerated dose.[1] Second-line agents include niacin and omega-3 fatty acids although efficacy is limited and should not be used as monotherapy.[4]

Conclusion

HTG acute pancreatitis is a rare presentation with an unclear pathophysiology and multiple risk factors. Fibrates, preferably fenofibrate, remain the mainstay of therapy both in the acute and long-term management setting with TG goals of <500 mg/dL. Other risk factors such as diabetes and obesity should be tightly managed. Benefits of other treatments are unclear and remain an area of further research.

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