

Early Plasmapheresis for Severe Hypertriglyceride-Induced Pancreatitis

A Case Report and Review of the Literature

September 24, 2014 · Case Reports and Clinical Pearls

Thomas P. Waring¹, Prashant Grover²

¹ University of Connecticut School of Medicine, ² Saint Francis Hospital and Medical Center

Waring TP, Grover P. Early Plasmapheresis for Severe Hypertriglyceride-Induced Pancreatitis: A Case Report and Review of the Literature. PulmCCM Journal. 2014 Sep 24 [last modified: 2014 Sep 28]. Edition 1.

Abstract

Triglycerides are an independent risk factor for adverse cardiovascular events and a potential mediator for pancreatic induced inflammation. We present a case of hypertriglyceride-induced pancreatitis that resolved after plasmapheresis, and review the current literature on plasmapheresis as a treatment for pancreatitis caused by hypertriglyceridemia.

Introduction

Hypertriglyceride induced pancreatitis (HTGP) is a potentially life threatening condition. Without prompt recognition and treatment, moderate to severe pancreatitis can rapidly evolve into pancreatic necrosis and ultimately death.¹ Triglycerides in general account for approximately 18% of total body weight.² Triglycerides (TG) are biologic lipids composed of a glycerol pillar to which three fatty acids are attached. These serve as a foundation to more complex biologic membranes. Normal triglyceride metabolism maintains safe levels less than 150mg/dl. Levels in excess of 1000 mg/dl are a risk factor for the development of pancreatitis.³ The sheer size of these macromolecular particles can impede pancreatic blood flow and produce local acinar ischemia. The disturbance of the acinar structure liberates pancreatic lipase. Pancreatic lipases degrade chylomicrons; the largest of the lipoproteins, producing pro-inflammatory free fatty acids.⁴ This pro-inflammatory state can accelerate pancreatic damage and produce local tissue necrosis.

Clinical Case

We report a case of a 52-year-old male, who presented to the emergency department with a chief complaint of abdominal pain associated with anorexia and nausea of three days duration. He has a past history of diabetes type II, hyperlipidemia, and hypothyroidism. Admission laboratory studies revealed a triglyceride level of 17,200 mg/dl, lipase 7,326 U/L, glucose 537 mg/dl, bicarbonate <5 mmol/L and anion gap of 28. A whole blood aliquot had a grossly milky appearance (Figures 1 and 2).



Fig. 1: Lipid-rich blood sample at 6 hours.

60 mL whole blood aliquot 6 hours after collection (before plasmapheresis was performed), showing layering of lipids.



Fig. 2: Lipid-rich blood sample at 24 hours.

24 hours later, the same whole blood aliquot's appearance has changed with dissolution of triglycerides to free fatty acids.

A CT scan of his abdomen showed peri-pancreatic inflammation without necrosis. He was admitted to the intensive care unit for DKA and pancreatitis. He was placed on an insulin and heparin infusion. A plasmapheresis catheter was placed twelve hours after admission. He received one cycle of plasmapheresis with a resultant decrease in total triglyceride levels of 15,000 mg/dl (Figure 3). His abdominal pain resolved after twenty-four hours. His anion gap normalized and he tolerated a low fat diet.

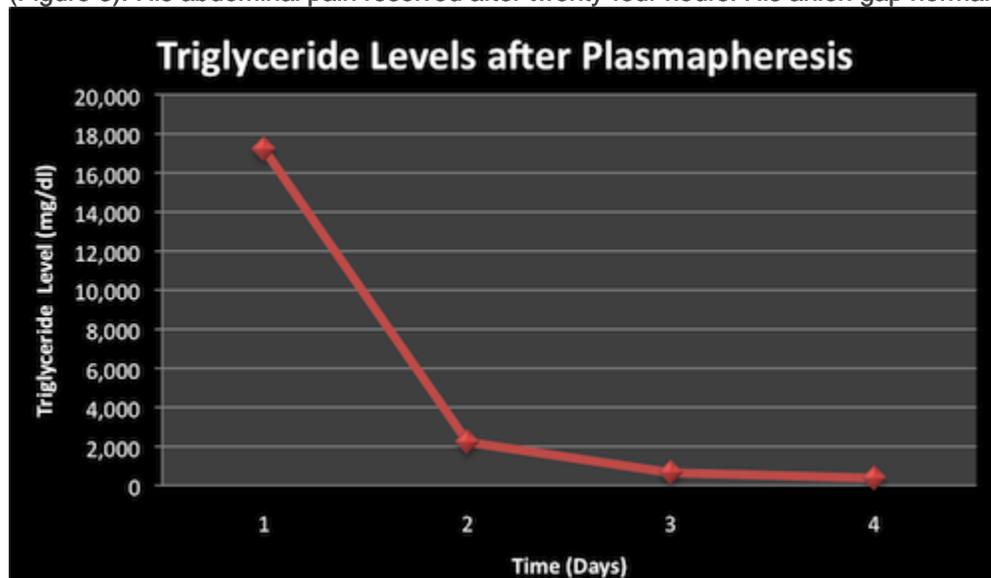


Figure 3. Decline in triglycerides during hospitalization. One cycle of plasmapheresis was initiated within 12 hours of admission, along with insulin and heparin infusions.

Discussion

Triglycerides are an independent risk factor for adverse cardiovascular events and a potential mediator for pancreatic induced inflammation.¹⁻⁵ Collectively, diet, genetic variability, diabetes and alcohol intake are the commonest explanations for elevated triglycerides. When glycogen stores reach critical threshold in the liver, circulating glucose is shunted into a fatty synthesis

pathway.⁶ Glucose is converted to acetyl-CoA, thus producing fatty acids. These fatty acids are incorporated into triglyceride molecules and transported from the liver in the form of very-low-density lipoproteins (VLDL), ultimately to be stored in adipose tissue.

Insulin therapy is the mainstay for the reduction of severe triglyceride levels. Insulin induces lipoprotein lipase (LPL) production.⁷ LPL is a water soluble enzyme of the lipase gene family. Similarly, enzymes in this genus are the hepatic lipases and endothelial lipases. Lipoprotein lipases are found coupled to the luminal side of the endothelium.⁸ Its main function is to hydrolyze triglycerides packed into the chylomicron. In one report by Monga et al, the use of an insulin infusion at the outset of known severe hypertriglyceridemia lowered triglycerides by 7,000 mg/dl in ninety-six hour period.⁹ Mikhail et al in 2005 used an insulin drip protocol of three to nine units/hour and continued for four days while keeping the patient euglycemic, and noted a resultant drop in triglycerides by 8,000 mg/dl.¹⁰

Heparin therapy, although reserved for severe cases of hypertriglyceridemia, has a similar mechanism of action to that of insulin. Heparin promotes release of hepatic lipase and lipoprotein lipases from the endothelial surface of the capillary.¹¹ In a report by Cole et al, in 2009, the use of a heparin infusion at 600 units/hour resulted in a substantial 6,000 mg/dl reduction in total triglyceride levels over a forty hour period.¹² There has been varying reports on heparin use in severe hypertriglyceridemia. Bolus dose heparin has been used with success to lower triglyceride levels.^{13,14} In one report the authors recommended heparin bolus dosing at 18 units/kg at 4-6 hour intervals.¹⁵ There is insufficient evidence to advise on the superiority of continuous vs. bolus dosing heparin administration in this setting.

Plasmapheresis is an extracorporeal therapy designed to separate whole blood into portions. In the setting of severe hypertriglyceridemia it serves to remove the triglyceride component of the blood along with toxic proteases.¹⁶ In general, plasmapheresis is employed to remove alloantibodies, toxins, immune complexes and monoclonal proteins. Conditions commonly associated with plasmapheresis are Myasthenia Gravis, Thrombotic Thrombocytopenia Purpura and Guillian Barre syndrome. It has also been utilized in transplant rejection.

Typically, a large bore double or triple lumen catheter is inserted into a central vein; commonly the internal jugular vein. Flow rates are typically 350 to 400 mL/min and infusion pressure should never exceed 25 PSI. Therapy is aimed at removal of two to three liters of plasma via a machine with filtration properties. That volume removed is then replaced with either 5% albumin or fresh frozen plasma. The machine separates the blood in two separate filtration steps. First, the plasma is removed from the cellular portion and second the globulin removed from albumin. Using membrane coated antibodies, specific lipoproteins can be removed. According to the American council for Apheresis, severe hypertriglyceridemia is currently a Class III indication for plasmapheresis (specific role not determined).¹⁷ Ewald et al in 2009 showed that a single session of plasmapheresis can lower triglycerides by 70%.¹⁸ Similarly, Yeh et al reported that a single cycle of plasmapheresis lowered triglycerides by 65% and a second cycle by 80%.¹⁹

Risks of plasmapheresis are low, although bleeding and trauma at the site of catheter insertion are possible. Hypersensitivity reactions to fresh frozen plasma if used in the exchange have been reported.

Experience with plasmapheresis in acute hypertriglyceride-induced pancreatitis is limited. Most of the experience is limited to case reports and case series and there are no consensus guidelines on optimal therapy. Overall, however, plasmapheresis has been reported safe and effective. It is unclear the number of cycles necessary and the timing in which plasmapheresis should be initiated. It is also unclear if plasmapheresis augments hospital stay and/or mortality.²⁰ It is clear that insulin and heparin either as mono- or dual therapy can reduce triglycerides substantially. The concomitant use of plasmapheresis is an additional therapy to aid in removal of circulating pro-inflammatory molecules and potentially avoid transition to overt pancreatic necrosis.

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