

# Hypertriglyceride induced Pancreatitis.

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## Introduction

Hypertriglyceride (HTG) is an associated cause of pancreatitis. It is seen in about 7% of cases after excluding the most common causes, gallstones and alcohol.<sup>1</sup> Primary causes of HTG include Familial combined Hyperlipidemia or familial hypertriglyceridemia. It can also be secondary to poorly controlled diabetes, medications, obesity, pregnancy and alcohol intake. Rarer causes include glycogen storage disorders and lipodystrophies.<sup>2</sup>

Fredrichson Classification divides Familial Hyperlipidemia into type I to type V based on the lipoproteins after electrophoresis. Familial Hypertriglyceridemia is classed as type IV and in a recent study by Linares et al, 92% of patients were type IV and about 20% had a history of acute pancreatitis.<sup>2</sup>

The Endocrine Society classifies serum triglyceride levels as

- Normal: TG <150mg/dl (<1.7mmol/L)
- Mild: TG 150-199mg/dl (1.7-2.3mmol/L)
- Moderate: TG 200-999mg/dl (2.3-11.2mmol/L)
- Severe: >1000mg/dl (11.2-22.4mmol/L)
- Very severe: >2000mg/dl (>22.4mmol/L)

(1mmol=88.5mg/dl).<sup>2</sup>

The risk of pancreatitis based on serum levels has not been fully established. It has been found that a level >200 increases the risk by 25%.

Triglycerides are carried as VLDLs and chylomicrons (10:1). Free fatty acids are generated by endothelial lipoprotein lipase enzyme via hydrolysis of triglycerides and chylomicrons. The mechanism of HTG induced pancreatitis remains unclear but includes pancreatic lipase generation of free fatty acids, stimulated by cholecystokinin which causes mitochondrial toxicity and intralobular necrosis and hemorrhage. A number of studies suggest that patients with HTG tend to have more of a severe clinical presentation of pancreatitis and at risk of worsening complications.

There is a higher risk of HTG induced pancreatitis in poorly controlled diabetics. The risk of pancreatitis in patients with a normal triglyceride level is 5.2% and levels between 500-2000 was 15%. This is due to insulin resistance causing a greater production of VLDL from the liver and reduced apoB synthesis leading to increased triglyceride levels.<sup>2</sup>

## Case

A 51-year-old gentleman who worked as a delivery driver was carrying out his daily delivery presented to the emergency department with a one day history of epigastric pain radiating to the back. He had a BMI of 31, no phenotypic features of lipodystrophy, no cutaneous features of dyslipidemia on examination. His past medical history included hypertension, type 2 diabetes and previous pancreatitis for which he had been placed on Simvastatin. His admission bloods are shown below

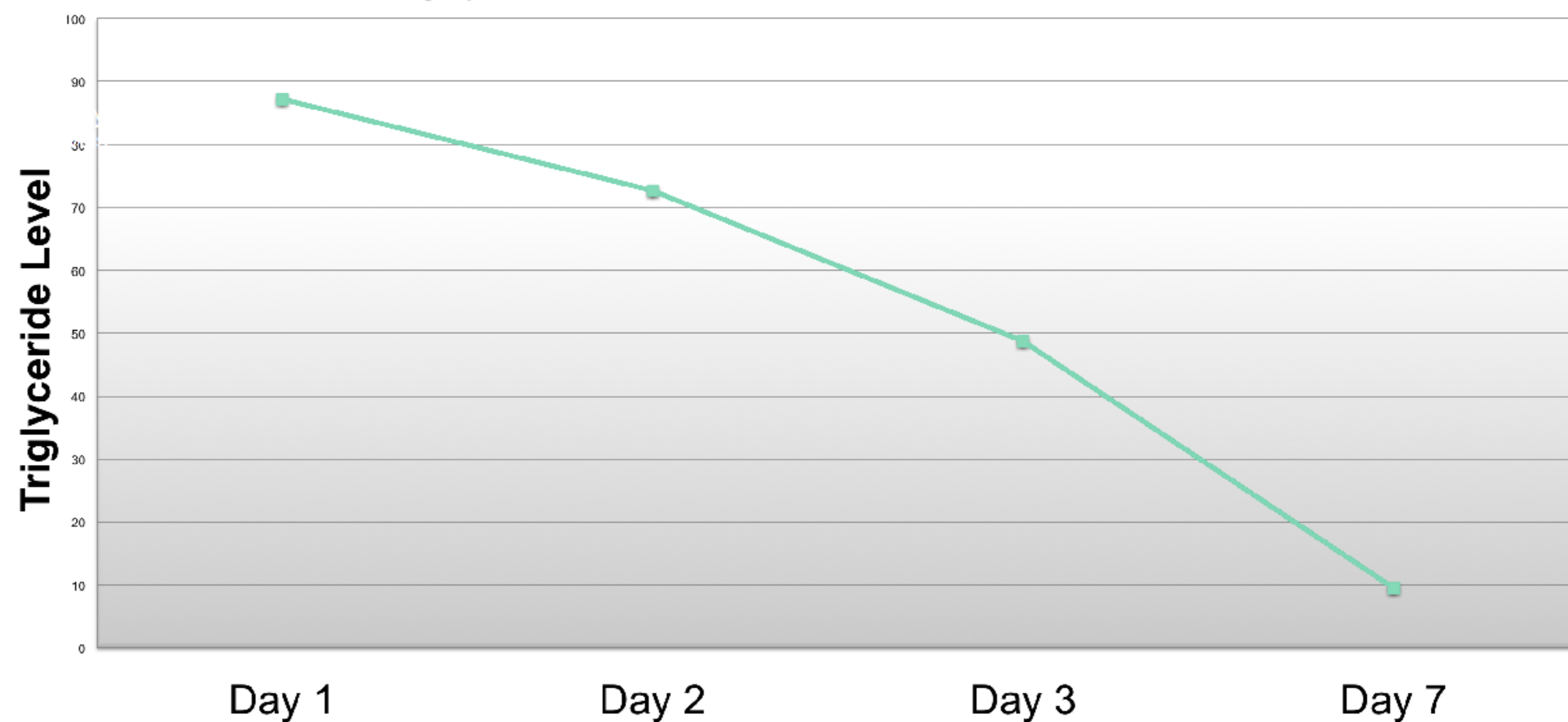
Blood	Result
Hb	141g/L
Wcc	11.1 X10 <sup>9</sup>
Cr	75 umol/L
Crp	287mg/L
Amylase	893u/L
Triglycerides	87.2nmol/L
Cholesterol	20.5nmol/L
HbA1c	81

His CT showed pancreatic oedema and fat stranding consistent with acute pancreatitis. Following this, an abdominal ultrasound showed no evidence of gallstones. There was no known family history of hyperlipidaemia and he was teetotal excluding these causes making hypertriglycerides the likely cause.

He was initially treated with intravenous fluids, analgesia and was kept nil by mouth. Intravenous insulin with 10% dextrose and heparin infusion 0.6ml/ hour was started based on his clinical symptoms and elevated serum triglyceride levels. Within 24 hours, the triglyceride level had significantly reduced and by 7 days of his stay, his levels had decreased to 10nmol/L. This can be shown in graph 1.

In addition to his acute management, he was commenced on fenofibrate, omega 3 and converted to Atorvastatin. His pain improved and he was discharged on subcutaneous Lantus and Novorapid.

A graph showing the reduction in serum triglyceride levels with treatment



## Discussion

Hypertriglyceridemia should be excluded as a cause of pancreatitis when patients are admitted to hospital. Two factors must be present to establish the diagnosis of pancreatitis. These factors include epigastric pain, elevated enzyme levels and radiological imaging suggestive of pancreatitis, which are present in this case. In addition, amylase levels can also be affected by triglyceride levels above 500mg/dl due to interference with the assay. The presence of two secondary factors increases the likelihood of a higher triglyceride level. In this case, this gentleman having a high BMI and poorly controlled diabetes increased his risk of developing HTG induced pancreatitis.

Different therapies have been used to manage acute pancreatitis. Intravenous fluids reduce triglyceride levels by blocking VLDL release from the liver. The fasting state can also reduce levels and therefore, initial triglyceride levels should be sent within 24 hours of admission to avoid inaccurate results..

Intravenous insulin and heparin have also been used in the acute management of HTG induced pancreatitis. Insulin causes a surge of lipoprotein lipase which breaks down triglycerides. Heparin has been shown to transiently increase the endothelial release of lipoprotein lipase.<sup>1</sup> Apheresis can be used to rapidly reduce the serum triglyceride levels, however, there has been a number of risks associated with this treatment and would only be considered if levels of triglyceride were still greater than 1000mg/dl after 24-48 hours despite intravenous fluids and fasting.

Long term management of HTG induced pancreatitis includes lifestyle modification into diet and weight monitoring and ensuring a good diabetic control. Fibrates are well recognised as a form of treatment as they reduce plasma triglyceride level and raise HDL cholesterol by 20%.

Omega 3 reduce triglyceride levels by 20-50%.

## Learning points.

Triglyceride levels should be checked on admission when suspecting pancreatitis.

Secondary factors increase the risk of elevated triglyceride level and should be obtained in the history.

Pancreatic rest and analgesia is important part of treatment. Novel therapies such as insulin and heparin can be used in the acute phase. Long term should be aimed at targeting HbA1c and triglyceride levels to avoid future recurrences.

## References

- 1) Scherer J, Singh V, Pitchumoni CS, Yadav D. Issues in hypertriglyceridemic pancreatitis- An update. J Clinical Gastroenterology. 2014;48(3) 195-203
- 2) Berglund, J D Brunzell, AC Goldberg, Il Goldberg, F Sacks, M Murad, A Stalenhoef. Evaluation and Treatment of hypertriglyceridemia. An endocrine society clinical practice guideline. J Clinical Endocrinology Metabolism September 2012, 98 (9) 2969-2989