

Use of Apheresis and Insulin for Hypertriglyceridemia-induced Pancreatitis and Diabetic Ketoacidosis

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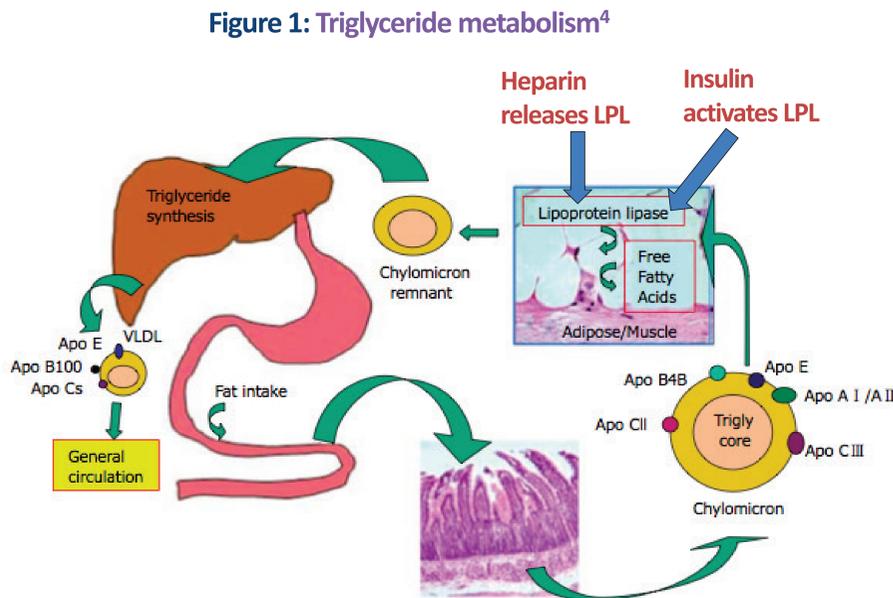


CLINICAL RELEVANCE

- Acute pancreatitis (AP) is a common gastrointestinal disease that may result in multiple organ failure and death¹
 - Gallstones & alcohol are the most common causes of AP¹
 - Hypertriglyceridemia (HTG) causes 1-4% of cases, and should be suspected if triglycerides (TG) are > 1,000 mg/dL in the absence of gallstones or history of significant alcohol use¹
 - Clinical management of hypertriglyceridemia-induced pancreatitis (HTGP) is based primarily on anecdotal evidence and case reports
- Concurrent diabetic ketoacidosis (DKA) and AP have been described in the literature
 - DKA may be a risk factor for AP, but it is uncertain if AP triggers DKA or vice-versa²
 - The optimal management of patients that present with AP, HTG, and DKA is unknown^{2,3}

Table 1: Proposed treatments for acute HTGP

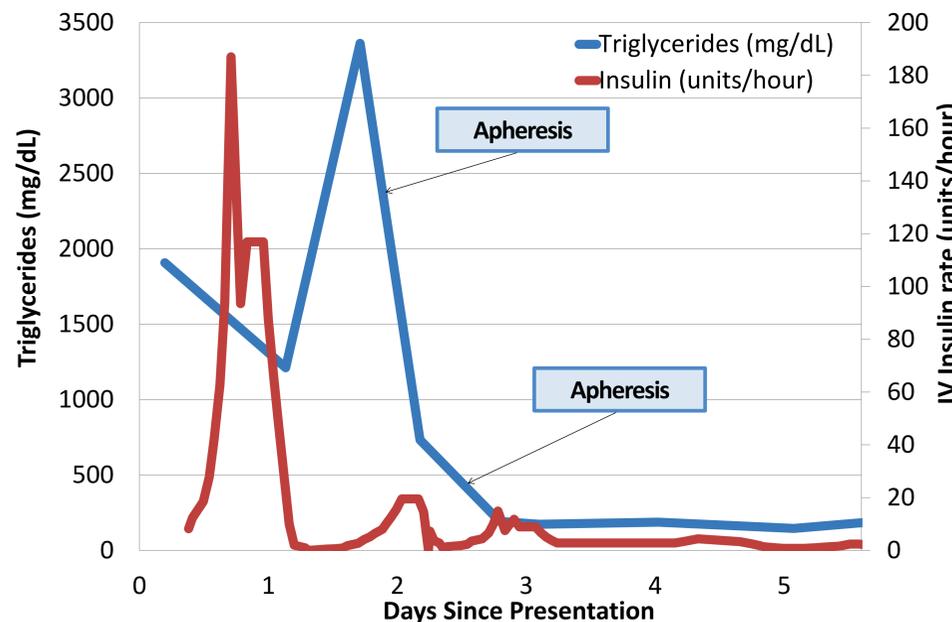
Intervention	Proposed Mechanism ^{3,5}
Insulin	<ul style="list-style-type: none"> Activates lipoprotein lipase (LPL) to accelerate lipolysis of chylomicrons
Heparin	<ul style="list-style-type: none"> Stimulates release of endothelial LPL May ↓ LPL activity with long-term use
Apheresis	<ul style="list-style-type: none"> Eliminates TG and proteases Replaces protease inhibitors



CASE REPORT

- 30 year-old male presented with 10 day history of worsening epigastric pain
- PMH: type 1 diabetes, familial HTG, and AP
- Day 1
 - Laboratory and imaging studies consistent with HTGP and DKA
 - Glucose 257 mg/dL, CO₂ 6 mmol/L, anion gap 30 mmol/L, beta-hydroxybutyrate 105.2 mg/dL, lipase 475 units/L, TG 1907 mg/dL
 - Abdominal/pelvis CT scan showed peripancreatic fluid and infiltration
 - Intubated for respiratory distress
 - IV insulin protocol initiated for DKA (Figure 2)
 - Following protocol, insulin was increased to a maximum of 187 units/hr
 - Titrated off within 24 hours as ketosis and hyperglycemia had resolved
- Day 2
 - Renal replacement therapy initiated for acute kidney injury
 - IV insulin restarted to treat HTGP, but remained < 4 units/hr
 - Lipase increased to 1173 units
 - TG increased to 3362 mg/dL (Figure 2)
 - Apheresis initiated due to inadequate response to insulin and illness severity
 - After 2 sessions, TG decreased to 192 mg/dL
 - Heparin 5000 units subcutaneous every 12 hours was administered from admission until first apheresis for a total of four doses
- On day 9 transitioned subcutaneous insulin and TG remained <500 mg/dL
- Hospitalization complicated by severe hemorrhagic pancreatitis, candidemia, and pneumonia
- Extubated on day 11 and left the intensive care unit on day 17
- Discharged on day 38 with insulin detemir and omega-3 fish oil

Figure 2: Plasma TG and IV insulin administration rate over time



DISCUSSION

- The relationship between AP, DKA, and HTG is complicated, making identification of the primary cause difficult²
 - AP can exacerbate DKA, and HTG with DKA is common²
 - Optimal management is unknown since there are no large trials or consensus statements^{2,3}
- Treatment of DKA requires insulin to resolve ketosis
- Strategies to manage acute HTGP include apheresis, heparin, and insulin^{3,5} (Table 1 & Figure 1)
 - Insulin activates LPL to facilitate TG metabolism
 - Heparin stimulates epithelial release of LPL
 - Apheresis directly removes TG/proteases and provides protease inhibitors via donor plasma
 - The most appropriate dosing of insulin for HTGP is not known, but starting at 0.1 – 0.3 units/kg/hr and titrating to TG level is reasonable³
- Use of continuous IV insulin, subcutaneous heparin, and apheresis resolved DKA and HTGP in our patient (Figure 2)
 - It is unknown if continued use of a weight-based insulin regimen would have avoided the need for apheresis
 - The contribution of heparin to resolve HTGP is uncertain
- With concurrent DKA and HTGP, IV insulin may be prematurely discontinued while TG are still critically high
 - Exercise caution when using insulin nomograms/protocols
 - Consider using a fixed, weight-based dose to avoid titrating off once ketosis resolves and blood glucose normalizes
 - It is reasonable to continue IV insulin until TG < 1000 mg/dL⁵, but the most appropriate length of therapy is uncertain
 - Communication of goals of therapy is paramount to ensure insulin is continued until resolution of both DKA and HTGP

CONCLUSIONS

- IV insulin appears to be safe and effective for HTGP with concurrent DKA, but establishing goals of therapy is essential
- Use of apheresis results in immediate reduction in TG levels, but well-conducted trials are necessary to support this practice³

REFERENCES & DISCLOSURES

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