Inpatient Insulin Management for Severe Hypertriglyceridemia
Care Process Model Synopsis

Objectives

- Decrease TG level with the use of insulin (insulin drip titrated to max of 0.3 unit/kg/hour).
- Dextrose infused in parallel to prevent hypoglycemia and/or maintain euglycemia.
- Consider IVF to maintain hydration

Background

Hypertriglyceridemia has different etiologies, categorized into primary(genetic) or secondary due to conditions that disturb lipid metabolism (Berglund et al., 2012; Valaiyapathi & Ashraf, 2017). A review of the clinical characteristics of 124 pediatric patients with severe hypertriglyceridemia (Richardson et al., 2018) showed that about a third (n = 46) had diabetes and insulin resistance-related etiology, another third (n = *48*) had hematologic-oncologic-related process. The remaining etiologies reported were renal disease (n = 12), total parental nutrition (TPN)-related (n = 6), or miscellaneous (including genetic conditions).

- SHTG related to diabetes and insulin resistance includes type 1 diabetes, type 2 diabetes, or as part of the metabolic syndrome, which includes conditions of obesity, insulin resistance, impaired glucose tolerance, hypertension, and hypertriglyceridemia (Berglund et al., 2012). Although rare overall, it is typical for diabetic ketoacidosis (DKA) and SHTG with or without pancreatitis to co-exist even in the pediatric population, as both are insulin-deficient states (Fick et al., 2017; Sharma et al., 2017; Wolfgram & Macdonald, 2013; Zaher et al., 2019). SHTG can also present in the absence of DKA (Richardson et al., 2018) or as an initial presentation for new type 2 diabetes mellitus not in DKA with SHTG induced AP (Farooqi et al., 2021).
- SHTG related to hematologic-oncologic process includes patients with various diagnoses of the hematologic or oncologic type, with approximately 50% having acute lymphoblastic leukemia (Richardson et al., 2018). Chemotherapeutic drugs used in patients with SHTG include polyethylene glycol (PEG)–asparaginase, vincristine, and doxorubicin (Richardson et al., 2018).
- SHTG related to renal disease, TPN-related, or miscellaneous. Renal disease includes nephrotic syndrome, chronic renal failure, lupus nephritis, Wegener granulomatosis, and focal segmental glomerulonephritis (Richardson et al., 2018). The patients with severe SHTG solely due to TPN were relatively younger (Richardson et al., 2018). Miscellaneous etiology includes lipoprotein lipase (LPL) deficiency, lipodystrophy, HIV, and septic shock (Richardson et al., 2018).

As the authors did not discuss the clinical presentation of SHTG, but rather other conditions it can be associated with, one should suspect possible SHTG if any of the risk factors noted above are observed clinically.

The most worrisome complication of SHTG is acute pancreatitis (AP) (Garg & Rustagi, 2018; Hoff & Piechowski, 2021; Valaiyapathi & Ashraf, 2017). The presentation will be similar to other causes of AP (Garg & Rustagi, 2018), such as abdominal pain, nausea, and vomiting. Serum TG of ≥ 1000 mg/dL increases the risk to develop AP; approximately 5% risk with serum TG > 1000 mg/dL and 10-20% risk at serum TG >2000 mg/dL (Tan et al., 2020; Valaiyapathi & Ashraf, 2017). Therefore, rapid lowering of TG is necessary. One adult case series (Tan et al., 2020) reported that SHTG-induced acute pancreatitis has a higher ICU admission rate than other etiologies of AP.

Lipoprotein lipase (LPL) is the critical enzyme involved in TG hydrolysis in the circulating chylomicrons and very-low-density lipoproteins (Valaiyapathi & Ashraf, 2017). Therefore, SHTG develops due to deficient or absent LPL activity (Valaiyapathi & Ashraf, 2017).

There are limited guidelines on the acute management of SHTG, even in adult literature (Hoff & Piechowski, 2021). Therapies implemented include fasting, insulin, heparin, and plasmapheresis (Valaiyapathi & Ashraf, 2017). A retrospective observational study comparing the combination of insulin and heparin therapy (IHT) to plasma exchange/plasmapheresis showed that both are effective in rapidly lowering SHTG (Jin et al., 2018). However, the IHT was less expensive, less invasive, and had fewer side effects than plasma exchange/plasmapheresis. Both insulin and heparin activate or release LPL; however, the heparin effect is short-lived (Valaiyapathi & Ashraf, 2017) and, therefore, not routinely recommended due to rebound hypertriglyceridemia and risk of hemorrhage (Garg & Rustagi, 2018). Therefore, this care process model will only discuss insulin therapy.

Insulin activates LPL activity by accelerating chylomicron degradation, thus lowering TG levels (Garg & Rustagi, 2018; Valaiyapathi & Ashraf, 2017). Intravenous insulin is preferred for ease in titration and its short half-life (Valaiyapathi & Ashraf, 2017), although subcutaneous insulin can also be used (Lee & Kim, 2020).

The largest case series to date evaluating intravenous insulin used for SHTG included 23 adult patients (Hoff & Piechowski, 2021). The study reported patients remained on IV insulin for a median of 60 hours (2.5 days). Median time

to attain a TG level < 500 mg/dL was 75 hours (3.1 days); however, *n* = 9 (39%) of patients did not experience a drop of TG < 500 mg/dL before discharge (Hoff & Piechowski, 2021). No correlation was reported between the initial TG level and the length of time on IV insulin, nor the resolution of SHTG (Hoff & Piechowski, 2021). This study mimics other literature, that is, the need for insulin infusion for resolution of SHTG can vary in duration, mostly within 3-5 days (Tan et al., 2020). A review of hospital management of SHTG in children recommended a continuous insulin infusion of 0.1-0.3 units/kg/h while maintaining euglycemia (Valaiyapathi & Ashraf, 2017). Oral medications such as fibrates or omega-3 fatty acids are not effective if TG > 1800 mg/dL (Valaiyapathi & Ashraf, 2017).

Target Users

- Emergency Department physicians
- Hospitalists
- Endocrinologists
- Gastroenterologists
- Inpatient floor nurses

Clinical Definitions

Severe hypertriglyceridemia (SHTG) is serum triglyceride (TG) of 1000-1999 mg/dL, and very severe hypertriglyceridemia is serum TG of 2000 mg/dL and above, as defined by the 2012 Endocrine Society's Clinical Practice Guidelines (Berglund et al., 2012).

Care Management Recommendations

- ***Emergency Department***
  - The initial goal is to recognize SHTG; checking triglyceride levels when the patient first presents to the hospital should be prioritized. If a patient has DKA and hyperglycemic hyperosmolar syndrome (HHS), please review DKA and HHS guidelines for further management. If with known DM but not in DKA or HHS, follow this SHTG protocol. If the patient is on home insulin, discuss the home insulin regimen with the inpatient endocrinology team. Initial blood work will include BMP, TG level, and POC glucose. As SHTG increases the risk for acute pancreatitis, lipase and CBC are also indicated, and gastroenterology should be consulted if pancreatitis is diagnosed. Provide stabilization care as clinically indicated.
  - IV insulin should be initiated at 0.1 unit/kg/hour and titrated based on the triglyceride level. IVF with 10% dextrose can be started at 1.5x maintenance and infused in parallel with IV insulin to prevent hypoglycemia or maintain euglycemia. Endocrinology should be consulted to initiate IV insulin. The goal is to decrease TG level with insulin (IV insulin titrated to a maximum of 0.3 unit/kg/hour). Patients may also need IVF to maintain hydration, especially if not tolerating oral/enteral intake.

- ***Inpatient***
  - IV insulin will be titrated based on the TG level (Tan et al., 2020). The authors suggested a decrease in TG level of less than 20% from baseline or every 12 hours as the cut-off for titrating up the IV insulin infusion while maintaining euglycemia. However, given the short half-life of IV insulin and the goal of rapid TG lowering, the recommendation is to monitor TG levels every 6 hours. If TG does not decrease by at least 20% from the previous check, then IV insulin should be titrated upward by 0.05 unit/kg/hour every 6 hours to a maximum of 0.3 unit/kg/hour while maintaining euglycemia. As mentioned earlier, there are limited guidelines on managing SEVERE hypertriglyceridemia even in the adult literature (Hoff & Piechowski, 2021).
  - Monitor Point of Care (POC) (blood glucose) BG every 1 hour and titrate dextrose IVF to maintain euglycemia (100-180 mg/dL). If the POC BG < 80 mg/dL, increase the dextrose IVF to a maximum of 2x/maintenance. If the patient continues to be hypoglycemic despite maximizing dextrose IVF, decrease the insulin infusion rate by 0.05 units/kg/hr, as a last resort, temporarily stopping the insulin infusion. If the POC BG levels rise to > 100 mg/dL, restart IV insulin at 0.1 unit/kg/hr.
  - Regularly monitor the BMP for electrolyte abnormalities, which may be secondary to insulin and IVF infusion. If the patient becomes hyperchloremic (Cl > 115 mmol/L), switch the IVF from D10NS (normal saline) to D10 ½ NS, keeping the rest of the IVF components the same. The expectation is that the patient will be on insulin and IVF infusion for a few days—regular monitoring of fluid status for any signs of fluid overload should occur.
  - If the patient has acute pancreatitis, trend hemoglobin and hematocrit (CBC) at least daily.

- Goal TG is < 500 mg/dL (when achievable) for insulin discontinuation. TG can significantly increase postprandial or rebound (Valaiyapathi & Ashraf, 2017). If TG stays between 500-1000 mg/dL and does not further drop in 2-3 days, discuss further recommendations with the inpatient endocrinology team.
- Consider diet initiation if the patient is stable, states hunger, and is without any gastrointestinal symptoms. Initiate a no-fat (clear liquid) diet, then gradually transition to a low-fat diet (<10-15% of total calories or <30g/day) as tolerated (Tan et al., 2020; Valaiyapathi & Ashraf, 2017). If the patient is tolerating oral-intake or enteral feeds, IVF may be discontinued. If not tolerating oral intake or enteral feeds, discuss with gastroenterology.
- See power plan for Severe Hypertriglyceridemia

- ***Discharge***
  TG < 1000 mg/dL and tolerating oral intake (Valaiyapathi & Ashraf, 2017).

Care questions answered
This standard work is based on consensus, as the evidence is sparse to guide patient care

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Approval Process

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Emergency Department	Oct 2021
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Version History

Date	Comments
Nov-21	Version one - algorithm and synopsis created
March 2026	Version two – updated documents to reflect the naming convention of the new EMR (EPIC) and other standard work of EBP

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