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Management of Hypertriglyceridemia-Induced Acute Pancreatitis in a Nondiabetic Patient

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Abstract

Hypertriglyceridemia-induced acute pancreatitis treatment strategies are not well defined in current literature or guidelines. One therapy option is an insulin infusion accompanied by a dextrose infusion to avoid hypoglycemia. The purpose of this case report is to highlight dosing considerations for dextrose infusions in nondiabetic patients. We describe a case of hypertriglyceridemia-induced acute pancreatitis in a 34-year-old nondiabetic female patient treated with a reduced-dose insulin infusion, complicated by hypoglycemic episodes requiring dextrose infusion titrations. Empirical initiation of a higher dextrose concentration infusion with glucose level titrations should be considered to avoid hypoglycemia for nondiabetic patients treated with an insulin infusion to lower triglyceride levels. In this case, clinical pharmacy assistance was imperative for successful treatment with a reduced-dose insulin infusion and titrated dextrose infusion in the management of hypertriglyceridemia-induced acute pancreatitis.

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Acute pancreatitis is an inflammatory condition of the pancreas with classic symptoms including acute-onset epigastric abdominal pain, often accompanied by nausea and vomiting. The most common causes of acute pancreatitis are secondary to gallstones, alcohol, genetic risk factors, medications, post—endoscopic retrograde cholangiopancreatography, and less commonly hypertriglyceridemia, which occurs in approximately 2% to 4% of cases.[1,2] It is proposed that hypertriglyceridemia induces acute pancreatitis from the hydrolysis of triglycerides in the pancreas into free fatty acids, resulting in lipotoxicity.[3] Triglyceride levels greater than 500 mg/dL (to convert to mmol/L, multiply by 0.0113) increase the risk of acute pancreatitis.[2,4,5] Optimal management strategies are not well defined, given limited studies and case reports. Some therapy options that have been studied include insulin, heparin, and plasmapheresis.[6-10] Insulin therapy is commonly used and is an effective treatment strategy; however, the literature does not define dosing recommendations for concomitant dextrose infusions to prevent hypoglycemia. We present a case report of hypertriglyceridemia-induced acute pancreatitis in a nondiabetic female patient treated with insulin and dextrose infusions complicated by hypoglycemic episodes, requiring dextrose titration.

CASE REPORT

The patient, a 34-year-old white woman weighing 77.5 kg, had a medical history of familial hypertriglyceridemia with previous episodes of acute pancreatitis related to hypertriglyceridemia in 2016 and 2017. She presented to the emergency department with severe radiating abdominal pain and was admitted to the gastroenterology service, given the presentation similar to her previous episodes of pancreatitis. Associated symptoms included nausea, chest tightness, and bloating. She denied alcohol use in the preceding 12 months and had no history of tobacco use, illicit drug use, or use of estrogen products. Her family history was notable for paternal hypertriglyceridemia without any acute pancreatitis episodes. Her medications before admission included gemfibrozil 600 mg by

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mouth twice daily and pravastatin 10 mg by mouth daily, with reported compliance.

Physical examination findings were unremarkable, except for epigastric and left upper quadrant tenderness without rebounding or guarding. Her abdomen was soft and nondistended. Examination was negative for masses or hepatosplenomegaly. No imaging was performed. Pertinent admission laboratory values were as follows: serum triglyceride, 3496 mg/dL; total cholesterol, 709 mg/dL; plasma glucose, 98 mg/dL; hemoglobin A_{1c}, 4.7%; lipase, 197 U/L; lactate, 1.3 mmol/L; and white blood cell count, 13.9 × 10^9/L (to convert serum triglyceride to mmol/L, multiply by 0.0113; to convert total cholesterol values to mmol/L, multiply by 0.0259; to convert glucose value to mmol/L, multiply by 0.0555; to convert lipase value to μkat/L, multiply by 0.0167). The patient was diagnosed with hypertriglyceridemia-induced acute pancreatitis on the basis of presentation and pertinent laboratory values and was treated with insulin and dextrose infusions.

On day 1 of hospitalization, the patient was directed to eat nothing by mouth and received initial fluids as follows: 1000 mL bolus of NaCl 0.9% followed by lactated Ringer solution at 350 mL/h for 6 hours and subsequent lactated Ringer solution at 125 mL/h for 3.5 hours. After initial fluid resuscitation, she was started on an insulin infusion and concomitant dextrose infusion that was pharmacist directed (Table 1). The endocrinology service was consulted to assist with hypertriglyceridemia management and recommended that the insulin infusion be empirically reduced from the standard starting dose of 0.1 unit/kg per hour to 0.07 unit/kg per hour secondary to her baseline lower serum glucose concentrations. Insulin therapy was to be continued at the lower dose until triglyceride levels were less than 500 mg/dL. Triglyceride concentrations were collected twice daily (Figure 1). Blood glucose concentrations were collected hourly while the patient received the insulin infusion, and a hypoglycemic protocol was ordered (Figure 2). Hypoglycemia was defined by a glucose concentration of 70 mg/dL or lower or the presence of hypoglycemic symptoms. She continued gemfibrozil 600 mg by mouth twice daily and pravastatin 10 mg by mouth daily. Omega-3 fish oil, 2 g by mouth twice daily, was started. Pain was managed with hydromorphone, which exacerbated her nausea and was subsequently discontinued. No additional pain management was required.

TABLE 1. Dextrose Infusion Titrations With Glucose Concentrations[a,b]

Time (h)	Dextrose concentration	Dextrose infusion rate (mL/h)	Serum glucose concentration (mg/dL)
0	D5W	125	95
5.5	D10W	200	77
22.5	D20W	200	70
48.25	D20W	125	103
50.25		off	79
70	D20W	200	89
85		off	135

[a]D5W, dextrose 5% in water; D10W, dextrose 10% in water; D20W, dextrose 20% in water.
[b]To convert glucose values to mmol/L, multiply by 0.0555.

The intravenous insulin infusion was started at 0.07 unit/kg per hour with concomitant dextrose 5% in water infusion at 125 mL/h to avoid hypoglycemia. The initial glucose level was 95 mg/dL at approximately 11:00 on day 1. Glucose levels were obtained hourly with the following results: 100 mg/dL, 116 mg/dL, 86 mg/dL, and 77 mg/dL. A glucose level of 77 mg/dL resulted at 16:08, approximately 5 hours after starting of the insulin infusion. On the basis of that level, the dextrose infusion was increased to dextrose 10% in water infusion at 200 mL/h. Titratable instructions for nursing to adjust the dextrose infusion on the basis of blood glucose levels were added per pharmacy recommendation. If blood glucose concentration fell below 200 mg/dL, the rate was to be adjusted to 200 mL/h. If blood glucose concentration rose above 200 mg/dL, the rate was to be adjusted to 125 mL/h. If blood glucose concentration rose above 300 mg/dL, dextrose infusion was to be held until the blood glucose level dropped below 300 mg/dL. Subsequent hourly glucose levels remained low with the following results: 96 mg/dL, 100 mg/dL, 97 mg/dL, 99 mg/dL, and 96 mg/dL, despite dextrose 10% fluid administration.

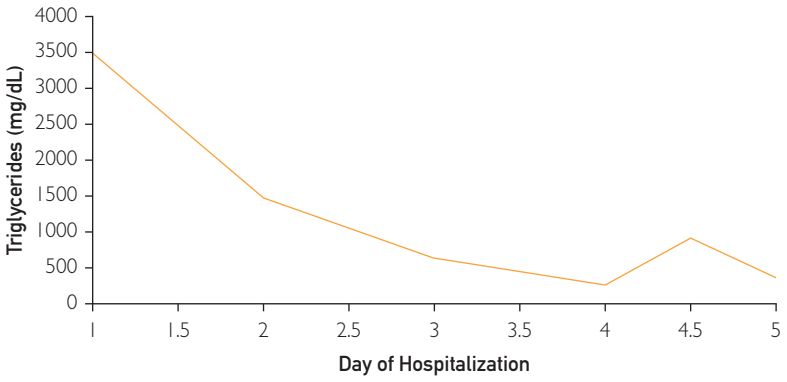

FIGURE 1. Triglyceride trend throughout hospitalization.

A glucose level of 55 mg/dL resulted at 20:59 on day 1. She was noted to be asymptomatic and was promptly treated with dextrose 50% in water 12.5 g intravenously that improved glucose concentration to 93 mg/dL. No adjustments to the dextrose infusion were made at that time as clinical pharmacy was unavailable. The next glucose levels resulted in 87 mg/dL and 65 mg/dL at 23:00 on day 1, which required an additional dextrose 50% in water 12.5 g intravenous bolus for the second asymptomatic hypoglycemic episode. Overnight, the dextrose infusion was not adjusted until the morning at 9:19 on day 2 of the infusion shortly after the result of an asymptomatic glucose level of 70 mg/dL and when clinical pharmacy was present. The dextrose infusion was increased to dextrose 20% in water infusion at 200 mL/h. Titratable instructions for nursing to adjust the dextrose infusion on the basis of blood glucose levels were added per pharmacy recommendation. If blood glucose concentration fell below 200 mg/dL, the rate was to be adjusted to 200 mL/h. If blood glucose concentration rose above 200 mg/dL, the rate was to be adjusted to 100 mL/h. If blood glucose concentration rose above 300 mg/dL, dextrose infusion was to be held until the blood glucose level dropped below 300 mg/dL. Her glucose levels ranged from 81 mg/dL to 175 mg/dL while she

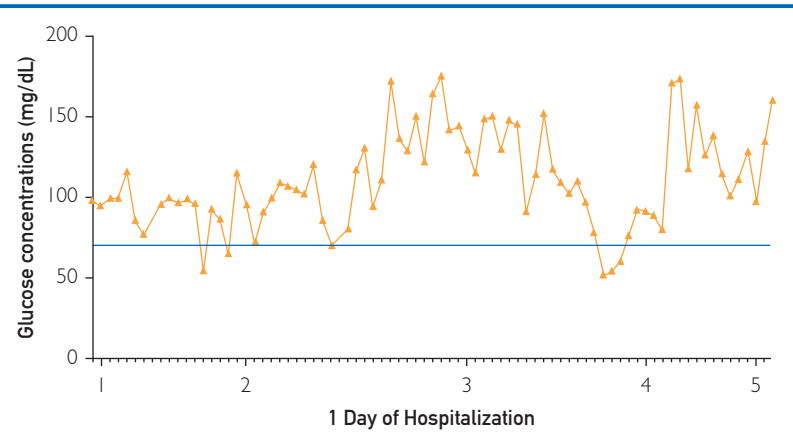

FIGURE 2. Glucose concentrations throughout hospitalization.

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was receiving this dextrose infusion. On day 3, at 11:30, the dextrose infusion was decreased to dextrose 20% in water at 125 mL/h, and the patient was started on a clear liquid diet. Triglyceride levels were measured at 427 mg/dL at 12:00 on day 3, and the insulin and dextrose infusions were stopped.

The patient was transitioned to an oral diet and remained hospitalized to ensure that triglyceride levels were maintained below 500 mg/dL with diet. On day 4 of the hospitalization, approximately 20 hours after maintaining an oral diet, triglyceride level was 916 mg/dL. An insulin infusion of 0.07 unit/kg per hour and dextrose 20% in water at 200 mL/h were resumed with titratable instructions based on previous dextrose 20% in water infusion. These infusions were maintained for 15 hours without any episodes of hypoglycemia until the triglyceride level was 372 mg/dL, at approximately 22:00 on day 4.

She was discharged on day 4 of hospitalization with fenofibrate 600 mg by mouth twice daily, pravastatin 10 mg by mouth daily, and omega-3 fish oil 2 g by mouth twice daily. It was recommended that she start orlistat 120 mg by mouth 3 times daily with meals as an outpatient.

Follow-up with the endocrinology service occurred at 2 weeks and 6 weeks after discharge with triglyceride levels noted at 280 mg/dL and 167 mg/dL, respectively. She reported compliance with her diet and medications: fenofibrate, pravastatin, omega-3 fish oil, and orlistat. At the 6-week follow-up postdischarge visit, the omega-3 fish oil was discontinued.

DISCUSSION

No consensus recommendations or guidelines currently exist for the management of hypertriglyceridemia-induced acute pancreatitis. Limited evidence and case reports describe efficacy with insulin, heparin, and plasmapheresis.[6-10] Insulin and heparin have been studied as concomitant and monotherapy options to induce lipoprotein lipase to degrade triglycerides. Controversy about heparin therapy exists as it may ultimately deplete lipoprotein lipase and inhibit degradation of triglycerides, increasing risk of recurrent hypertriglyceridemia-induced acute pancreatitis. This risk as well as coagulopathy risk was the reason that heparin was not selected for this patient. Plasmapheresis was not empirically considered because of cost and logistics compared with insulin therapy.

Various doses of insulin, including intermittent and continuous infusions, have been suggested on the basis of case reports and case series. The most consistent efficacy is reported with an insulin infusion at 0.1 unit/kg per hour with a concomitant dextrose 5% infusion to avoid hypoglycemia.[6-10] There is currently no evidence published regarding nondiabetic patients experiencing hypoglycemia during the treatment of hypertriglyceridemia-induced acute pancreatitis.

Unlike in this patient, diabetes mellitus type 2 is a common comorbidity of hypertriglyceridemia. These patients are less likely to experience hypoglycemia even while receiving a set-rate insulin infusion. Alternative considerations should be made for nondiabetic patients to avoid hypoglycemia during treatment of hypertriglyceridemia-induced acute pancreatitis. Evaluation of both the insulin infusion rate and the dextrose infusion concentrations and rates is imperative to provide effective therapy and to minimize risks of hypoglycemia.

As noted in our patient, a reduced insulin infusion rate of 0.07 unit/kg per hour was effective at acutely lowering triglyceride levels. It is unclear whether the reduction in the insulin infusion rate prolonged the time for triglyceride levels below 500 mg/dL to be achieved. Even with a reduction in the insulin infusion rate, hypoglycemia was a problem for our patient. We empirically started with a dextrose 5% infusion per literature recommendations, but the patient quickly required additional adjustments to avoid hypoglycemia. We elected to increase the dextrose infusion rather than to reduce the insulin infusion further to allow continued treatment of the patient's acute hypertriglyceridemia. A central line was not placed for administration of dextrose 20% in our patient. Placement of a central line could be considered as dextrose 20% exceeds the upper-limit osmolality for a peripheral line.

TABLE 2. Recommendation for Dextrose Infusion Titration Dosing in Nondiabetic Patients[a,b]

Glucose concentration	≤70 mg/dL or symptomatic hypoglycemic episode	71-180 mg/dL	>180 mg/dL
Dextrose infusion recommendations[c]	Increase glucose concentration by either doubling D10W rate or switching to D20W with same rate	Continue D10W at current infusion rate	Decrease glucose concentration by either reducing rate of D10W by half or switching to D5W with same rate

[a]D5W, dextrose 5% in water; D10W, dextrose 10% in water; D20W, dextrose 20% in water.
[b]To convert glucose values to mmol/L, multiply by 0.0555.
[c]Based on initial infusion with D10W at patient-specific maintenance intravenous fluid rate.

On day 1 of the dextrose and insulin infusion, clinical pharmacy was unavailable overnight, and given the complexity of the situation, the overnight physician and nursing staff were uncomfortable with adjusting the dextrose drip. The nurses elected to use the standard hypoglycemia protocol with dextrose pushes for hypoglycemic symptoms and low blood glucose readings. This highlights the importance of effective communication and education between physicians, nursing staff, and pharmacy for a successful application of a titratable dextrose infusion, especially when clinical pharmacy is unavailable.

From this clinical experience, consideration of alternative dextrose infusion dosing in nondiabetic patients is recommended to maintain the insulin infusion dose close to the therapeutic goal. Empirical dextrose therapy could be initiated with dextrose 10% in water infusion at a calculated maintenance intravenous fluid rate based on the patient's weight. The dextrose infusion should be titrated on the basis of glucose levels (Table 2). For glucose levels of 70 mg/dL and lower or a symptomatic hypoglycemic episode, we recommend increasing the glucose infusion concentration by doubling the dextrose 10% in water infusion rate or switching to dextrose 20% in water at the same initial infusion rate. If the glucose level is between 71 mg/dL and 180 mg/dL, we recommend continuing the current dextrose infusion rate. If the glucose level is above 180 mg/dL, we recommend decreasing the glucose infusion concentration by reducing the dextrose 10% in water infusion by 50% or switching to dextrose 5% in water at the same initial infusion rate. Development of a protocol could be considered, with recognition that it may require patient-specific adjustments to prevent glycemic complications.

Clinical pharmacy consultation is recommended, if possible, to ensure appropriate euglycemic control and to offer recommendations for dextrose infusion titration. In this case, the pharmacists implemented the initial dextrose infusion titration instructions and provided multivariable adjustments (ie, concentrations and rates) based on the patient's progress, laboratory results, and volume status. The clinical pharmacists were proactive with the gastroenterology service through interdisciplinary rounding and frequent chart monitoring. In addition, education was provided for physicians and nursing staff of the dextrose titration instructions. At our institution, clinical pharmacy is available from 7 o'clock in the morning to 10 o'clock in the evening. During pharmacy off-hours, it was recommended that the titration instructions and the hypoglycemia protocol be used if needed. The clinical pharmacists' assistance in management of dextrose titrations, in our case, was imperative for successful treatment and avoidance of adverse events.

Our recommendations in this single-patient case need to be applied cautiously, given other patient factors that may affect the blood glucose levels. It is recommended to have close blood glucose monitoring throughout the time the patient is receiving the insulin and dextrose infusions. These titration recommendations should not be applied to patients with a history of diabetes mellitus, and deviations from protocol are recommended when blood glucose or triglyceride goals are not being met.

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CONCLUSION

We present the case of a 34-year-old nondiabetic woman with hypertriglyceridemia-induced acute pancreatitis that was successfully treated with a reduced-dose insulin infusion and titrated dextrose infusion directed by clinical pharmacy.

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