Hypertriglyceridemia-Induced Acute Pancreatitis Treated with Insulin Therapy: A Case Series

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Case Report

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ABSTRACT:

Hypertriglyceridemia is a condition characterized by high levels of triglycerides in the blood, which can lead to recurrent episodes of acute pancreatitis. When the concentration of triglycerides in the blood exceeds 1000mg/dL, it can trigger acute pancreatitis attacks, but even lower levels can contribute to the severity of the condition. In addition to keeping the patient nil per oral, aggressive hydration and pain management are the mainstays of therapy. It is also crucial to use aggressive triglyceride-lowering therapies in the initial management to reduce complications. Insulin therapy is highlighted as an initial treatment option in this article for lowering triglyceride levels. This can improve patient outcomes and shorten the duration of hospitalization. This retrospective case series describes our experience with hypertriglyceridemia-induced acute pancreatitis at our acute medicine department and emphasizes the role of insulin therapy in its management.

Key words: Hypertriglyceridemia, Acute pancreatitis, Insulin therapy.

INTRODUCTION:

Acute pancreatitis is a life-threatening condition caused by inflammation of the pancreas, resulting in local injury, systemic inflammatory response syndrome, and organ failure.[1] The most common causes are gallstones and alcohol abuse, accounting for up to 70% of cases. Hypertriglyceridemia is the third most common cause, accounting for up to 7% of cases.[2] When serum triglyceride concentrations exceed 1000mg/dL, they can trigger acute pancreatitis attacks, but even lower levels can contribute to the severity.[3,4] In addition to keeping the patient nil per oral, aggressive hydration and pain management are the mainstay of therapy. It is also crucial to use aggressive triglyceride-lowering therapies in the initial management to reduce complications. Insulin therapy is highlighted as an initial treatment option in this article for lowering triglyceride levels, which can improve patient outcomes and shorten hospitalization duration.

METHOD:

This is a 2-year retrospective case series diagnosed with Hypertriglyceridaemia-Induced Acute Pancreatitis (HTG AP) in 2023 & 2024 at the Department of Acute Medicine on Square Hospitals Ltd, Dhaka, Bangladesh. The BISAP (Bedside index of Severity in Acute Pancreatitis) and Modified Marshall scores for organ dysfunction were used to determine Acute Pancreatitis severity. The results were expressed by using the mean and standard deviation.

RESULT:

A total of thirteen patients were included in the study. The clinical characteristics and presentation of the patients have been described in Table 1. There were 8 male and 5 female patients. The mean (± SD) age in the study was 37.23 ± 9.64 years. Ten patients had Type 2 diabetes and eleven patients had dyslipidemia. They have no history of pancreatitis. Acute pain in the abdomen radiating to the back and vomiting were the most common clinical symptoms at the time of presentation.

Table 1: Clinical presentation

Case no	Age (Years)	Gender	Comorbidities	Prior H/O pancreatitis	Clinical presentations	Addiction to alcohol
1	35	F	Diabetes Mellitus, Dyslipidemia	No	Abdominal pain, vomiting	No
2	53	F	Diabetes Mellitus, Dyslipidemia	No	Abdominal pain, vomiting	No
3	52	M	Diabetes Mellitus, Dyslipidemia	Yes	Abdominal pain, vomiting	No
4	27	M	Dyslipidemia	Yes	Abdominal pain, vomiting	Yes
5	44	F	Diabetes Mellitus, Dyslipidemia	No	Abdominal pain, vomiting	No
6	39	M	Diabetes Mellitus	No	Abdominal pain, vomiting	No
7	19	M	No	No	Abdominal pain, vomiting	No
8	40	M	Diabetes Mellitus, Dyslipidemia	No	Abdominal pain, vomiting	No
9	30	F	Diabetes Mellitus, Dyslipidemia	No	Abdominal pain, vomiting	No
10	39	M	Diabetes Mellitus, Dyslipidemia	Yes	Abdominal pain, vomiting	No
11	29	M	Dyslipidemia	Yes	Abdominal pain, vomiting	No
12	42	F	Diabetes Mellitus, Dyslipidemia	Yes	Abdominal pain, vomiting	No
13	35	M	Diabetes Mellitus, Dyslipidemia	Yes	Abdominal pain, vomiting	No

The biochemical parameters have been described in Table 2. The mean (± SD) amylase and lipase levels are 937.23 (± 991.13) and 4779.84 (± 5428.09) IU/mL, respectively. The mean (± SD) TG levels at the baseline were 6334.53 (± 9392.114) mg/dL.

Paired t-test was done to see the statistical significance of the reduction of triglyceride levels before and after treatment with IV insulin. P value 0.0399; which was statistically significant. Table 3 shows the paired t test.

In terms of acute pancreatitis severity, all thirteen patients had severe pancreatitis. After insulin administration, we observed a significant drop in triglyceride levels, reaching safe levels.

Four patients developed necrotizing pancreatitis and systemic inflammatory response syndrome (SIRS). Two of them required mechanical ventilation. Unfortunately, one of them passed away, while the other patient had an extended hospital stay.

At the time of discharge, all patients had fully recovered clinically. The severity and outcomes of these patients are detailed in Table 4.

DISCUSSION:

The exact cause of HTG-triggered pancreatic injury is not fully understood. Normally, our body's triglycerides (TGs) are packaged and transported through very low-density lipoproteins (VLDLs) and chylomicrons, which are large, low-density molecules. When there is excess TGs, pancreatic lipase breaks them down into free fatty acids (FFAs), which have pro-inflammatory and cytotoxic effects. The excess FFAs can also activate and convert acinar cell trypsinogen into trypsin, leading to acinar cell injury.[5] Another mechanism is the intrinsic toxicity of TGs to the pancreatic tissue. Non-esterified TGs can

Table 2: Biochemical parameters and presentation

Case no	Amylase (IU/mL)	Lipase (IU/mL)	Baseline TG level (mg/dL)	TG level after getting insulin therapy (mg/dL)	Duration of getting insulin therapy
1	1200	385	1434	390	48 hours
2	2100	1289	2600	183	44 hours
3	1584	17886	3886	436	38 hours
4	365	3692	4800	465	28 hours
5	3475	6558	35890	376	78 hours
6	1343	5346	4957	457	62 hours
7	110	5629	1913	262	48 hours
8	427	4254	1730	326	48 hours
9	168	527	5541	365	120 hours
10	646	13774	2531	251	30 hours
11	246	1827	1847	465	24 hours
12	268	325	2245	169	48 hours
13	252	646	12975	267	60 hours

* TG- Triglycerides

Table 3: Paired t-test

	Mean	Standard deviation	SEM	p value
Before treatment	6334.54	9392.11	2604.90	0.0399
After treatment	339.38	104.88	29.09	

* SEM- Standard Error of Mean

act as pro-inflammatory substances, increasing interleukin IL 1, IL6, IL 10 and tumor necrosis factor-α, causing systemic inflammatory response syndrome (SIRS). Additionally, intracellular lipid accumulation can lead to a faulty intracellular scavenging mechanism and mitochondrial dysfunction. Other mechanisms such as increased plasma viscosity due to hyperchylomicronemia can lead to decreased capillary blood flow, causing local pancreatic ischemia and necrosis.[6]

We administer intravenous (IV) insulin to patients with worrisome symptoms of HTGP.[3] Worrisome symptoms are – (i) hypocalcemia, (ii) lactic acidosis, (iii)Signs of worsening systemic inflammation (2 or more) i.e.; temperature, heart rate > 90 beats/min, respiratory rate 0f >20 breaths/ min or Pa CO2 <32mmHg, WBC >12,000cells/mL, <4000cells/mL, (iv) Signs of organ dysfunction or multiorgan failure as defined by Modifies Marshall scoring for organ dysfunction. Since insulin can lower both triglyceride and glucose levels, we use insulin to manage hyperglycemia in patients with HTGP and diabetes, which is defined as plasma glucose levels above 180 mg/dL.

In patients showing worrisome symptoms of HTGP, we usually start an IV infusion of regular insulin at a rate of 0.1 to 0.3 units/kg/hour, while closely monitoring blood glucose levels. For patients with blood glucose levels between 150 and 200 mg/dL, we provide a separate 25 percent dextrose infusion to prevent hypoglycemia caused by the insulin infusion. It's important to monitor triglyceride levels every 12 hours. Serum glucose levels should be checked every hour, and the insulin and 25 percent dextrose infusion should be adjusted accordingly. IV insulin should be discontinued when triglyceride levels are below 500 mg/dL (5.6 mmol/L).[7]

The use of intravenous (IV) insulin may be more effective than subcutaneous insulin in severe cases of hypertriglyceridemia-induced acute pancreatitis (HTGP).[8,9] IV insulin is also easier to titrate than subcutaneous administration of insulin. A continuous infusion of IV insulin was found to be effective in treating patients with severe HTGP, both with and without type 2 diabetes mellitus.[9]

Table 4: Severity and outcome

Case no	Severity of acute pancreatitis (BISAP * score)	Modified Marshal scoring for organ dysfunction	Complications	Duration of hospital stay	Outcome
1	Severe	2	None	7 days	Improved
2	Severe	2	None	7 days	Improved
3	Severe	5	None	10 days	Improved
4	Severe	10	Necrotizing pancreatitis, SIRS**	22 days	Improved
5	Severe	12	Necrotizing pancreatitis, SIRS**	8 days	Died
6	Severe	6	None	6 days	Improved
7	Severe	2	None	5 days	Improved
8	Severe	2	None	4 days	Improved
9	Severe	12	Necrotizing pancreatitis, SIRS**	11 days	Improved
10	Severe	2	None	4 days	Improved
11	Severe	2	None	3 days	Improved
12	Severe	10	Necrotizing pancreatitis, SIRS**	10 days	Improved
13	Severe	2	None	3 days	Improved

*BISAP Score – Bedside index of severity in acute pancreatitis
**SIRS – Systemic inflammatory response syndrome

Insulin has several effects on triglyceride metabolism. It reduces the production of VLDL triglycerides and lowers serum triglyceride levels by increasing the activity of lipoprotein lipase (LPL), an enzyme that breaks down chylomicrons and VLDL into glycerol and free fatty acids (FFAs).[10,11] Additionally, insulin inhibits hormone-sensitive lipase in adipocytes, which is responsible for releasing fatty acids from triglycerides. In severe acute pancreatitis associated with severe hypertriglyceridemia (HTG), the goal of insulin therapy is to counter the stress-induced release of fatty acids from adipocytes, promote triglyceride storage within adipocytes, enhance fatty acid metabolism in insulin-sensitive cells, reduce peripheral insulin resistance, and primarily correct hyperglycemia. Our study found a significant reduction in TG levels within 48 hours after starting insulin therapy.

This reduction is more pronounced when the treatment is initiated early after the onset of symptoms, thereby reducing complications of acute pancreatitis. Out of thirteen patients, four developed SIRS. They presented to our center 48 hours after the onset of severe abdominal pain. One of them required mechanical ventilation and plasma exchange for hypertriglyceridemia but unfortunately, she died. Compared to previous data when patients were treated conservatively without insulin therapy, they needed longer hospital stays and experienced more complications.

CONCLUSION:

Patients with HTGP require urgent and aggressive management to reduce TG levels because the disease presentation is particularly severe and may result in grave complications. The use of insulin therapy, along with close monitoring of blood glucose levels, can be an appropriate and cost-effective therapeutic approach. This paper not only highlights the utility of insulin therapy for HTGP but also emphasizes the need for concerned physicians to evaluate this treatment approach in larger, multicenter studies. Long-term management using both pharmacological and non-pharmacological therapies aimed at maintaining serum triglycerides within normal limits is required to prevent recurrent attacks of HTGP.

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