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Case Report

Insulin Infusion for the Management of Patients with Severe Hypertriglyceridemic Pancreatitis

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Abstract

A Acute pancreatitis secondary to hypertriglyceridemia is mainly observed in severely elevated triglyceride to a level above 11.3 mmol/L. Different treatment methods have been described for treatment of hypertriglyceridemic pancreatitis, including plasma exchange and insulin therapy. The outcomes of insulin therapy are not well-detailed in the United Arab Emirates. We studied 9 patients confirmed to have severe hypertriglyceridemic pancreatitis requiring hospitalization. All patients were managed successfully with insulin infusion and the target triglyceride level below 5.6 mmol/L was achieved within an average of 5 days duration of therapy. Early intervention in this group of patients will help avoid serious complications. We conclude that insulin infusion is a cost-effective, less invasive, and valid treatment approach in patients with hypertriglyceridemia-induced acute pancreatitis.

Introduction

Hypertriglyceridemia refers to an increase in the fasting triglyceride measurement to above 1.7 mmol/L. Risk factors associated with hypertriglyceridemia are familial causes, metabolic syndrome, excess alcohol, and sedentary lifestyle [1]. A cross-sectional study carried out in the Northern Emirates of the United Arab Emirates (UAE) to assess the prevalence of hypertriglyceridemia in adults showed 29% of 824 participants had high triglyceride levels [2]. Untreated hypertriglyceridemia can lead to complications, including acute pancreatitis of which hypertriglyceridemia is the third most common cause worldwide [3]. Acute pancreatitis is mainly observed with severely elevated triglycerides to a level above 11.3 mmol/L [3,4]. Management of hypertriglyceridemia is typically lifestyle modification and triglyceride-lowering medications. For acute pancreatitis related to hypertriglyceridemia, the literature describes different treatment modalities, including insulin therapy and plasmapheresis [4,5]. The outcomes of two patients managed with plasmapheresis for hypertriglyceridemia in Dubai have been reported [4], but the outcomes of insulin treatment for hypertriglyceridemia are not well-described in the UAE.

Aim

The aim of this study was to report the outcome of patients having severe hypertriglyceridemia treated with insulin infusion.

Methods

Data Collection and Analysis

We reviewed 9 patients confirmed to have Hypertriglyceridemic Pancreatitis (HTGP) requiring hospitalization. The study was conducted at Sheikh Shakhbout Medical City, Abu Dhabi, UAE and data was obtained retrospectively from patient's electronic medical records. We analysed the clinical parameters of these patients, and the response achieved with insulin therapy.

It is a comprehensive study collection from patient medical charts looking at various variables. The patient demographic characteristics includes age, gender, and nationality. Confirmed cases of HTGP were only studied and this was confirmed based on elevated triglyceride levels, confirmed imaging of pancreatitis, and elevated lipase levels. Other causes of pancreatitis including gallbladder disease, alcoholism, or abnormal calcium levels were ruled out. All patients were initiated on insulin infu-

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sion upon admission and was stopped after achieving the desired triglyceride level below 5.6 mmol/L.

Case Series and Results

We had a total of 9 patients diagnosed with HTGP requiring hospitalization. The median age when first diagnosed with HTGP was 32 years. All patients had a level of triglyceride above 11.3 mmol/L and were started on insulin therapy on admission. Our standard regimen was intravenous insulin at a rate of 0.1U/Kg/hr, adequate hydration, measurement of triglyceride levels twice daily, hourly check of blood glucose levels and stopping insulin infusion once triglyceride levels were below 5.6 mmol/L. The insulin infusion rate was increased by 0.05 U/Kg/hr if serum triglyceride does not decrease by at least 25-50% in the first 24 hours. The maintenance fluid included dextrose with close monitoring of blood glucose levels as to avoid hypoglycemia. The patients all had dietitian review, inpatient education about lifestyle modification, and were placed on triglyceride-lowering agents upon discharge with outpatient clinic follow-up (Table 1).

Table 1: Characteristics of patients diagnosed with HTGP.

Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Age - first diagnosed	29	38	27	26	38	30	32	39	30
Nationality	India	Egypt	UAE	Syria	Bangladesh	Pakistan	UAE	Egypt	Bangladesh
Gender	Male	Male	Female	Male	Male	Male	Male	Male	Male
Alcohol consumption	Occasional	No	No	No	Occasional	No	No	No	No
Admission diagnosis	HTGP	HTGP	HTGP	HTGP	HTGP	HTGP	HTGP	HTGP	HTGP
Abdomen Imaging	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gallbladder disease	No	No	No	No	No	No	No	No	No
Hypocalcaemia	No	No	No	No	No	No	No	No	No
Liver function test	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Previous history of pancreatitis	No	No	Yes	Yes	No	No	Yes	Yes	No
Lipase level IU/L*	233	1315	275	196	947	418	125	242	195
Triglyceride level mmol/L**	14.5	20	24.4	26.9	13	29.6	39.6	40.9	38.6
Insulin infusion stop day	Day 2	Day 5	Day 4	Day 2	Day 2	Day 3	Day 12	Day 6	Day 6
Hypoglycaemia	None	None	Day 3	No	Day 2	None	Day 6	None	None
Length of hospital stay	3 days	6 days	13 days	3 days	4 days	4 days	13 days	7 days	9 days

*Reference range for lipase level is 12 – 60 IU/L
**Reference range for triglyceride level is 0.5 – 1.7 mmol/L

Table 2: Treatment of acute HTGP.

Drug	Mechanism	Duration	Advantage	Complications
Plasmapheresis	Removal of circulating triglycerides and chylomicrons	49-97% reduction in a single session	Rapid	-Costly -Allergy -Infection -Central line related complications
Insulin	LPL* activation	50-75% reduction in 2-3 days	-Non invasive -Cheaper -Availability	-Hypoglycemia
Heparin + Insulin	Release and activation of LPL	50% within the first 24 hours	-Non invasive -Cheaper -Availability	Used of heparin increase risk of rebound hypertigrlycerdemia and Haemorrhage
Alternative therapies reported in literature	Combined blood purification therapy High volume hemofiltration and hemoperfusion			

*LPL – lipoprotein lipase

Discussion

Hypertriglyceridemia accounts for 4-10% of all cases of acute pancreatitis. HTGP tends to have a more severe course and higher complication rate as compared to other aetiologies of pancreatitis [6,7]. The mechanism of hypertriglyceridemia causing acute pancreatitis is complex and not clearly understood. Hypertriglyceridemia and chylomicronaemia form toxic structures that damage platelets and vascular endothelium. Also, they increase plasma viscosity and cause capillary plugging. These result in increased inflammatory response, ischemia, acidosis and trypsinogen activation leading to acute pancreatitis [7,8].

No standard international guidelines exist for the treatment of HTGP. The management approach should be focused on both

acute and long-term treatment to prevent recurrence. The initial treatment of acute pancreatitis from any cause includes bowel rest, nutritional support, intravenous fluid hydration, pain management and illness severity stratification. Different treatment modalities have been proposed for rapid triglyceride reduction in the acute settings of HTGP (Table 2) [6-12]. As per the American Society of Apheresis, plasmapheresis remains most effective in severe cases and can be considered if the patient exhibits one of the following: (i) lactic acidosis, (ii) hypocalcemia, (iii) worsening inflammatory response, (iv) worsening organ dysfunction or multiorgan dysfunction [9,13].

The approach we intended to utilize in our patients, was insulin infusion therapy with the standard regime as specified earlier. Similar standard regimes are proposed in the literature with promising outcomes [8]. As seen in our patients, the target triglyceride level was achieved between 2-6 days of hospitalization except for one patient who required 12 days of insulin therapy. The length of stay correlated with the initial triglyceride level and 3 of the patients with initial level above 35 mmol/L had at least 6 days of hospital stay. All patients had successful recovery without any complications during hospitalization. This proves the effectiveness of insulin therapy in the management of HTGP.

Maintenance therapy includes lifestyle modification and pharmacological treatment to achieve good control of triglyceride levels below 5.6 mmol/L and more ideally below 1.7 mmol/L [7,8,14]. As per the American College of Cardiology, the best long-term pharmacologic options in prevention of acute pancreatitis are fenofibrates and omega -3 fatty acid [15]. Two emerging novel agents, apolipoprotein C-III (apoC-III) and angipoietin-like 3 (ANGPTL3) inhibitors, showed 70-90% reduction in plasma triglyceride levels and could potentially decrease the complications associated with uncontrolled hypertriglyceridemia [14].

Conclusion

Rapid initiation of treatment is vital in patients with HTGP to prevent life threatening complications. Insulin infusion is a cost-effective approach and the target triglyceride level below 5.6 mmol/L can be achieved within an average of 5 days duration of therapy. The potential adverse effect of hypoglycemia can be prevented by close monitoring of blood glucose levels. Our study helps to characterize patients treated for hypertriglyceridemia-induced acute pancreatitis with insulin in the Middle East and demonstrates insulin as a cost-effective and valid alternative to more aggressive treatment modalities proposed in the literature [16]. This review also provides insight that could contribute to international consensus guidelines toward the treatment of HTGP.

Author Statements

Authors Contribution

All authors were involved in the data collection and analysis. The work was divided equally among all members. All authors read and approved the final manuscript.

Ethical Approval and Consent to Participate

Ethical approval was obtained from SSMC research ethical committee to have access to patient medical charts. As this is a retrospective review of patients' records, consent is not required.

Human and Animal Rights

No Animals/Humans were used for studies that are base of this research.

Consent for Publication

Verbal and written informed consent were not obtained from the patients for publication, as this is a retrospective study with no direct patients' participation.

Availability of Data and Materials

Data used in this report is available in the patient's electronic medical record and is available for review.

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Conflict of Interest

The author declares no conflict of interest, financial or otherwise.

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