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# Severe hypertriglyceridemia-induced pancreatitis successfully managed with therapeutic plasma exchange: Report from India

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#### **Abstract:**

Hypertriglyceridemia (HTG) is the third most significant risk factor for acute pancreatitis after gallstones and alcohol. Therapeutic plasma exchange (TPE) has been considered a possible treatment for HTG-induced pancreatitis, especially in severe and refractory cases. Here, we report one such clinical experience with a patient of severe HTG-induced pancreatitis. He was treated with TPE along with intravenous insulin, statins, and fibrates. TPE resulted in immediate relief of symptoms as well as a marked improvement in laboratory values, with 74.5% reduction in triglycerides after a single session. TPE can be successfully utilized as an adjunct in HTG-induced pancreatitis.

#### **Keywords:**

Hypertriglyceridemia, pancreatitis, therapeutic plasma exchange

## Introduction

Hypertriglyceridemia (HTG) is an independent and important risk factor for adverse cardiovascular events and pancreatitis.[1] HTG is defined by fasting serum triglyceride (TG) levels of >150 mg/dL. HTG is classified as mild (150-199 mg/dL), moderate (200–999 mg/dL), severe (1000–1999 mg/dl), and very severe (>2000 mg/dL).[1] Primary causes of HTG include mutations in genes encoding lipoprotein lipase and its activator Apo C-II, while secondary causes comprise diabetes mellitus (DM), hypothyroidism, pregnancy, and medications. Severe HTG may result in significant morbidity and complications, such as acute pancreatitis, chronic abdominal pain, hepatosplenomegaly, eruptive xanthomas, lipemia retinalis, peripheral neuropathy, memory loss/dementia, and dyspnea.

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Early clinical recognition and treatment of HTG-associated pancreatitis is important to prevent pancreatic tissue damage and necrosis. The management of HTG is generally conservative, such as fat-restricted diet, lipid-lowering medications, heparin, insulin, and noncaloric intravenous (i.v) fluids. According to the American Society for Apheresis guidelines-2016, hypertriglyceridemic pancreatitis is a Category III (not established) disease indication for performing therapeutic plasma exchange (TPE) (2016) and decision-making should be individualized.<sup>[2]</sup> We present a case of HTG-induced pancreatitis where such a decision to perform TPE worked out very well for the patient.

## **Case Report**

A 34-year-old male, a known case of DM type 2, presented to the emergency department with the chief complaints

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Submission: 04-07-2017 Accepted: 05-12-2017 of abdominal pain, nausea, vomiting, and decreased appetite for 3 days. The patient had a history of a similar episode 2 years back which necessitated hospital admission, when he was found to have HTG-induced pancreatitis. He was then managed conservatively and was discharged on oral hypoglycemic and lipid-lowering agents. However, his compliance was poor; he discontinued his medications few weeks after previous discharge from the hospital.

During the present admission, his laboratory investigations revealed a grossly lipemic sample with TG: 2610 mg/dl, total cholesterol: 797 mg/dl, very low-density lipoprotein (VLDL): 973 mg/dl, high-density lipoprotein: 21 mg/dl, LDL: 133 mg/dl, serum amylase levels: 162 U/l, serum lipase: 426 U/l, Fasting Blood sugar: 250 mg/dl, glycated hemoglobin: 10.94%, procalcitonin: 56 ng/ml, and C-reactive protein: 252.8. The complete blood counts, liver and kidney function tests, blood culture, urine culture, and calcium were unremarkable. Vital parameters were within the normal limits.

Ultrasonography of the upper abdomen showed Grade-1 fatty changes in liver, small amount of hyperechoic biliary sludge in gallbladder, and hypoechoic and swollen pancreas with slight blurring of peripancreatic margins. Chest X-ray was normal.

A provisional diagnosis of HTG-induced pancreatitis was made. The patient was started on insulin infusion, statins and fenofibrate, i.v fluids, i.v ceftriaxone, and other symptomatic treatment. In view of severe HTG, TPE was planned by the team of gastro-physician and apheresis physician. Central venous access was obtained in the right jugular vein. TPE was performed within 12 h of admission and was carried out with a COM.TEC® cell separator (Fresenius Kabi, AG 61346 Bad Homburg, Germany), using the standard plasma exchange kit (PL1). 1.5 volume of plasma (3787 ml) was exchanged using 5% albumin as replacement fluid. TG levels were reduced to 663 mg/dl after one session (single procedure) of TPE. There was a significant improvement in other laboratory parameters such as total cholesterol, VLDL cholesterol, and LDL cholesterol which were reduced to 227 mg/dl, 178 mg/dl, and 30 mg/dl, respectively. In view of clinical and laboratory improvement, the patient was managed conservatively.

The patient was relieved of symptoms of abdominal pain and nausea after TPE, thereafter. TG levels were further reduced to 461 mg/dl on the following morning. The patient was discharged a day after on statins and fenofibrate in stable condition. After 6 months of follow-up, the patient continues to be asymptomatic and is maintaining normal lipid profile on lipid-lowering medication.

#### Discussion

HTG is one of the common causes for acute pancreatitis after gallstones and alcohol. Serum concentration >1000 mg/dl is a significant risk factor for acute pancreatitis. Diagnosis of pancreatitis requires two of the following three criteria – clinical signs and symptoms consistent with pancreatitis, markedly increased pancreatic enzyme levels (three or more times the upper limit), and pancreatic alterations on imaging. In the presence of HTG, the serum amylase and lipase levels may be sometimes spuriously normal or only mildly elevated. Hence, in such cases, diagnosis should be made on the basis of clinical judgment and prompt treatment should be given. [4] In this patient, the pancreatic enzymes were not markedly elevated that could be due to HTG.

Patients with severe HTG-induced pancreatitis are in a urgent need of a fast and effective means for lowering TG levels to prevent organ damage. TPE is an effective method for rapid reduction of TG levels below 1000 mg/dl and for relieving the patients from the symptoms in acute phase of the disease. TPE involves removal of 1–1.5 volumes of plasma through centrifugation or filtration under transient anticoagulation and replacing it by 5% human albumin or fresh frozen plasma. TPE is relatively a safe procedure with few complications. [5] Our patient did not experience any adverse event during the 3-h TPE procedure.

In most of the case studies and reports, TPE was done in patients with severe HTG or in patients refractory to the conventional treatment [Table 1].

In our patient, TPE was done in combination with medical therapy in view of severe HTG and a single session of TPE reduced TGs by 74.5%, which was higher than reductions (61%–70%) shown in similar studies. [6-9]

Table 1: Other publications on the use of therapeutic plasma exchange in hypertriglyceridemia

Reference study	Number of patients	Indication of TPE	Replacement fluid	Percentage reduction in TG levels
Yeh et al.[6]	17	Hyperlipidemic pancreatitis	FFP and 5% albumin	66
Stefanutti et al.[7]	17	Refractory to conventional management	5% albumin	60
Kyriakidis <i>et al.</i> [8]	10	Hyperlipidemic pancreatitis	FFP	61
Syed <i>et al</i> . <sup>[9]</sup>	4	HTG-induced pancreatitis	5% albumin	70

TPE = Therapeutic plasma exchange, TG = Triglycerides, FFP = Fresh frozen plasma, HTG = Hypertriglyceridemia

Gubensek *et al.*<sup>[10]</sup> observed a mean reduction of 59% in TG levels with TPE as compared to 27% with conservative management over approximately 24 h, which was significantly lower than the reduction by TPE and concluded that TPE effectively reduced TG levels at a faster rate than the conservative treatment and is associated with a low rate of complications. According to Kyriakidis *et al.*, TPE should be performed as early as possible, within the first 48 h to prevent irreversible organ damage and prevent further attacks of pancreatitis.<sup>[8]</sup> In our patient, TPE was done within 12 h and the patient was relieved of acute symptoms following the session of TPE.

TG levels were further reduced to 461 mg/dl the next day following one session of TPE with medical management. No further TPE was performed and the patient was managed conservatively in accordance with the study of Ewald and Kloer<sup>[11]</sup> which states that TPE should be performed until TG levels have been lowered to <500 mg/dl.

#### Conclusion

Along with conventional management, TPE can be an effective part of the therapeutic armamentarium in patients with severe HTG, as it rapidly lowers the TG levels and should be performed as early as possible in suitable patients.

## **Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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#### Conflicts of interest

There are no conflicts of interest.

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