Clinical Case Report

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Double filtration plasmapheresis in treatment of acute pancreatitis associated with severe hypertriglyceridemia

Three case reports

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Abstract

Rationale: Severe hypertriglyceridemia is the 3rd-leading cause of acute pancreatitis. Current treatment option for hypertriglyceridemia associated with acute pancreatitis is mainly supportive measures, including adequate fluid supply, pain management, and broad-spectrum antibiotics if necessary. Extracorporeal method by mean of plasmapheresis is effective in reducing serum level of triglyceride. It has been proposed to have therapeutic potential in limited small sample studies.

Patient concerns: A retrospective review of therapeutic effect of double filtration plasmapheresis in treating hypertriglyceridemia associated with acute pancreatitis was conducted by enlisting 3 patients who meet the criteria for the present study.

Diagnoses: Three patients met the criteria for hypertriglyceridemia (serum level >800 mg/dL) associated with acute pancreatitis (either with elevated serum level of lipase and/or amylase and/or with computed tomography evidence of acute pancreatitis).

Interventions: Patients received double filtration plasmapheresis.

Outcomes: We found that an effective reduction of triglyceride was achieved on an average of 84.7% as a result of a single session of plasmapheresis. All 3 of our patients survived, but needed extended hospitalization.

Lessons: A substantial clinical trial is required to further assess the effectiveness of plasmapheresis in managing of acute pancreatitis in the setting of hypertriglyceridemia.

Abbreviations: CT = computed tomography, DFPP = double filtration plasmapheresis, ED = emergency department, HTG = hypertriglyceridemia, HTG-AP = hypertriglyceridemia associated-acute pancreatitis, ICD-9 code = International Classification of Diseases, 9th Revision, PE = plasma exchange, TG = triglyceride.

Keywords: acute pancreatitis, double filtration plasmapheresis, hypertriglyceridemia

1. Introduction

Severe hypertriglyceridemia (HTG) is currently the 3rd-leading cause of acute pancreatitis after alcohol and gallstones in the United States.[1] It accounts for between 2% to 26% among patients from all causes of acute pancreatitis.[2] Additionally, it is responsible as a main cause of morbidity and mortality with a reported incidence of 40 per 100,000 persons in the Western population.[3] It is generally believed that triglyceride (TG) levels of >1000 mg/dL (11.3 mmol/L) trigger acute pancreatitis and its serious complications. This threshold, however, is arbitrary and the level above which acute pancreatitis might occur is actually unknown.[4] Current management for hypertriglyceridemia associated-acute pancreatitis (HTG-AP) remains supportive methods such as adequate fluid supply, pain control, and broad spectrum antibiotics if necessary.[5] Further medical treatment can include the use of insulin and heparin drip.[6] Plasmapheresis has been proposed to reduce TG level in HTG-AP with varied results.[7–10] Many of those studies have been limited by small sample sizes, probably related to the fact that there is lack of strong evidence supporting its clinical application and also presence of widely available oral lipid lowering agents.

Plasma exchange (PE) has been claimed to be superior to double filtration plasmapheresis (DFPP) in reducing serum level of TG in severe lipemia patients.[7] But technical difficulty and potential transfusion relation complications in PE may raise concern of patient safety in this treatment modality. DFPP is a semiselective method in which the first filter separates the whole blood from the plasma, then the plasma is passed through a second filter that prevent the passage of high-molecular weight molecules.[11] In many diseases, compared with PE, DFPP is considered to be equally effective in treating many diseases except

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thrombotic thrombocytopenic purpura.[12] But DFPP has the advantage of reducing the risk of allergic reaction using fresh-frozen plasma as replacement fluid in PE. Human albumin can be used as the alternative replacement fluid, but it is much more expensive relative to plasma.[13] Thus, we are interested to explore the therapeutic potential of DFPP on HTG-AP and further scrutinize the patients' outcome.

2. Methods

2.1. Ethical approval statement

We have obtained the approval from the Joint Institutional Review Board of the Taipei Medical University to conduct a retrospective study at the Taipei Medical University-Wan Fang Hospital.

2.2. Consent for publication statement

All 3 patients had given their consent to be included in the manuscript.

2.3. Selection criteria

Adult (age ≥ 21 years) medical records from January 1, 2010 to December 31, 2017 were reviewed. Using International Classification of Diseases, 9th Revision code for therapeutic plasmapheresis, we have found in total of 30 qualifying patients. We then excluded 27 patients receiving plasmapheresis for various other indications such as Guillain–Barre syndrome, myasthenia gravis, and rapid progressive glomerulonephritis. DFPP as HTG-AP therapy was considered if the patients were found to have TG levels >1000 mg/dL, 11.29 mmol/L (normal: <150 mg/dL) and had clinical evidence of acute pancreatitis diagnosed either by abdominal computed tomography (CT) or significantly elevated of serum lactate dehydrogenase levels (2–4 times of normal; normal 11–82 U/L). The criteria for the further sessions of DFPP are that if the patient's TG remained >1000 mg/dL, then further sessions of DFPP would be performed until TG <1000 mg/dL. We found 3 patients received DFPP for HTG-AP. Table 1 summarized the baseline characteristics of the all 3 patients.

2.4. Outcome assessment

Levels of TG, APACHE II score, number of DFPP sessions, duration of hospitalization, and survival outcomes before and after DFPP procedures are the main outcome measure assessments.

2.5. DFPP procedure

DFPPs were performed in our establishment in cases where lipid-lowering agents were contraindicated or whose condition in urgent need for rapid TG removal as a lifesaving procedure. Vascular access was established with a double-lumen central venous catheter insertion into the femoral vein. DFPP was performed using filtration-based device HF440 (Infomed, Geneva, Switzerland). Anticoagulants were not used during DFPP. Each treatment lasted for 2 to 3 hours, and the average apheresis volume was approximately 4200 mL per session of DFPP (3500–5000 mL).

Table 1

Baseline characteristics of patients.

Case	Case 1	Case 2	Case 3
Age	39	34	36
Gender	Male	Female	Female
BMI, kg/m^2	35	29.6	19.5
Alcohol use	Yes	No	No
Diabetes mellitus	Yes	No	No

BMI = body mass index.

2.6. Case reports

2.6.1. Case 1. A 39-year-old male patient with a medical history of hypertension and type 2 diabetes mellitus presented himself to the emergency department (ED) with acute abdominal pain. The finding of physical examination showed diffuse abdominal tenderness, but no guarding or rebound tenderness. Laboratory studies revealed the results of a lipase serum level of 188 U/L (normal fasting range: 11–82 U/L; 3.13 μmol/s L, range: 0.18–1.37 μmol/s L) and serum TG level of 1926 mg/dL (21.8 mmol/L). CT imaging finding showed focal inflammatory changes extending from the pancreatic head to the duodenum that was consistent with focal acute pancreatitis (groove pancreatitis). The patient was kept nothing by mouth and received pain control, intravenous fluid, antibiotics with meropenem 500 mg every 8 hours intravenously. The patient was started on DFPP, and a total of 5000 mL of plasma volume had been filtered (50 mL/kg body weight). Day 1 after DFPP, his serum TG was decreased to 893 mg/dL (10.1 mmol/L). He tolerated DFPP well without developing of any complications. The patient continuously received intravenous insulin infusion to sustain falling of serum TG levels. He remained under intensive care treatment for another 5 days. He was reassigned to general ward on Day 6, followed by a 30 days hospitalization. With continual prescribed fenofibrate 200 mg treatment, the patient had TG level 349 mg/dL (3.9 mmol/L) at the time of discharge.

2.6.2. Case 2. A 34-year-old female patient with history of pancreatitis secondary to HTG (with poor compliance with gemfibrozil 600 mg/d) presented herself to our ED with nausea, emesis, and abdominal pain. The finding of physical examination revealed diffuse abdominal tenderness with hypoactive bowel sound. Laboratory studies revealed a lipase level of 1759 U/L (normal fasting range: 11–82 U/L; 29.3 μmol/s L, range: 0.18–1.37 μmol/s L) and TG level of 11,754 mg/dL (132.8 mmol/L). The finding of CT imaging was consistent with focal acute pancreatitis. The patient was kept nothing by mouth, and was treated with pain management, intravenous fluid, antibiotics with meropenem 500 mg every 8 hours intravenously. She was started on DFPP, and a total of 4000 mL of plasma had been filtered (60 mL/kg of body weight). After DFPP, her serum TGs decreased to 2030 mg/dL (22.94 mmol/L). She tolerated DFPP well without development of any complications. Although her TG serum level was reduced to 373 mg/dL (4.21 mmol/L) on the 3rd day after admission, but she required surgical drainage and followed by a prolonged hospital stay. She was discharged from the hospital on day 52 after initial presentation to our hospital. In continual medical treatment with fenofibrate 200 mg, the patient had TG level 195 mg/dL (3.9 mmol/L) at the time of discharge.

2.6.3. Case 3. A 36-year-old female patient, gravida one at 26th week 2 days gestational age, who had suffered from sudden onset of epigastric pain with nausea for 1 day. She had a history of HTG under medical treatment, but her TG treatment had been discontinued since her pregnancy. The finding of physical examination revealed diffuse abdominal tenderness, without

Table 2

Laboratory data of patients before and after each session DFPP.

Case	Case 1	Case 2	Case 3	Normal ranges
TSH, IU/mL	4	4.77	4.02	0.38–5.33
Total cholesterol, mg/dL	298	1461	2185	<200
LDL-C, mg/dL	50	143	93	<130
HDL-C, mg/dL	35	38	15	>40
Lipase on admission, U/L	188	1758	405	11–82
Amylase on admission, U/L	47	294	415	29–103
Time laps before initiation of DFPP, h	12	24	24	
BISAP score	1	1	2	
Ranson score on admission	0	1	1	
Ranson score at 48 h	3	2	6	
APACHE II before DFPP	14	16	12	
APACHE II after DFPP	1	14	9	
TG at presentation, mg/dL	1926	11,754	10,385	<150
TG before apheresis, mg/dL	1926	2030	2575	
TG after apheresis, mg/dL	349	373	272	
TG on discharge, mg/dL	320	195	440	
Number of apheresis session	1	2	2	
Length of hospitalization, d	33	52	25	
Outcomes	Survived	Survived	Survived	

DFPP = double filtration plasmapheresis, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TG = triglyceride, TSH = Thyroid- Stimulating Hormone.

any presence of muscle guarding or other evidence of peritoneal irritation. Laboratory studies revealed a serum lipase level of 405 U/L (normal fasting range: 11–82 U/L; 6.75 μmol/s L, range: 0.18–1.37 μmol/s L) and TG level of 10,385 mg/dL (117.35 mmol/L). Abdominal ultrasound imaging was consistent with acute edematous pancreatitis.

The patient was kept nothing by mouth, and was provided pain management and intravenous fluid. On 3rd day of admission, her respiratory distress has progressively worsened. The patient received an emergency cesarean delivery due to the wellness concern for both mother and child. Large amount of purulent fluid was drained from the peritoneal cavity. The finding of abdomen and pelvis CT showed edematous pancreas with peripancreatic heterogeneous fluid accumulation, without any evidence of necrosis, pseudocyst, thrombosis, or other extra-pancreatic abscess. She received DFPP on the 3rd and 5th day of admission, and a total volume of 4500 and 4000 mL of plasma were filtered on the 3rd and 5th day, respectively (65 mL and 60 mL/kg body weight). On the 6th day of admission, she recovered from pulmonary edema, and was weaned off from the mechanical ventilation. Her TG serum level was reduced to 440 mg/dL (4.97 mmol/L). She tolerated DFPP well without development of any complications. The patient was discharged on the 22nd day of admission, and had continued to be on oral fenofibrate 200 mg/d. The patient and her baby remained well with no sequelae at follow-up clinic later.

3. Discussion

HTG is a well-established cause of acute pancreatitis. Numerous studies have reported that serum level of TG can be effectively reduced by the extracorporeal methods in patients complicated with acute pancreatitis. But there are no randomized clinical trials exist to support the therapeutic role of apheresis in HTG-AP. Those evidences merely from case reports and case series[14–17] have suggested beneficial effects of plasmapheresis in reducing TG serum levels, circulating activated enzymes, and proinflammatory mediators. An observation study suggested that TG levels are not correlated with disease severity (i.e., APACHE II) or to influence mortality or length of hospital stay.[18] Based upon those background information, HTG-AP is currently considered in category III indication for plasmapheresis and graded 2C in the American Society of Apheresis 2016 apheresis guideline.[19,20]

Using DFPP in reduction of TG, our patients achieved 84.7% of TG reduction (Table 2). This record is higher than the previous reported experiences of 60% to 70% TG reduction with DFPP,[21] and is compatible with therapeutic PE method in TG reduction of 84.5%.[22] Both case 1 and case 2 were discharged uneventfully, but they required for more than a month of prolonged hospital stay. In the case 3, both mother and baby survived and remained healthy after the discharge (case 3).

Previously studies suggested that a rapid decrease in TG serum levels is the key to the successful management of HTG-induced pancreatitis.[23] Our study showed the promising effect in reducing serum TG levels with DFPP in our patients, but this treatment did not have any obvious influence on the patients' survival or length of hospitalization (Table 2). As many studies suggested, the timing of initiation of DFPP might crucial.[10,24] There are several reports showing that maximal reduction in morbidity and mortality can be achieved when apheresis is used as early as possible.[8,25] All of our patients received DFPP within 24 hours after symptoms onset.

Furthermore, the APACHE II scores averaged 16.3 ± 4.8 in our patients. The risk of mortality is 44% when APACHE II score >15 in patients with acute pancreatitis.[26] All of our patients survived, but early initiation of DFPP treatment seemed to have no obvious influence on the patient's length of hospitalization. The severity of disease is the possible factor to explain the need for extended period of hospitalization in our patients.

4. Summary

The current evidence and our experience do not support the role of DFPP in reducing mortality or morbidity rate from HTG-AP. But it is an effective therapeutic option in addition to conservative medical treatment including pharmacological therapy, diet, and

lifestyle changes to lower serum TG level. Whether the effect of DFPP in lowering TG level can be translated into survival benefit is unknown. Therefore, randomized controlled studies are needed to definitely verify its survival benefit.

Author contributions

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