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Acute pancreatitis due to hypertriglyceridemia: Plasmapheresis versus medical treatment

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Abstract:

OBJECTIVE: Hypertriglyceridemia (HTG) is the third-most common cause of acute pancreatitis. Plasmapheresis is an extracorporeal treatment method used for treatment. This study aimed to investigate the efficacy of medical treatment and plasmapheresis in patients with acute pancreatitis due to HTG.

METHODS: This was a retrospective cross-sectional study. The patients were divided into two groups according to the treatment they received as those who received only medical treatment and those who performed plasmapheresis with medical treatment. According to the treatment received by the patients; clinical, demographic, and laboratory data, Ranson scores, and bedside index of severity in acute pancreatitis (BISAP) scores, decrease in triglyceride levels in 24 h, length of hospital stay, and outcomes were recorded.

RESULTS: Forty-seven patients were included in the study. The level of triglyceride decreases at the 24th h was 59.7% ±17.3% in those who received medical treatment and was 70.4% ±15.1% in those who received plasmapheresis (P = 0.032). Receiver operating characteristic curve analysis was performed to predict the need for plasmapheresis treatment, area under the curve (AUC) value of the triglyceride level was the highest (AUC: 0.822, 95% confidence interval: [0.703–0.940]; P < 0.001), the sensitivity and specificity were 83.3% and 72.4%, respectively, and the cut-off value of triglyceride was accepted as 3079.5 mg/dL.

CONCLUSION: Plasma triglyceride levels and BISAP score on admission may help physicians to predict the need for plasmapheresis. Plasmapheresis helps to rapidly reduce triglyceride levels in patients with HTG-associated acute pancreatitis.

Keywords:

Bedside index of severity in acute pancreatitis, hypertriglyceridemia, lipemic index, pancreatitis, plasmapheresis

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Introduction

Acute pancreatitis is a life-threatening acute inflammatory disease. Diagnosis is made by the presence of two of the following criteria: abdominal pain, a three-fold increase in serum amylase and lipase levels, and radiologic findings.[1] Hypertriglyceridemia (HTG) is the third-most common cause of acute pancreatitis after gallbladder (biliary system) diseases and alcohol, and accounts for 1%–14% of all acute pancreatitis cases.[2,3]

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Box-ED Section

What is already known on the study topic?

- Among all the causes of acute pancreatitis, hypertriglyceridemia (HTG) ranks third after gallstone disease and chronic alcohol abuse
- Conventional treatment (fasting, fluid resuscitation, nutritional support, proper pain management, traditional lipid-lowering drugs, insulin therapy, and heparin infusion) and therapeutic plasma exchange are the treatment options.

What is the conflict on the issue? Has it important for readers?

- Rapid reduction in triglyceride levels may reduce the risk of developing complications, length of hospital stay, and mortality.

How is this study structured?

- This study was conducted as a single-center, retrospective, cross-sectional study with 47 adult patients' data on HTG-associated acute pancreatitis (HTG-AP) treatment options.

What does this study tell us?

- Bedside index of severity in acute pancreatitis scores and triglyceride levels were found to be statistically significantly higher in HTG-AP patients who underwent plasmapheresis
- Plasmapheresis significantly reduced serum triglyceride levels. However, there was no statistically significant difference between the two treatment groups in any of the systematic complications and mortality.

The pathophysiology of HTG-associated acute pancreatitis (HTG-AP) is not known exactly. Free fatty acids emerge as a result of the breakdown of excess triglycerides by pancreatic lipase. Free fatty acids are toxic and are thought to cause ischemia and necrosis in the pancreas by increasing plasma viscosity with increased chylomicrons.[4,5]

Acute pancreatitis may occur when the plasma triglyceride level is above 500 mg/dL, but its frequency increases when it is above 1000 mg/dL (11.3 mmol/L), and this increased level of plasma triglyceride causes more severe acute pancreatitis.[6] However, the plasma triglyceride level that causes acute pancreatitis and whether the clinic is more severe than other etiologies of acute pancreatitis remains unclear.[1,3,7] Amylase analysis can also be negatively affected by the presence of lipemia, which can cause a diagnosis of acute pancreatitis to be missed. This is especially troubling as high serum triglyceride is a risk factor for acute pancreatitis, and therefore, samples from acute pancreatitis patients may be lipemic and mask raised amylase activity.[8] Therefore, in patients with high clinical suspicion of acute pancreatitis, if amylase values are normal and lipemic index >+1 lipemia/turbidity (LIP) level >40 mg/dl), plasma triglyceride level and abdominal computed tomography will help the diagnosis.

In the treatment of HTG-AP, there are medical treatment methods and extracorporeal treatment methods such as plasmapheresis. In conventional treatment, fluid resuscitation, nutritional support, proper pain management, traditional lipid-lowering drugs, insulin therapy, heparin infusion, and if necessary, antibiotics are available.[9] Plasmapheresis, on the other hand, is an extracorporeal treatment method that helps rapid clearance of triglycerides and chylomicrons from plasma. However, insufficient clinical studies are showing that plasmapheresis is more effective than medical therapy in the treatment of HTG-AP.[10]

This study aimed to determine the treatment option (medical treatment/medical treatment + plasmapheresis) of patients with HTG-AP in the emergency department and to evaluate the rate of decrease in serum triglyceride levels at the 24th h according to treatment modalities.

Methods

Study design and setting

This study was a retrospective cross-sectional study. It was conducted in a tertiary hospital with approximately 290,000 annual emergency admissions. Patients over the age of 18 years who were admitted to the emergency department between July 1, 2019 and December 31, 2020, and were diagnosed with having HTG-AP were included in the study. The study was started after obtaining approval from the Cukurova University Medical Faculty Non-Interventional Clinical Research Ethics Committee, through its meeting number 111 and decision 67, dated May 21, 2021.

Selection of participants

The data were recorded on a uniform data collection form. The data were accessed through hospital information operating system records and patient files. The diagnosis of acute pancreatitis was confirmed by clinical findings, elevated amylase, and lipase values, and computed tomography of the abdomen. Patients with high lipemic index (>+1 or LIP >40 mg/dl) and triglyceride levels >1000 mg/dL in biochemical parameters were hospitalized with the diagnosis of HTG-AP. Patients aged under 18 years, pregnant women, patients with acute pancreatitis due to other etiologic causes (gallstones, alcohol, infection, hypercalcemia, hyperparathyroidism, pancreaticobiliary tumor), and

patients whose data could not be reached fully were excluded from the study.

According to the treatment they received, the patients were divided into two groups as those who received only medical treatment and those who performed plasmapheresis with medical treatment. Fluid resuscitation, nutritional support, insulin infusion, heparin/low-molecular-weight heparin, proton-pump inhibitors, fenofibrate, proper analgesics, and antibiotics if necessary were given to all patients as medical treatment. The plasmapheresis treatment decision was made in line with the patient's clinical findings, laboratory tests, radiological imaging methods, the decision of the consultant physician, and recommendations of the American Society for Apheresis (ASA). ASA revised the recommendation level of plasmapheresis in acute hypertriglyceridemic pancreatitis as category 3 Grade 1C (application of apheresis based on observational data, the optimal role of apheresis therapy could not be determined; the decision is left to the physician) and recommended plasmapheresis if available.[11,12] In line with this recommendation, patients with triglyceride levels of ≥1000 mg/dL, severe abdominal pain, moderate acute pancreatitis according to the Atlanta classification, and patients who underwent plasmapheresis in the first 24 h were included in the study. According to the Atlanta classification, moderate pancreatitis is defined as transient organ failure and involvement of two or more of the three organs (respiratory, cardiovascular, renal) used in the Marshall score system. Follow-up triglyceride levels were measured at the end of the 24th h in both patient groups. The rate of triglyceride decrease, the length of hospital stays (days), and the rate of complications were evaluated.

Therapeutic plasmapheresis exchange (TPE) was performed on the patients with the Prismaflex TPE 2000 (Baxter Medical Ab. Kista, Sweden) device for 2–4 h, taking into account the patient's weight, hematocrit level, and parenteral treatments. Plasmapheresis was performed with albumin or plasma. A double-lumen centrifuge was used in all TPE procedures. A central venous catheter (double-lumen catheter) was used in patients in whom vascular access from the peripheral vein was not suitable. Plasma volume was changed once (rarely twice) during each TPE procedure and replaced with a bicarbonate-based electrolyte solution with 30 g/L albumins. Anticoagulation in plasma apheresis was performed with ADC-A anticoagulation citrate dextrose solution.

Data collection and measurement

In addition to the demographic characteristics of the patients, laboratory parameters, Bedside Index of Severity in Acute Pancreatitis (BISAP) scores,[13] Ranson scores[14] on admission to the emergency room, treatment option (medical treatment, plasmapheresis), length of hospital stay, systematic complications (fever, ARDS, acute renal injury, etc.) and outcomes (discharge, mortality) were recorded.

Lipemic index values were obtained using the serum index function of the Beckman Coulter AU2700 (Beckman Coulter Inc., Brea CA, USA, 2017) analyzer. Bichromatic turbidity test was performed. Patient samples were diluted with icterus and hemolysis (LIH) reagent and the absorbance was measured at 6 wavelengths. If the LIP level was <40 mg/dl, the samples were considered lipemicly normal (LIP referans level [+1] =40–99 mg/dl, [+2] =100–199 mg/dl, [+3] =200–299 mg/dl, [+4] =300–500 mg/dl, [+ 5] = >500 mg/dl).[15] Samples could be lipemic for a number of reasons (e.g. taken soon after a high-fat meal or due to a hyperlipidemia of either primary of secondary cause.[8]

Patient samples were diluted with jaundice and hemolysis (LIH) reagent and absorbance was measured at 6 wavelengths. Samples were considered normal as lipemic if the LIP level was <40 mg/dl (LIP reference level [+1] =40–99 mg/dl, [+2] =100–199 mg/dl, (+3) =200–299 mg/dl, [+4] =300–500 mg/dl, [+5] = >500 mg/dl.[15] Samples may be lipemic for a number of reasons (e.g. immediately after a high-fat meal or due to hyperlipidemia of any of the secondary causes).[8]

The BISAP scores and Ranson scores of all patients were calculated and recorded on admission. The BISAP score includes five parameters: blood urea nitrogen (BUN) >25 mg/dL, Glasgow Coma Scale <15, systemic inflammatory response syndrome, age >60 years, and the presence of pleural effusion on imaging. Each parameter contributes one point to the score. A BISAP score of 0–2 is associated with low mortality and 3–5 with high mortality.[13] Ranson's scores consist of 11 criteria. Five criteria are calculated during hospitalization and six are calculated 48 h later. Each criterion contributes one point to the score. Based on the calculated score, the severity and prognosis of pancreatitis are estimated. Age, white blood cell count, glucose, lactate dehydrogenase, and aspartate aminotransferase levels are checked during hospitalization. At the 48th h after hospitalization, a decrease in hematocrit, and increases in BUN, calcium, arterial oxygen, base deficit, and fluid sequestration are calculated. According to Ranson's criteria, the severity of pancreatitis is mild if the score is 0–3 and severe if the score is 4–11. According to Ranson's criteria, mortality is estimated as 2% if the score is 0–2 points, 15% if the score is 3–4 points, 40% if the score is 5–6 points, and 100% if the score is 7–11 points.[14]

Sample size

The sample size was estimated with G*Power for Mac OS X (version 3.1.9.2; Universität Dusseldorf, Germany). Accordingly, with a Type-1 error of 5%, a Type-2 error of 5% (power 95%), and a two-sided analysis, the sample size was determined as 36 patients. Considering a possible protocol bias, adding 10% of patients to each arm was planned; hence, 40 were determined as the minimum number of patients to be included.

Statistical analysis

The SPSS version 22 package program was used in the statistical evaluation of the data obtained in the study (SPSS Inc., Chicago, Illinois, USA). As descriptive statistics, mean and standard deviation are given for those with normal distribution, and minimum, maximum, median, and 25%–75% percentile values were given for those that did not show normal distribution. The Chi-square test was used to compare categorical variables, Student's *t*-test was used for comparisons between two groups in cases of normal distribution, and the MannWhitney *U*-test was used in cases of nonnormal distribution. A receiver operating characteristic (ROC) curve was used to investigate the accuracy of the triglyceride level, lipemic index, and BISAP score at the time of admission in predicting the need for plasmapheresis. The Youden index, which took the highest sensitivity and specificity point on the ROC curve, was used to determine the cut-off value. To investigate the accuracy of the diagnostic test, sensitivity and specificity parameters were calculated with a 95% confidence interval and presented as a table. $P < 0.05$ were accepted as statistically significant.

Results

During the study period, 501 patients were diagnosed with acute pancreatitis in the emergency department. Fifty-six of these patients were diagnosed with HTG-AP. The data of 7 of these patients could not be fully reached. Two patients did not accept treatment and left the emergency department voluntarily. A total of 47 patients with HTG-AP and plasma triglyceride levels above 1000 mg/L were included in the study. Medical treatment only was administered to 29 patients (Group 1) and plasmapheresis was applied to 18 patients (Group 2) [Figure 1].

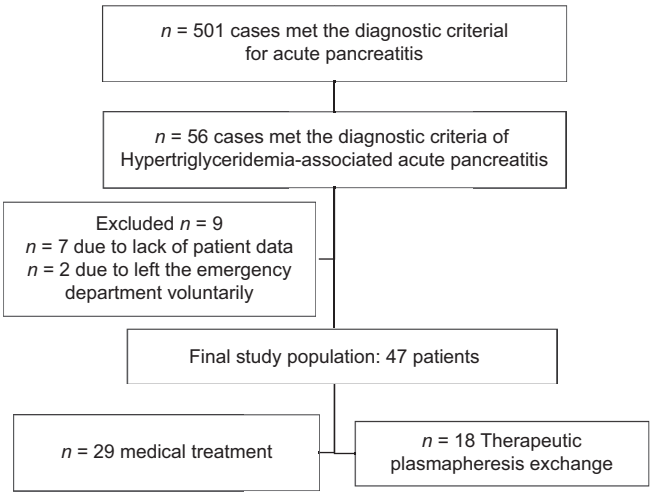

Figure 1: Flow chart of the patients included in the study

The distribution of the patients according to the treatment they received, their demographic characteristics, comorbidities, and the presence of obesity (body mass index >30 kg/m^2) are summarized in Table 1. Of all the patients, 44.7% (n = 21) were female and 55.3% (n = 26) were male. Of the patients who underwent plasmapheresis, 61.1% (n = 11) were female and 38.9% (n = 7) were male. There was no statistically significant difference between the treatments given according to sex (P = 0.074). The mean age of the patients who underwent plasmapheresis was 37.2 ± 10.5 years, and the mean age of the patients who received medical treatment was 41.3 ± 5.4 years (P = 0.081).

BISAP scoring was used to determine the severity of acute pancreatitis in the patients. The BISAP scores were found to be statistically significantly higher in those who underwent plasmapheresis (1.34 ± 0.6 vs 1.94 ± 1, P = 0.014) [Table 1].

Ranson's score was calculated on admission to the emergency department. There was no statistically significant difference between the Ranson score on admission and the preferred treatment method of the patients (1.28 ± 1.2 vs. 1.28 ± 0.8, P = 0.995) [Table 1].

The triglyceride levels of the patients were measured at the time of hospitalization and the 24th h after treatment. The mean plasma triglyceride level was statistically significantly higher in those who underwent plasmapheresis (2809.4 ± 1986.7 vs. 5427.1 ± 2569.6, P = 0.001). The level of triglyceride decrease in 24 h was 59.7% ±17.3% in those who received medical treatment and 70.4% ±15.1% in those who underwent plasmapheresis. The percentage of triglyceride reduction in 24 h was statistically significantly higher in patients who underwent plasmapheresis (P = 0.032). The lipemic index was higher in patients who underwent plasmapheresis (4.7 ± 2.1 vs. 6 ± 1.2, P = 0.014) [Table 1].

The ROC curve analyses performed to determine the prediction of plasmapheresis treatment need by serum triglyceride level, lipemic index, and BISAP scores are shown in Figure 2. It was determined that the triglyceride area under the curve (AUC) value was the highest (AUC: 0.822, 95% confidence interval [CI]:

Table 1: Characteristics of the patients according to treatment

Variable	Group 1 (*n*=29)	Group 2 (*n*=18)	*P*
Age (mean±SD)	41.4±10.5	37.2±5.4	0.081
Gender, *n* (%)			
Female	10 (34.4)	11 (61.1)	0.074
Male	19 (65.6)	7 (38.9)	
Comorbidity, *n* (%)			
Hypertension	2 (6.8)	2 (11.1)	0.615
Hyperlipidemia	18 (62)	9 (50)	0.416
Diabetes mellitus	8 (27.6)	9 (50)	0.120
Past pancreatitis	9 (31)	4 (22.2)	0.511
Obesity (BMI >30)	2 (6.8)	2 (11.1)	0.615
BISAP score (mean±SD)	1.34±0.6	1.94±1	**0.014***
Ranson score (mean±SD)	1.28±1.2	1.28±0.8	0.995
Laboratory parameters (median) (25%-75%)			
WBC (10^3 µL)	13.5 (10-18)	14.6 (10.8-17.7)	0.638
Hemoglobin (g/dL) (mean±SD)	15.2±2.5	16.7±3.2	0.088
Hematocrit (g/dL) (mean±SD)	39±4.5	39±5.7	0.992
Platelet (10^3 µL)	286 (235-337)	327.5 (254-405)	0.078
Glucose (mg/dL)	143 (109-240)	229.5 (165-303)	0.168
Aspartate transaminase (U/L)	31 (23-42)	39 (16-56)	0.470
Alanine transaminase (U/L)	17 (11-24)	17.5 (3-34)	0.835
Gamma glutamyl transferase (U/L)	29 (19-43)	29 (14-55)	0.734
Alkaline phosphatase (U/L)	68 (62-94)	66.5 (59-107)	0.776
Calcium (mmol/L)	9.3 (8.9-9.6)	8.5 (7-9.5)	0.062
LDH (U/L)	313 (203-406)	328 (234-412)	0.638
Total bilirubin (mg/dL)	0.5 (0.3-0.7)	0.6 (0.5-0.8)	0.207
Direct bilirubin (mg/dL)	0.1 (0.1-0.1)	0.1 (0.1-0.1)	0.866
Amylase (U/L)	181 (84-301)	329 (157-655)	0.054
Lipase (U/L)	322 (185-781)	587.5 (410-1563)	**0.039***
Triglyceride (mg/dL) (mean±SD)	2809.4±1986.7	5427.1±2569.6	**0.001***
C-reactive protein (mg/L)	11.2 (5.3-21)	20.8 (9.7-27.4)	0.053
BUN (mg/dL)	10.7 (8.8-13)	9.3 (7-12.6)	0.288
Creatinine (mg/dL)	0.7 (0.5-0.8)	0.7 (0.4-0.9)	0.800
Lipemic index (mean±SD)	4.7±2.1 (3.9-5.5)	6±1.2 (5.3-6.5)	**0.014***
Systematic complications, *n* (%)			
Fever	3 (10.3)	4 (22.2)	0.100
ARDS	0	2 (11.1)	
Acute renal injury	2 (6.8)	0	
Diabetic ketoacidosis	0	1 (5.6)	
Arrhythmia	0	1 (5.6)	
İntraabdominal abscess	1 (3.4)	0	
Length of hospital stay (days) (mean±SD)	6.2±5.9	19.8±26.2	**0.043***
Mortality, *n* (%)	0	2 (11.1)	0.275

*Bold text indicates a statistically significant difference with a $P<0.05$. Group 1: Medical treatment, Group 2: Plasmapheresis. BISAP: Bedside ındex of severity in acute pancreatitis, SD: Standard deviation, BMI: Body mass index, ARDS: Acute respiratory distress syndrome, WBC: White blood cell, BUN: Blood urea nitrogen, LDH: Lactate dehydrogenase

0.703–0.940; $P < 0.001$) [Table 2]. When the cut-off value determined for the prediction of plasmapheresis need was accepted as 3079.5 mg/dL for the triglyceride level, the sensitivity was calculated as 83.3% and the specificity as 72.4%. The AUC value of the BISAP score was calculated (AUC: 0.681, 95% CI: 0.518–0.844; $P = 0.039$). When the cutoff value of the BISAP score was accepted as 1.5, the sensitivity was calculated as 61.1% and the specificity as 72.4%. The AUC value of the lipemic index was calculated (AUC: 0649, 95% CI: 0.493–0.805; $P = 0.088$). When the cutoff value for the lipemic index was accepted as 3.5, the sensitivity was calculated as 94.4% and the specificity as 34.5% [Table 2].

There was no statistically significant difference between the two groups in any of the systematic complications (fever, ARDS, acute renal injury, diabetic ketoacidosis, arrhythmia, intraabdominal abscess) ($P = 0.100$). The length of stay in the hospital was statistically significantly longer in patients

Table 2: Receiver-operating characteristics analysis of triglyceride, bedside ındex of severity in acute pancreatitis score, lipemic index values for the need of plasmapheresis

	AUC	SE	95% CI	Cut-off	Sensitivity-95% CI	Specificity-95% CI	+LR	–LR	*P*
Triglyceride	0.822	0.061	0.703-0.940	3079.5	83.3 (58.6-96.4)	72.4 (52.8-87.3)	3.1	0.2	**<0.001***
BISAP	0.681	0.083	0.518-0.844	1.5	61.1 (35.8-82.7)	72.4 (52.8-87.3)	2.3	0.5	**0.039***
Lipemic index	0.649	0.080	0.493-0.805	3.5	94.4 (72.7-99.9)	34.5 (17.9-54.3)	1.4	0.1	0.088

*Bold text indicates a statistically significant difference with a *P*<0.05. BISAP: Bedside ındex of severity in acute pancreatitis, LR: Likelihood ratio, AUC: Area under the curve, SE: Standard error, CI: Confidence interval

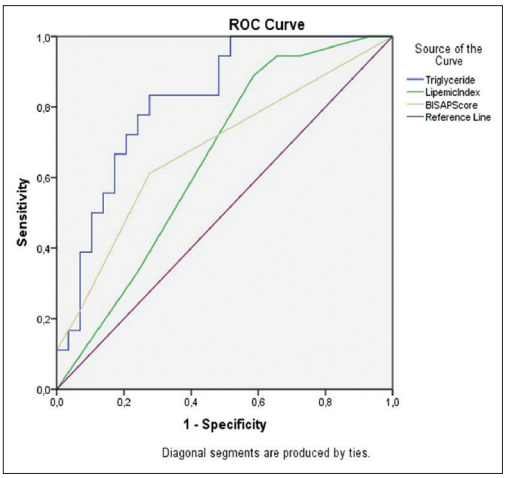

Figure 2: ROC curve showing of triglyceride, BISAP score, lipemic index values for the need of plasmapheresis. ROC: Receiver operating characteristic, BISAP: Bedside index of severity in acute pancreatitis

who underwent plasmapheresis (6.2 ± 5.9 days vs. 19.8 ± 26.2 days, *P* = 0.043) [Table 1].

Although there was no mortality during hospitalization in patients who received medical treatment only, two of the patients who underwent plasmapheresis died during hospitalization. There was no statistically significant difference between the groups in terms of mortality during hospitalization (*P* = 0.275).

Discussion

In our study, the level of triglyceride decrease in 24 h was statistically significantly higher in patients who underwent plasmapheresis (70.4% ±15.1%) than those who received medical treatment (59.7% ±17.3%) (*P* = 0.032). Triglyceride level (AUC: 0.822, 95% CI: 0.703–0.940; *P* < 0.001) and BISAP score (AUC: 0.681, 95% CI: 0.518–0.844; *P* = 0.039) are helpful in determining the need for plasmapheresis treatment of patients.

Although there are studies in the literature stating that the clinical course of the disease in HTG-AP is not different from acute pancreatitis with other etiologies,[1] studies have also been published showing that it is associated with more severe disease[16] and higher mortality.[17] Patients with severe disease may present with systemic inflammatory response, pancreatic necrosis, sepsis, and organ failure, resulting in death in 20%–25%.[18] Therefore, rapid reduction of serum triglyceride levels can reduce mortality and complications. Although drugs such as fibrates, niacin, and statins are effective in the long term, they are not helpful in the acute phase.[3] In recent years, there have been studies on reducing triglyceride levels with continuous insulin infusion and heparin therapy. Insulin reduces triglyceride levels by stimulating lipoprotein lipase activity. Heparin also reduces triglyceride levels by causing the release of lipoprotein lipase from the endothelium into the circulation and by causing the release of hepatic triglyceride hydrolase.[19,20] However, the use of heparin is controversial because it may cause bleeding in the pancreatic bed and exacerbate the clinical condition. Dhindsa *et al*. investigated the efficacy of insulin infusion in 51 patients with HTG-AP with triglyceride levels above 1000 mg/dL, they showed that the triglyceride level decreased below 1000 mg/dL on the 3rd day.[21] Coskun *et al*. reported a decrease in triglyceride concentrations to <500 mg/dL 3 days after regular intravenous insulin therapy in 12 patients that they followed up with the diagnosis of HTG-AP.[22]

Chylomicrons are triglyceride-rich lipid particles that cause ischemia by occluding pancreatic capillaries, and they also cause the release of pancreatic lipase. Increased lipase causes an increase in cytotoxic free fatty acids in the circulation. These fatty acids cause vascular endothelial cell damage, erythrocyte aggregation, and pancreatic ischemic injury, both by causing acute pancreatitis and by activating toll-like receptor-2 (TLR2) and TLR-4 receptors.[17,23] Therefore, it is important to reduce triglyceride levels without delay. Plasmapheresis should be started early to increase clinical benefit, reduce complications, and provide an early rapid decrease in triglyceride levels. In our study, patients underwent plasmapheresis in the first 24 h of their admission. Compared with patients who received medical treatment only, the rate of triglyceride reduction at 24 h was statistically significantly higher in patients who underwent plasmapheresis.

In studies comparing both treatment modalities in patients with HTG-AP, it was stated that plasmapheresis was of critical importance, although there was no significant difference in terms of complication development, lowering triglyceride rates, mortality, and morbidity.[24,25] High triglyceride concentrations

can be the trigger of acute inflammatory reactions and plasmapheresis can support the enzyme lipoprotein lipase, which breaks down fatty acids, and can ensure that triglycerides are cleared from the plasma. Based on this, a study reported a 70% reduction in triglyceride levels after one plasmapheresis session and recommended plasmapheresis in the first 24 h to achieve a target triglyceride level of <500 mg/dL.[26] In a study in which triglyceride levels were rapidly reduced by 70% or more, it was suggested that this rapid decrease ended multi-organ failure and improved shock.[27] Some studies emphasized that the prognosis after plasma exchange might depend on the timing of the initiation of plasma exchange.[28] In our study, plasmapheresis was performed on the patients in the first 24 h, and a 70.4% decrease was observed in triglyceride levels after a single session. The time of initiation of treatment may play an important role in complications and the severity of HTG-AP, but there are insufficient studies on this subject; more studies are needed.

Li *et al*. compared the scoring systems in the course of HTG-AP in 238 patients and emphasized that BISAP scoring might be the best system to predict the severity and prognosis of the disease.[29] In our study, when the patients were compared according to the treatment they received, the triglyceride levels, and BISAP scores of the patients who underwent plasmapheresis were statistically significantly higher. There is no definite opinion in the literature about which patients should be treated with plasmapheresis in the first 24 h. There is no study in the literature examining the triglyceride levels and BISAP scores in predicting the need for plasmapheresis, and prospective studies with larger numbers of patients are needed.

In our study, when the patients' mortality and morbidity were compared according to the treatment they received, complications were observed more frequently in the plasmapheresis group. However, it was not statistically significant. No mortality was observed in patients who received medical treatment, but two patients who underwent plasmapheresis died. A meta-analysis including 15 observational studies has shown that plasmapheresis has a tendency to assist in the reduction of serum TG in the first 24 h after admission, whereas it fails to improve the clinical outcomes, including systematic complications (respiratory failure/ARDS, acute renal injury, and hypotension), local complications, the requirement for surgery, and hospitalization duration. At the same time, there was no evidence that plasmapheresis causes more in-hospital deaths. This may be due to selection bias considering that all the included studies were nonrandomized controlled trials, in which the clinicians decided on the choice of treatment, and reasonably, plasmapheresis would be the option for the more severe patients.[30] Similarly, in our study, the decision of plasmapheresis was decided by the clinician according to the severity of the patient's clinic. This is why complications and mortality are higher.

Limitations

Our study has some limitations. The study was conducted in a single center and the number of patients was low. The treatment selection of the patients was made according to the clinician's decision, similar to other studies in the literature. This selection may be seen as biased. Prospective, multicenter studies with large patient populations are needed to base patient selection on more objective decisions and the most effective treatment options.

The study was also designed retrospectively. Due to some technical problems and a lack of trained personnel in our hospital, plasmapheresis could only be applied to patients between July 1, 2019 and December 31, 2020. The duration of the study has been designed according to the dates when plasmapheresis can be performed in our hospital. Even though seasonal variation has been proved in the levels of some blood lipids, reports regarding minimum and peak values of serum TG according to the seasons have yielded contradicting results.[31] Therefore, it is doubtful whether the duration of our study for 1.5 years will cause a limitation in terms of the seasonal cycle. However, the incompleteness of this seasonal cycle can be seen as a limitation.

Conclusion

Although there is insufficient evidence that early performance of plasmapheresis will be beneficial in HTG-AP, it may be beneficial to perform it in addition to medical treatment because an earlier and rapid decrease in plasma triglyceride levels may affect the clinical course. Although the decision on which patients should be treated with plasmapheresis is often taken by the clinician according to the severity of the patient, the plasma triglyceride level and BISAP score may help physicians to predict the need for plasmapheresis according to the data of our study.

Authors' contributions

GKS, MG, SS, and SA were the coordination researcher of the study and were concerned with study design, implementation, study monitoring, data collection, and interpretation. GKS, SS, MG, SA, and NKU were involved in the study design, study monitoring and supervision, and interpretation of data. MG, SA, NKU, YC, and MSS were researchers and were involved in data collection and interpretation. GKS, SS, MG, SA, NKU, YC, and MSS were involved in study design, statistical analysis, and data interpretation. All authors reviewed the drafts and approved the final version of the article for submission.

Conflicts of interest

None Declared.

Ethical approval
The Ethical Committee of Cukurova University approved the study and confirmed that the protocol was compatible with the second Declaration of Helsinki (Approval date: May 21, 2021, Decision number: 67 Meet number: 111).

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