Contents lists available at ScienceDirect

Transfusion and Apheresis Science

Use of the APACHE II score to assess impact of therapeutic plasma exchange for critically ill patients with hypertriglyceride-induced pancreatitis

Shazia Nakhoda [a,*], Ann B. Zimrin [b], Maria R. Baer [b], Jennie Y. Law [b]

[a] Department of Internal Medicine, University of Maryland Medical Center, 22 South Greene Street, Baltimore, Maryland 21201, USA
[b] Division of Hematology/Oncology, Marlene and Stewart Greenebaum Comprehensive Cancer Center, University of Maryland Medical Center, 22 South Greene Street, Baltimore, Maryland 21201, USA

ARTICLE INFO

ABSTRACT

Objectives: Hypertriglyceridemic (HTG) pancreatitis carries significant morbidity and mortality and often requires intensive care unit (ICU) admission. Therapeutic plasma exchange (TPE) rapidly lowers serum triglyceride (TG) levels. However, evidence supporting TPE for HTG pancreatitis is lacking.
Methods: Ten patients admitted to the ICU for HTG pancreatitis underwent TPE at our institution from 2005–2015. We retrospectively calculated the Acute Physiology and Chronic Health Examination II (APACHE II) score at the time of initial TPE and again after the final TPE session to assess the impact of triglyceride apheresis on morbidity and mortality associated with HTG pancreatitis.
Results: All 10 patients had rapid reduction in TG level after TPE, but only 5 had improvement in their APACHE II score. The median APACHE II score decreased from 19% to 17% after TPE, correlating with an 8% and 9% decrease in median predicted non-operative and post-operative mortality, respectively. The APACHE II score did not differ statistically before and after TPE implementation in our patient group (p = 0.39).
Conclusion: TPE is a clinically useful tool to rapidly lower TG levels, but its impact on mortality of HTG pancreatitis as assessed by the APACHE II score remains uncertain.

1. Introduction

Hypertriglyceridemia accounts for 1–4% of all acute pancreatitis cases and is seen in patients with primary disorders of lipid metabolism. Severe hypertriglyceridemia is defined as triglyceride (TG) levels >1000 mg/dL [1]. Exacerbation of underlying hypertriglyceridemia by secondary factors such as uncontrolled diabetes mellitus, alcohol abuse, medications, and pregnancy can result in acute pancreatitis [2,3]. Acute pancreatitis is the leading gastrointestinal cause of hospitalization in the United States [4]. Compared to alcohol-induced and other non-hypertriglyceride-associated causes of pancreatitis, hypertriglyceridemic (HTG) pancreatitis has a more severe clinical course and less favorable outcomes, including increased length of stay and more frequent need for both intensive care admission as well as surgical intervention [5,6].

Elevated TG levels increase the number of chylomicrons in circulation, which can obstruct the pancreatic capillary bed, causing ischemia. Pancreatic lipase degrades exposed chylomicrons to free fatty acids, which further propagates cytotoxic injury and leads to release of inflammatory mediators, ultimately resulting in acute pancreatitis [7]. Per guidelines created by the American Society for Apheresis, HTG pancreatitis currently has a category III indication for therapeutic plasma exchange (TPE), defined as a clinical scenario in which the optimal role of apheresis is not established and decision making is individualized per physician discretion. The paucity of data regarding the impact of TPE on clinical outcomes in patients with HTG pancreatitis prompts the need for further investigation [8].

The Acute Physiology and Chronic Health Examination (APACHE) II score is a well validated scoring system used to predict severity of acute pancreatitis in critically ill patients requiring intensive care [9]. Other scoring systems specifically used for predicting mortality in acute pancreatitis include the Ranson score, the bedside index of severity in acute pancreatitis (BISAP) score, and the commuted tomography (CT) severity index. However, the Ranson score is not intended for interval monitoring as it is calculated

* Corresponding author. N3E09, Education Office, Department of Medicine, University of Maryland Medical Center, 22 S. Greene St., Baltimore, MD 21201, USA. Fax: +1 410 328 0267.
E-mail address: snakhoda@umm.edu (S. Nakhoda).

based on clinical parameters at two specific time points. Due to the absence of certain clinical data necessary for calculation, the BISAP and CT severity index could not be determined for all patients in our study and as such neither was utilized as our assessment tool [10–12]. While the APACHE II score was initially developed to predict estimated mortality in patients requiring intensive care and later validated to risk stratify patients based on severity of pancreatitis, recent studies have utilized the APACHE II score in evaluating change in clinical status over time [13,14]. We retrospectively examined changes in APACHE II score to assess the impact of TPE on mortality in critically ill patients with HTG pancreatitis.

2. Materials and methods

Twelve patients underwent TPE for HTG pancreatitis at our institution from 2005 to 2015. HTG pancreatitis was defined by the presence of 3 criteria on admission: 1) acute abdominal pain, 2) nausea and/or vomiting, and 3) elevated amylase and/or lipase greater than 2 times the upper limit of normal (upper limit of normal for amylase, 133 units/L and lipase, 300 units/L), in the setting of *severe* hypertriglyceridemia (TG level >1000 mg/dL) or *very severe* hypertriglyceridemia (TG level > 2000 mg/dL). Of these 12 patients, 2 patients were excluded because they underwent TPE in a non-intensive care unit or as an outpatient. Retrospective review of the electronic medical record was performed for the remaining 10 patients. Collected data were used to calculate the patient's APACHE II score immediately prior to initiation of TPE and immediately following the last TPE session. All patients underwent TPE using the Spectra Optia® Apheresis System, manufactured by Terumo BCT, with 5% albumin as replacement fluid and acid citrate dextrose solution as the anticoagulant. All patients received aggressive intravenous fluids and pain control. In cases of concurrent uncontrolled hyperglycemia, intravenous insulin was also administered [15]. Data in normal distribution were analyzed using *t*-test. Categorical data were analyzed using a chi-square test. This study was approved by the Institutional Review Board.

3. Results

3.1. Patient characteristics and clinical outcome

Median age of patients requiring TPE for HTG pancreatitis at our institution was 35 years (range, 31–52 years). The median number of days in the ICU was 13 (range, 2–87 days). All 10 patients had rapid improvement in their triglyceride level following TPE, with a median TG level of 2625 mg/dL (range, 1114–5289 mg/dL) on initiation of TPE and a median TG level of 415 mg/dL (range, 192–681 mg/dL) at completion of TPE. Patients received a median of 2 TPE sessions (range, 1–4). All TPE sessions occurred in daily succession. The first TPE session was conducted on a median of day 2.5 of admission (range days 1–6). The need for repeat TPE on the following day was determined by triglyceride level after TPE. Cessation of further TPE was indicated if the patient had a TG level <500 mg/dL or based on physician discretion if the patient had a down trending TG level approaching 500 mg/dL (Table 1).

Risk factors for HTG pancreatitis present on admission included alcohol abuse (40%), a family history of familial hypertriglyceridemia (40%), and moderate to poor control of diabetes mellitus type II, as defined by a hemoglobin A1c (HbA1c) >8% (40%). All 10 patients survived to discharge or transfer back to the referring medical center. The median length of ICU admission was 13.5 days (range, 2–87 days). 40% of patients required pancreatic surgery either during their hospitalization or within 3 months of discharge. All 4 cases requiring surgery underwent exploratory laparotomy after TPE initiation. Decision to proceed with surgery was based on worsening imaging findings, clinical deterioration, and/or rising intra-abdominal pressures (Table 1). In addition, 50% of patients were re-admitted to our institution for recurrent HTG pancreatitis. Of the 8 patients discharged from our institution, 7 were given triglyceride-lowering therapy (fenofibrate or gemfibrozil) and 5 received statin therapy for cardiovascular risk reduction. No patients received outpatient apheresis for management of their elevated triglycerides following discharge.

3.2. Effectiveness of TPE as assessed by APACHE II score

The median APACHE II score in our patients was 19 (range, 10–30) before TPE. At the conclusion of TPE, the median APACHE II score was 17 (range 10–26), which corresponded to an 8% decrease in median predicted non-operative mortality and a 9% decrease in median predicted post-operative mortality (Table 2). Five of the 10 patients had improvement in their percent-predicted mortality based on change in their APACHE II score after TPE. The predictive mortality score worsened in 2 patients, while the remaining 3 patients had no change following TPE. There was no statistically significant difference between APACHE II scores before and

Table 1
Demographic data, risk factors present on admission, and clinical outcome.

Case	Demographics		Risk factors			TPE		Clinical outcomes		
	Age	Gender	Alcohol abuse	HbA1C >8.0	Reported family history of HTG	# of TPE	Day of first TPE within hospitalization	Need for surgery	Length of ICU stay	Survival
1	36	M	Y	N	N	4	2	N	*22*	Y
2	51	F	N	N	Y	2	4	Y	43	Y
3	30	F	Y	Y	Unk	4	2	Y	14	Y
4	52	M	N	Y	Unk	2	7	N	20	Y
5	43	F	N	Y	Y	3	3	Y	13	Y
6	23	F	N	N	Y	1	3	N	6	Y
7	34	M	N	Y	N	1	6	N	5	Y
8	31	M	Y	N	N	1	1	N	13	Y
9	35	F	Y	N	N	2	1	N	2	Y
10	48	M	N	N	Y	2	2	Y	87	Y
Mean	38.3					2.2	3.1		22.6	
Median	35.5					2	2.5		13	
%		50% F 50% M	40%	40%	40%			40%		100%

Patient features including demographic data, risk factors for HTG pancreatitis present on admission (reported history of alcohol abuse, reported family history of hypertriglyceridemia, uncontrolled diabetes defined as a documented HbA1C >8% during hospitalization), specifics of TPE intervention (day of hospitalization on which TPE was initiated and number of TPE sessions) and clinical outcomes.