Original Article

Plasmapheresis as treatment for hyperlipidemic pancreatitis ☆

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ABSTRACT

Background: Severe hypertriglyceridemia with an accumulation of chylomicrons and triglyceride figures >1000 mg/dL can cause acute pancreatitis, a potentially fatal complication. The option of rapid reduction in triglyceride concentrations is attractive and possible with plasmapheresis.
Methods: We present the results of an analysis of 11 patients admitted to the intensive care unit with severe hypertriglyceridemic pancreatitis and treated with plasmapheresis. The procedure was repeated until serum triglycerides were below 1000 mg/dL. We recorded anthropometric, clinical data as well as final outcome.
Results: In eight patients a single plasma exchange was sufficient to reduce triglyceride figures <1000 mg/dL. Only three patients died, all with the worst severity indexes and who experienced the longest delay before the procedure.
Conclusions: Our results, together with a review of the literature, confirm the need for a randomized clinical trial to compare conventional treatment vs. plasmapheresis in patients with severe hypertriglyceridemic pancreatitis.

1. Introduction

Hypertriglyceridemia is associated with severe complications, such as acute pancreatitis [1–4], as well as being a cardiovascular risk factor [5,6]. The usual treatment of hypertriglyceridemia includes dietary restrictions and lipid-lowering drugs [7]. However, situations exist that may require the urgent rapid and efficient reduction in blood levels of triglycerides. In these situations plasmapheresis has proven a valid and safe technique for the treatment of severe hypertriglyceridemia complicated by acute pancreatitis [8]. In addition, plasma exchange has been used to prevent acute pancreatitis in patients with severe hypertriglyceridemia who don't respond to conventional diet and drugs, as a multicenter study recently showed [9].

Plasmapheresis is the procedure by which plasma is separated from the blood and processed to eliminate certain components. The plasma is then usually reinfused back into the patient, though on occasions it may be completely eliminated and replaced by an isovolumetric substance. Plasmapheresis is a simple extracorporeal process that can be carried out as either an emergency or programmed procedure. It is particularly indicated in neurological, hematological and rheumatologic diseases and involves minimum adverse effects [10]. The filtering techniques in plasmapheresis include double or cascade filtration, where a first filter separates the whole blood from the plasma, with the plasma then being passed through a second filter with smaller pores that prevent the passage of high-molecular weight molecules, in this case triglycerides. The benefits may go beyond the mere reduction in triglyceride levels, and include, for example, the removal of excess proteases and replacement of consumed protease inhibitors [8].

Experience in the treatment of hypertriglyceridemia with apheresis is still scarce. Most of the literature refers to single cases [11–16], though a recent excellent review summarizing six reports involving more than ten patients shows that the technique results in drastic reductions of 60% in serum triglycerides in just a few hours [17]. Due to the lack of controlled and randomized trials in this field, the American Society for Apheresis' recommendation for the procedures is only Grade 2C [18].

The aim of this study is to describe the usefulness of plasmapheresis in critical patients admitted to our center with a diagnosis of hyperlipidemic pancreatitis.

2. Methods

This observational, retrospective study comprised patients admitted to the Intensive Care Unit of the Hospital Universitario Virgen de la Victoria, Malaga, with lipidemic pancreatitis and who were treated with plasmapheresis between 1 January 2007 and 31 December 2011. In addition to serum triglyceride concentrations >1000 mg/dL, at the time of admission to the emergency department the patients had to fulfill clinical (suggestive abdominal pain), analytical (elevated serum amylase and lipase or urine amylase three times the upper limit of normal) and radiological (abdominal CT) criteria of acute pancreatitis.

We gathered information on demographic data, a family history of dyslipidemia, and a personal history of dyslipidemia, medical treatment of dyslipidemia, diabetes, hypertension, previous episodes of pancreatitis, alcohol consumption, and smoking, as well as biochemical and hematological data. The patients were classified for severity according to their APACHE II [19,20], the Ranson criteria [21] and Balthazar score [22].

The plasmapheresis sessions were done using Prismaflex (Prismaflex TPE 2000, Gambro Industries, Hospal S.A. Intensive Care, Barcelona, Spain). The exchange volume was adjusted according to the formula $[1 - (\text{hematocrit}/100)] \times \text{weight} \times 0.07$ [23]. In general, two liters of plasma were exchanged per session, with the procedure lasting about three hours. The replacement was done with a 5% albumin solution. The serum triglycerides were measured again six hours after the procedure, which was repeated if the figure was greater than 1000 mg/dL.

For each patient data were recorded on the number of plasmapheresis sessions, the exchange volume, the replacement solution, procedure time, complications or adverse effects during the procedure, as well as any other procedures associated with the stay in the Intensive Care Unit (need for mechanical ventilation, vasoactive drugs, hemofiltration). A record was also made of other complications, ICU stay, onset of respiratory distress syndrome, state of the patient on discharge from the ICU, follow-up after ICU discharge, triglyceride levels at hospital discharge, and hospital stay.

The variables were analyzed using SPSS 17.0. The qualitative variables are shown as number of cases (%) and the quantitative variables as means, with the standard deviation when relevant.

3. Results

The study included 11 patients (see Table 1). Their mean age was 40.6 years (range: 27–51 years), and 6 (54%) were men. The most usual personal history was alcohol consumption, in 8 patients (72%), followed by prior primary hypertriglyceridemia in 5 (45%), hypertension in 3 (27%) and type 2 diabetes mellitus in 2 (18%). Only one of the patients with hypertriglyceridemia was taking lipid-lowering drugs prior to the episode (Gemfibrozil); that patient was taking also estrogens as birth-control pill before the attack. In six patients who have assessed body mass index at admission, the median value was 28.1 kg/mt^2 (interquartile range 23.1–30.0). All subjects with type 2 diabetes were treated with insulin infusion to keep blood glucose <180 mg/dL avoiding hypoglycemia.

Most of the patients (72%, 8 patients) had acute grade E pancreatitis, according to the Balthazar classification. Only 2 patients met one Ranson criterion at the first evaluation, 3 met two criteria, 2 met three and 4 met four criteria. The median APACHE II was 13 (IQR 9–18), corresponding to an expected mortality of 24.7%.

Eight (72.7%) patients received one plasmapheresis session, 2 (18.2%) received two sessions, and just one (9.1%) patient required

three sessions. At the start of the plasmapheresis sessions, the median (interquartile range) triglyceride concentration was 2138 (1338–2540) mg/dL and at the end it was 395 (335–485) mg/dL, representing a reduction of 81% (69–84). All the patients attained triglyceride concentrations <1000 mg/dL by the end of the procedure (Fig. 1), and the level at hospital discharge was 173 (96–454) mg/dL.

Tolerance to the plasmapheresis was good; three cases had hypervolemia which was successfully treated with IV furosemide. Ten of the 11 patients experienced some type of complication during their ICU stay; 5 had ARDS of whom 4 required mechanical ventilation for 8 days; 4 patients needed continuous venovenous hemofiltration due to renal failure, which was completely reversed in 3 patients. Three patients died during their ICU stay, one of them after 17 days due to severe nosocomial pneumonia and the other two, after 52 and 53 days, due to multiple organ failure syndrome. All patients who died had necrotic-hemorrhagic pancreatitis. Compared with those who survived, those who died had met significantly more Ranson criteria on admission [median 4 (IQR 4–4) vs. median 2.5 (IQR 2.0–3.0), p < 0.05] and a tendency towards a higher APACHE II score [median 18 (IQR 15–20) vs. median 11 (IQR 8.2–15), p = 0.08] and lower pre-plasmapheresis triglyceride levels (median 1338 (IQR 1314–1863) vs. 2230 (IQR 1994–2689), p = 0.08) (Fig. 2). Analysis of the time between symptom onset and plasmapheresis showed no significant differences, as the median time was 55 h (IQR 22–118) in those who died and 49 (IQR 29–59) in those who survived.

4. Discussion

Our series provides data on 11 consecutive patients who underwent plasmapheresis due to acute pancreatitis and severe hypertriglyceridemia. This sample can be considered representative of this situation as more patients were male, most were in their 30s or 40s, a high percentage consumed alcohol and two out of eleven had type 2 diabetes mellitus. These figures are concordant with two previous series from our center [4,24] and those of other groups [25–28].

Plasmapheresis proved very efficient and after the procedure all the patients had triglyceride levels <1000 mg/dL, a figure below which the concentration of chylomicrons is scarce and the risk of pancreatitis exceptional [24,29]. Only a few adverse effects were noted, and limited to just three episodes of hypervolemia, which were successfully treated with diuretics. However, plasmapheresis was unable to prevent a fatal outcome in three of the 11 patients treated. Various different factors may be involved in this situation. First, the three patients who died were admitted to the ICU with the most advanced grade of acute pancreatitis, as they all met four Ranson criteria simultaneously, a grade E on the Balthazar scale and an APACHE-II score >15. These results are comparable to those of other series, as mortality in patients with hypertriglyceridemic pancreatitis and three or more Ranson criteria was 15–30% [30]; and in another series, an APACHE II score >8 increased

Table 1
Demographic and clinical data.

Patient	Age	Time[a]	Gender	Comorbidities	Balthazar	Ranson	APACHE II	TG$_1$	Sessions
1	47	53	Female	DL. HTN. DM.	E	1	13	2173	1
2	46	45	Male	DL. Alcohol.	E	2	20	2132	1
3	36	18	Female	DL DM	E	2	8	2288	1
4	27	61	Female	Alcohol	E	4	15	1949	2
5	29	83	Male	DL	C	3	12	2739	1
6[b]	48	22	Male	Alcohol	E	4	20	1863	3
7[b]	44	55	Male	Alcohol	E	4	15	1314	2
8	42	29	Female	Acohol	C	2	5	2540	1
9[b]	43	118	Male	Alcohol	E	4	18	1338	1
10	34	32	Male	HTN. Alcohol	E	3	10	1290	1
11	51	54	Female	DL. HTN. Alcohol	D	1	9	5238	1

DL = dyslipidemia. HTN: hypertension. DM: diabetes mellitus. TG$_1$: serum triglycerides (mg/dL) at admission in emergency ward.
  [a] Time (hours) since first symptom to plasmapheresis.
  [b] Patient died.