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• CLINICAL RESEARCH •

Therapeutic plasma exchange in patients with hyperlipidemic pancreatitis

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Abstract

AIM: To clarify the effectiveness of plasma exchange by comparing the mortality and morbidity before and after the intervention of plasma exchange.

METHODS: Plasma exchange has been available as an optional therapy for hyperlipidemic pancreatitis since August 1999 in our hospital. The patients were assorted into 2 groups (group I: before August 1999 and group II: after August 1999). Group I consisted of 34 patients (before the availability of plasma exchange). Group II consisted of 60 patients (after the availability of plasma exchange). Twenty patients in group II received plasma exchange after giving their consent. The mortality and morbidity were compared between group I and group II. Furthermore, the patients with severe hyperlipidemic pancreatitis (Ranson's score≥3) were analyzed separately. The mortality and morbidity were also compared between those receiving plasma exchange (group A) and those who did not receive plasma exchange (group B).

RESULTS: There was no statistical difference in the mortality, systemic and local complications between group I and group II. When the patients with severe hyperlipidemic pancreatitis were analyzed separately, there was no statistical difference between group A and group B.

CONCLUSION: Plasma exchange can not ameliorate the overall mortality or morbidity of hyperlipidemic pancreatitis. The time of plasma exchange might be the critical point. If patients with hyperlipidemic pancreatitis can receive plasma exchange as soon as possible, better result may be predicted. Further study with more cases is needed to clarify the role of plasma exchange in the treatment of hyperlipidemic pancreatitis.

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INTRODUCTION

Hypertriglyceridemia (HTG) is a rare cause of pancreatitis. Hyperlipidemic pancreatitis (HLP) secondary to HTG presents typically as an episode of acute pancreatitis or recurrent acute pancreatitis or rarely as chronic pancreatitis[1]. The typical clinical profile of HLP is a patient with preexisting lipid abnormality along with the presence of secondary factors (such as poorly controlled diabetes mellitus, alcohol abuse, pregnancy, or a medication) that can induce HTG[1]. It is generally accepted that a TG level more than 1 000 mg/dL is needed to precipitate an episode of acute pancreatitis[2]. It is postulated that hydrolysis of TG by pancreatic lipase into free fatty acid is toxic to pancreatic endothelium and acinar cells[3]. In an animal study, hyperlipidemia could intensify the course of acute edematous pancreatitis and necrotizing pancreatitis[3].

Plasmapheresis has been claimed to reduce triglyceride level rapidly in HLP[4-11] and is believed to halt the progression of HLP[8-10]. Actually, experiences of plamapheresis in HLP are limited and only sporadic cases were reported[5-11]. There was no control study in the past concerning whether plasmapheresis could improve the mortality or morbidity of HLP. Our aim was to analyze the benefits of plasma exchange by comparing the mortality and morbidity of HLP patients with those without receiving such an intervention.

MATERIALS AND METHODS

Patient characteristics

From September 1992 to June 2003, a total of 862 patients with acute pancreatitis were reviewed and 94 patients were consistent with hyperlipidemic pancreatitis (HLP). As plasma exchange has been available as an optional therapy of HLP since August 1999 in our hospital, the patients were assorted into 2 groups (group I: before August 1999 and group II: after August 1999). Group I consisted of 34 patients (before the availability of plasmapheresis) and group II consisted of 60 patients (after the availability of plasmapheresis). Twenty of 60 patients in group II received plasma exchange after giving their consents. The Ranson's score was used for assessment of the severity of pancreatitis. Half of the patients receiving plasma exchange were severe cases (Ranson's score≥3). The anatomical change of acute pancreatitis was assessed according to the Balthazar's grading. The enrolled criteria of plasma exchange in HLP were as followings: (1) overt symptoms of acute pancreatitis, (2) pancreatitis proved by CT, ultrasound or elevation of pancreatic enzymes, (3) triglyceride (TG) >1 000 mg/dL and lactescent serum, (4) exclusion of other causative conditions, such as gall stone, trauma or neoplasm, (5) patient's agreement. The mortality and morbidity between group I and group II were compared.

Furthermore, the patients with severe HLP (Ranson's score≥3) were analyzed separately. We divided the patients with severe HLP (a total of 29 patients) into 2 groups. Group A received plasma exchange, while group B did not receive the intervention. The mortality and morbidity between group A and group B were also compared.

The secondary factors inducing HTG in our patients included diabetes mellitus (46 patients), alcoholic consumption (32 patients) and oral contraceptive (one patient). The median time for starting plasma exchange was 3 d after symptom onset (range, 2-6 d).

Apheresis

Plasma exchange was carried out using membrane filtration in a KM 8800 membrane plasmapheresis monitor (Kuraray, Osaka, Japan) with a Plasmacure plasma separator (Kuraray, Osaka, Japan) to separate plasma from blood. One calculated plasma volume was processed during each session of plasma exchange. One course of plasma exchange treatment consisted of one or two daily sessions based on the doctor 's decision, single session in 13 patients and two sessions in 7. Heparin was used as the anticoagulant. Either a double lumen catheter in a central vein (fifteen patients) or a dialysis catheter in an antecubital vein (five patients) was used for vascular access. Replacement fluid was given with fresh frozen plasma (FFP) in 8 patients and isovolumetric 5 % albumin solution in 12 patients.

Statistical analysis

t-test and chi-square test were used for statistical analysis. $P<0.05$ was considered statistically significant.

RESULTS

The demographic characteristics of all the patients are summarized in Table 1. The mean age and sex distribution were similar in both groups. The initial mean TG level was around 1 900 in both groups. The severity of pancreatitis was predicted by the Ranson's criteria. Severe pancreatitis (Ranson's scroe$\geq$3) was 20.6% in group I and 36.7% in group II (P=0.105). The anatomical change of pancreatitis was assessed according to the Balthazar's grading system and 54.2% of group I and 41.3% of group II were belonged to Balthazar grade D or E (P=0.305).

The mortality rate, systemic and local complications of both groups are demonstrated in the Table 2. The systemic complication was defined by the Atlanta definition[12]: (1) pulmonary insufficiency, $PaO_2 < 8$ kPa, (2) renal insufficiency, Cr > 2 mg/dL, (3) shock, SBP<12 kPa, (4) UGI bleeding >500 mL/24 h. The local complications included abscess and pseudocyst formation. There was no significant difference between group I and group II in mortality and complications. Further comparison of individual items of systemic and local complications between the two groups revealed no statistical differences (Tables 3, 4).

Table 1 Demographic characteristics

	Group I (n=34)	Group II (n=60)	P value
Age (yr)	40.8±6.8	42.3±8.9	0.394
Initial TG	1 922±1 287	1 913±612	0.966
DM (%)	38(13/34)	55(33/60)	0.118
Alcohol (%)	44(15/34)	28.3 (17/60)	0.121
Ranson >3(%)	20.6(7/34)	36.7(22/60)	0.105
Balthazar D, E (%)	54.2(13/24)	41.3(19/46)	0.305

Table 2 Comparison of mortality and morbidity between patients before and after availability of plasma exchange

	Group I (%, n=34)	Group II (%, n=60)	P value
Mortality (%)	5.9(2/34)	6.7(4/60)	0.881
Systemic complications (%)	17.6(6/34)	18.3(11/60)	0.934
Local complications (%)	11.8(4/34)	6.7(4/60)	0.395

When severe hyperlipidemic pancreatitis (Ranson's score$\geq$3) was analyzed separately (Table 5), the mortality rate, systemic and local complications of group A (with plasmapheresis) and group B (without plasmapheresis) were not statistically different (P=0.369, 0.153, 0.454, respectively).

The mean serum concentration of TG and lipase fell significantly after plasma exchange. The serum TG level declined from 2 019±780 mg/dL to 691±331 mg/dL (65.8% reduction) and the serum lipase level declined from 4 007±355 U/L to 447±35 U/L (88.8% reduction).

Table 3 Comparison of systemic complications between patients before and after the availability of plasma exchange

	Group I (%, n=34)	Group II (%, n=60)	P value
ARF	17.6(6/34)	10(6/60)	0.286
UGI bleeding	0(0/34)	8.3(5/60)	0.084
Shock	8.8(3/34)	10(6/60)	0.852
ARDS	11.8(4/34)	10(6/60)	0.790

ARF: Acute renal failure; ARDS: Acute respiratory distress syndrome.

Table 4 Comparison of local complications between patients before and after availability of plasma exchange

	Group I (%, n=34)	Group II (%, n=60)	P value
Abscess	17.6(6/34)	10(6/60)	0.286
Pseudocyst	0(0/34)	8.3(5/60)	0.084

Table 5 Comparison of patients with severe hyperlipidemic pancreatitis receiving plasma exchange and not receiving plasma exchange

Ranson >3	Group A: PE(+) (%, n=10)	Group B: PE(-) (%, n=19)	P value
Mortality	30(3)	15.8(3)	0.369
Systemic complications	70(7)	42.1(8)	0.153
Local complications	10(1)	21.1(4)	0.454

PE (+): With plasma exchange; PE (-): Without plasma exchange.

DISCUSSION

The association between hyperlipidemia and acute pancreatitis was first described by Speck in 1865[1]. Studies on patients with familial HTG and their longterm follow-up have shown that extreme elevation of TG occurred during episode of acute pancreatitis[13]. It has been generally believed that a TG level of more than 1 000 mg/dL was needed to precipitate an acute pancreatitis[2]. The hypothesis of hyperlipidemic pancreatitis is that pancreatic damage was resulted from toxic injury to the capillary endothelium and the damage of pancreatic acinar cells was caused by free fatty acids liberated by pancreatic lipase[3]. Conservative treatment (fasting, lipid lowering drugs, insulin or fluid restoration) might decrease TG level slowly in a time span of days to weeks[14]. In contrast, plasmapheresis might remove excessive lipid from serum in about 2 h[4,6]. Sporadic reports about plasmapheresis used in hyperlipidemic pancratits were seen in the past[4-10]. They all concluded that plasmapheresis was helpful for treating or preventing acute hyperlipidemic pancreatitis. However, no control study to assess the value of plasmapheresis in the treatment of hyperlipidemic pancreatitis is available.

Different methods have been used in plasmapheresis. Plasma exchange is superior to double filtration in the removal of excessive TG because the membrane of plasma separator was usually blocked by the larger particles of chylomicron[6]. We used plasma exchange with replacement of albumin or fresh frozen plasma (FFP) in the treatment of HLP in this study. FFP could supply lipoprotein lipase and apolipoprotein from the healthy donor[13]. Lipoprotein lipase and apolipoprotein were essential for the catabolism of TG[13].

In our study, plasma exchange could remove TG effectively

from turbid plasma in a short time (about 2 h). TG declined from 2 019±780 mg/dL to 691±331 mg/dL (65.8% reduction). It was also postulated that plasmapheresis could remove circulating activated enzymes and inflammatory mediators[15], but its beneficial effects in pancreatitis has not been proved[10]. The serum lipase level declined from 4 007±355 U/L to 447±35 U/L (88.8% reduction) after plasma exchange in our patients.

Despite the marked reduction in TG and lipase after plasma exchange, we could not achieve statistically significant improvement in the mortality and morbidity after the intervention of plasma exchange. The mortality was 5.9% before the intervention (group I) and 6.7% after the intervention (group II). The rate of systemic complications (acute renal failure, UGI bleeding, shock, or pulmonary insufficiency) was 17.6% in group I and 18.3% in group II. The rate of local complications (abscess or pseudocyst) was 11.8% in group I and 6.7% in group II. While individual items of complications were considered, there were still no statistical differences between the two groups.

When the patients with severe HLP (Ranson's score$\geq$3) were analyzed separately, the mortality rate was 30% in group A (with plasma exchange) and 15.8% in group B (without plasma exchange). The mortality in severe HLP was not decreased by plasma exchange. The rate of systemic complication was 70% in group A and 42.1% in group B (P=0.153). The rate of local complication was 10% in group A and 21.1% in group B (P=0.454). Again, plasma exchange was not able to alter the complication rate significantly.

Why could plasma exchange not improve the mortality and morbidity in HLP? We proposed that the time of plasmapheresis might be the critical point. If patients with HLP could receive plasma exchange as soon as possible, better result might be expected[5].

In conclusion, plasma exchange fails to improve the overall mortality and morbidity of HLP in our study. Further study with more cases is needed to clarify the role of plasmapheresis in the treatment of HLP.

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