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RAPID COMMUNICATION

Effect of admission hypertriglyceridemia on the episodes of severe acute pancreatitis

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Abstract

AIM: To investigate the effect of admission hypertriglyceridemia (HTG) on the episodes of severe acute pancreatitis (SAP).

METHODS: One hundred and seventy-six patients with SAP were divided into HTG group (n = 45) and control group (n = 131) according to admission triglyceride (TG) ⩾ 5.65 mmol/L and < 5.65 mmol/L, respectively. Demographics, etiology, underlying diseases, biochemical parameters, Ranson' s score, acute physiology and chronic heath evaluation Ⅱ (APACHE Ⅱ) score, Balthazar's computed tomography (CT) score, complications and mortality were compared. Correlation between admission TG and 24-h APACHE Ⅱ score was analyzed.

RESULTS: SAP patients with HTG were younger (40.8 ± 9.3 years *vs* 52.6 ± 13.4 years, P < 0.05) with higher etiology rate of overeating, high-fat diet (40.0% *vs* 14.5%, P < 0.05) and alcohol abuse (46.7% *vs* 23.7%, P < 0.01), incidence rate of hypocalcemia (86.7% *vs* 63.4%, P < 0.01) and hypoalbuminemia (84.4% *vs* 60.3%, P < 0.01), 24-h APACHE Ⅱ score (13.6 ± 5.7 *vs* 10.7 ± 4.6, P < 0.01) and admission serum glucose (17.7 ± 7.7 *vs* 13.4 ± 6.1, P < 0.01), complication rate of renal failure (51.1% *vs* 16.8%, P < 0.01), shock (37.9% *vs* 14.5%, P < 0.01) and infection (37.4% *vs* 18.3%, P < 0.01) and mortality (13.1% *vs* 9.1%, P < 0.01). Logistic regression analysis showed a positive correlation between admission TG and 24-h APACHE Ⅱ score (r = 0 .509, P = 0.004).

CONCLUSION: The clinical features of SAP patients with HTG are largely consistent with previous studies. HTG aggravates the episodes of SAP.

Key words: Clinical study; Hypertriglyceridemia; Severe acute pancreatitis; Clinical features; Outcome

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INTRODUCTION

Hypertriglyceridemia (HTG) is a rare but well-recognized cause for severe acute pancreatitis (SAP), which has been intensively studied since Speck noted the association between hyperlipidemia and acute pancreatitis (AP) in 1865[1-4]. HTG can be a primary cause for AP which occurs in 1.3%-3.8% of AP patients, or secondary to other factors prior to the increase of lipid levels, or both[5]. Clinically, mild to moderate hyperlipidemia in AP patients, particularly in alcoholic pancreatitis patients, is often observed. However, it is difficult for clinicians to distinguish mild to moderate hyperlipidemia secondary to AP from marked HTG that primarily causes AP.

It is generally believed that a serum triglyceride (TG) level of more than 1000 mg/dL (about 11.3 mmol/L) is needed to precipitate AP, the reduction of which to well below 1000 mg/dL may effectively prevent further episodes[6]. Animal studies showed that HTG intensifies the course of AP including both edematous and necrotizing pancreatitis[7,8]. It was reported that TG would worsen pancreatic injury induced by AP when it reaches 5.65 mmol/L, thus playing a worth-noting role in predisposing mild pancreatitis to the vicious episode[9]. Extreme elevation of TG in AP patients with familial HTG can cause the so-called "hyperlipidemic abdominal crisis"[10]. However, it was also reported that

SAP patients with HTG can have pancreatic necrosis, pseudocysts, abscesses and other complications that can be seen in other types of pancreatitis with a different clinical course from other forms of AP[11]. Thus, the correlation between HTG and the severity of AP episodes is still uncertain.

In this study, the clinical features and the effect of HTG on the episodes of SAP were investigated with HTG as a coexisting medical condition of SAP.

MATERIALS AND METHODS

Patients

The diagnostic criteria for SAP formulated at the Bangkok World Congress of Gastroenterology 2002 in Thailand[12] were employed and organ failure was defined according to the Criteria of Clinical Diagnosis and Classification System for AP formulated by the Pancreatic Surgical Society of Chinese Medical Association in 1997[13] in this study. From March 2003 to December 2004, all patients diagnosed with SAP and admitted to West China Hospital of Sichuan University within 72 h after onset of symptoms were included. Patients were excluded if they had hepatic dysfunction or renal failure prior to the development of SAP.

Methods

One hundred and seventy-six SAP patients admitted to our hospital were enrolled and divided into HTG group (n = 45) and control group (n = 131) according to admission TG $\geqslant$ 5.65 mmol/L and TG < 5.65 mmol/L, respectively. Blood samples were collected at admission for biochemical examinations in Department of Laboratory Medicine of our hospital.

All patients received standardized comprehensive treatments[12]. The main protocols of treatment throughout the study were intensive care, oxygen inhalation, fasting, intermittent gastrointestinal decompression and fluid infusion. The balance of internal environment was maintained, prophylactic antibiotics were used for 7-14 d, H_2 receptor antagonists or proton pump inhibitors were given for 7 d. When the patients developed respiratory failure, a respirator was employed to assist respiration. When the patients developed hypoalbuminaemia, 20% of human serum album in 50 mL was used daily until the serum albumin value became normal. When serum lipid value was decreased to normal, fat emulsion was added in parenteral nutrition. During hospitalization, microbiological tests of sputum, urine, feces, or blood were performed, when the following susceptible clinical symptoms or signs appeared: body temperature $\geqslant$ 38.5℃ and white blood cell (WBC) count $\geqslant 20 \times 10^9$ /L, signs of peritoneal irritation (area) in more than 2 quadrants, and intractable malnutrition. Contrast-enhanced computed tomography (CECT) was performed to determine necrotic infection of (peri) pancreas. For those who were unsuitable for CECT evaluated by the investigator, magnetic resonance imaging was alternatively eligible. Ultrasound-guided fine needle aspiration (FNA) was performed for microbiological testing when air bubbles appeared in necrotic tissue of the (peri) pancreas. Bacterial infection was confirmed by positive culture or smear examination. Fungal infection was confirmed by positive fungi in no less than 2 different specimens by culture or smear examination.

The sex, age, etiology, underlying diseases, biochemical parameters and incidence of complications including acute respiratory distress syndrome (ARDS), renal failure, acute hepatitis, shock, encephalopathy, infection rate, and mortality, were confirmed by one of the investigators using a standard data collection instrument. The Ranson's score, 24-h APACHE Ⅱ score and admission Balthazar's CT score were calculated by a single investigator.

Table 1 Clinical features of patients in HTG and control groups

	HTG group (n = 45)	Control group (n = 131)
Sex (Male/Female)	27/18	72/59
Age (mean ± SD, yr)	40.8 ± 9.3	52.6 ± 13.4
	(24-61)[a]	(22-82)
Etiology, *n* (%)		
Overeating and high fat diet	18 (40.0)[a]	19 (14.5)
Alcohol abuse	21 (46.7)[b]	31 (23.7)
Gallstones	5 (11.1)[b]	37 (28.2)
L-Asparaginase chemotherapy	2 (4.4)	0
Pregnancy	6 (13.3)	0
Underlying diseases, *n* (%)		
Hypertension	6 (13.3)	15 (11.5)
Coronary heart disease	3 (6.7)	7 (5.3)
Atherosclerosis	3 (6.7)	9 (6.9)
Familial hyperlipidemia	6 (13.3)	11 (8.4)
Admission biochemical		
Serum glucose (mmol/L)	17.7 ± 7.7[b]	13.4 ± 6.1
Hypoalbuminaemia (%)	38 (84.4)[b]	79 (60.3)
Hypocalcaemia (%)	39 (86.7)[b]	83 (63.4)
Hypopotassemia (%)	16 (35.6)	50 (38.2)
Hyponatremia (%)	26 (57.8)	59 (45.0)
Ranson's score (mean ± SD)	4.7 ± 1.9	4.9 ± 2.0
24-h APACHE Ⅱ score (mean ± SD)	13.6 ± 5.7[b]	10.7 ± 4.6
Balthazar's CT score (mean ± SD)	5.4 ± 2.3	6.3 ± 5.4

[a]P < 0.05, [b]P < 0.01 *vs* control group.

Statistical analysis

Data were expressed as mean ± SD or percentage. Data in normal distribution were analyzed using t-test. Data in abnormal distribution were analyzed using Wilcoxon rank sum test. Categorical data were analyzed using chi-square test. The correlation between serum TG and 24-h APACHE Ⅱ score was analyzed using Logistic regression. P < 0.05 was considered statistically significant.

RESULTS

Clinical features

The clinical features of the patients in the HTG and control groups are summarized in Table 1. There were no statistical differences in sex distribution and incidence

Table 2 Incidence of complications and mortality in HTG and control groups *n* (%)

	HTG group (n = 45)	Control group (n = 131)
Complications		
ARDS	29 (64.4)	61 (46.6)
Renal failure	23 (51.1)[b]	22 (16.8)
Acute hepatitis	20 (44.4)	38 (29.0)
Shock	17 (37.9)[b]	19 (14.5)
Encephalopathy	10 (22.2)	24 (18.3)
Infection	17 (37.4)[b]	24 (18.3)
Death	14 (31.1)[b]	12 (9.1)

[b]$P < 0.01$ *vs* control group.

rate of underlying diseases between the two groups. Patients in the HTG group were younger ($P < 0.05$) with a higher rate of overeating and a high fat diet ($P < 0.05$) and alcohol abuse ($P < 0.01$) and less gallstones ($P < 0.01$). The Ranson's score and initial Balthazar's CT score were not statistically different between the two groups, but the 24-h APACHE Ⅱ score was higher in the HTG group than in the control group ($P < 0.01$). The incidence rate of hypokalemia and hyponatremia had no difference and was higher in the HTG group than in the control group ($P < 0.01$), and admission serum glucose was higher in the HTG group than in the control group ($P < 0.01$).

Complications and mortality

There were no statistical differences in complications such as ARDS, acute hepatitis and encephalopathy between the two groups. However, more complications, such as renal failure, shock and infection occurred in the HTG group than in the control group ($P < 0.01$). The mortality was higher in the HTG group than in the control group ($P < 0.01$) (Table 2).

DISCUSSION

HTG-associated SAP is an uncommon, but potentially life-threatening disease[14]. HTG may be primary in origin (hereditary or sporadic genetic disorder of metabolism) or secondary (associated with an identifiable disease or condition and is reversible with control or eradication of that disease or condition) to other factors or both[15-17]. Although the exact pathogenesis of HTG-associated AP is not clear, it is thought to result from toxic injury to acinar cells and capillary endothelia by excessive free fatty acids from hydrolysis of TG[18,19]. Competitive oxidation of ethanol is also responsible for SAP by aggravating the level of serum lipids[20]. L-asparaginase-induced HTG is suggested as a possible mechanism of SAP[21,22]. HTG is the cause for gestational pancreatitis in 56% cases[23]. Elevated estrogen increases the synthesis of TG and depresses plasma postheparin lipolytic activities by inhibiting the removal efficiency of TG, and high-fat intake may be a cause for AP during pregnancy[24-27], which are largely consistent with the results of our study, showing that the patients with HTG were younger with more diet-associated etiologies including overeating, high-fat diet and alcohol abuse. SAP patients with HTG had a higher incidence of hypoalbuminaemia and hypocalcemia and a higher level of admission serum glucose, which may be associated with the aggravation of HTG, resulting from severe stress response and metabolic disorders[28].

The role of HTG in modulating disease course of AP is still controversial. Although studies demonstrated that HTG has no significant correlation to complications of disease or overall end-of-episode severity in AP patients[3,12]. It was reported that HTG is independently associated with the severity of AP and plays a role in the aggravation of acute necrotizing pancreatitis[29-31]. The results of our study show that the incidence of admission hypocalcaemia, a predictable index of SAP[32], and the 24-h APACHE Ⅱ score were higher in the HTG group than in the control group. The complications, such as renal failure, shock and infection, and the mortality were higher in the HTG group than in the control group, indicating that HTG aggravates SAP, leading to systemic complications and a high mortality rate of SAP.

In conclusion, the clinical features of HTG-associated SAP are largely consistent with previous studies. HTG aggravates SAP.

COMMENTS

Background

Hypertriglyceridemia (HTG) is associated with severe acute pancreatitis (SAP), which has long been recognized. HTG may be a primary etiology of SAP, and it is difficult for clinicians to identify it. Some previous studies suggest that HTG is independently associated with the severity of acute pancreatitis (AP) and plays a role in the aggravation of acute necrotizing pancreatitis. However, its mechanism underlying such a role is still controversial.

Research frontiers

HTG is a rare cause for pancreatitis. An elevated TG level is needed to precipitate the episode of AP, which is called "hyperlipidemic abdominal crisis". Moreover, recurrent pancreatitis may occur in patients with familial hyperlipoproteinemia. Which patients progress to the extremely dangerous state during SAP and specific strategy against its deterioration and recurrence are the major research field.

Innovations and breakthroughs

It is generally believed that the serum triglyceride (TG) level of more than 1000 mg/dL (about 11.3 mmol/L) is needed to precipitate AP, but the clinicians cannot identify mild to moderate HTG secondary to SAP with marked HTG that causes AP in the acute phase. This research used admission HTG as a coexisting factor for SAP patients at admission.

Applications

At present, the exact role of HTG in the development of SAP remains unclear. Our study, conducted in one of the largest institutions in China, showed that HTG could aggravate SAP and leads to a worse outcome of SAP patients, thus providing applicable and valuable evidence for prognostic evaluation of pancreatitis.

Terminology

AP is an acute inflammatory process in the pancreas involveing local or other organ systems. Severe AP is defined as the occurrence of organ failure. HTG is defined as an abnormal concentration of TG in the blood.

Peer review

This research investigated the effect of admission HTG on the severity of SAP, by regarding admission HTG as a coexisting factor for SAP. The study was well designed and its results are valuable.

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