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HYPERLIPIDEMIA IN ACUTE PANCREATITIS: CONCOMITANT DISORDER OR A CAUSE?

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Abstract. *Acute pancreatitis is a common condition with alcohol and gallstones being the most frequent etiologies. The aim of our study was to determine the prevalence of hyperlipidemia, its etiopathogenetic role and influence on outcomes in patients with acute pancreatitis.The study included 47 patients admitted to our clinic for acute pancreatitis during one year period. On admission patients with hyperlipidemia were compared to those without it, regarding following parameters: body mass index, Glasgow score, organ failure occurrence, local complications occurrence (pancreatic necrosis, pseudocyst, abscess, jaundice, gastric outlet syndrome), intensive care unit stay and death. The results of the study revealed high incidence of hyperlipidemia in 51% of examined acute pancreatitis patients with the prevalence of severe forms in more than half of these patients. Dominant lipid disorder was hypertriglyceridemia, followed by hypercholesterolemia. It was clearly demonstrated that patients with hyperlipidemia, especially hypertriglyceridemia, had more severe acute pancreatitis, higher incidence of complications and poorer outcome compared to normolipemic patients. Hyperlipidemia in patients with acute pancreatitis should be considered and treated by a clinician as a separate serious problem, both when being a cause and a concomitant disorder. Hypolipidemic therapy should be administered both in urgent acute pancreatitis settings and as a long-term treatment aimed to prevent inflammation recurrence by successful persistent serum lipid levels control.*

Key words: *Hyperlipidemia, acute pancreatitis*

Introduction

Acute pancreatitis (AP) represents a serious clinical issue in everyday surgical practice. Alcohol and gallstones are the most frequent etiologies of this potentially severe condition. Other causes, like metabolic, structural and iatrogenic, account for up to 25% of AP cases [1].

Yadav and Pitchumoni [2] remarked that in 1846 Speck [3] was the first who described an association of the hyperlipidemia (HLP) and AP. However, since then etiological correlation of lipid disorders and AP still remains unclear. Hyperlipidemia may be an epiphenomenon to AP, since secondary lipid abnormalities are commonly found in patients with alcohol-induced AP and diabetic, pregnant and obese patients [4]. Nevertheless, primary lipid disorders, especially hypertriglyceridemia (HTG) or chylomicronemia, may independently induce AP and are responsible for up to 7% of cases [1]. Contrary to HTG, hypercholesterolemia does not cause AP [2]. Also, it is still uncertain whether HLP influences the evolution and outcome of AP. In available literature it has been suggested both that the presence of HLP is associated with more severe forms of AP [5] and, alternatively, that it does not intensify the course of inflammatory disease [6]. Cameron et al. reported that association between lipid abnormalities and AP is more than coincidental stating that lipids may play an intermediary role in the pathogenesis of this disease [7].

The aim of our study was to determine the prevalence of HLP, its etiopathogenetic role and influence on outcomes in patients with AP.

Material and Methods

The data were collected prospectively and the study included patients admitted to our clinic for AP during one year period with serum amylase level two times higher than normal range (28–100 U/L) considered confirmatory [8]. Patients previously treated elsewhere for actual AP episode and those with exacerbated chronic pancreatitis and pre-existing organ failure were excluded. On admission complete laboratory investigation was performed and Body mass index (BMI) was calculated (kg/m2). Lipid status assessment was done within 24h of admission and included measurement of triglycerides (TG), cholesterol, low density (LDL) and very low density lipoproteins serum levels. Radiological "imaging" assessment included abdominal ultrasound within 48h of admission and multi-slice computed tomography

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examination performed on the 6th day after disease onset. The aetiology of AP was ascertained from history and collected examination data and disease severity was assessed by the Glasgow criteria and the occurrence of organ dysfunction. Lipid status assessment was repeated on discharge and, if elevated on discharge, serum lipids were measured again one month after discharge. Patients were categorized according to Fredrickson classification of HLP.

Patients with HLP on admission were compared to those without HLP regarding following parameters: BMI, Glasgow score (GS), organ failure occurence (OF), local complications (LC) occurrence (pancreatic necrosis, pseudocyst, abscess, jaundice, gastric outlet syndrome), intensive care unit (ICU) stay and lethal outcome (LO). The data were statistically analyzed using nonparametric Pearson's chi-squared test.

Results

From January 2012 to January 2013 there were 47 patients — 29 (62%) males and 18 (38%) females with average age of 41 years (range, 19–76) admitted for AP. Alcohol was the cause in 25 (53%) and gallstones in 22 (47%) patients. The incidence of potential additional etiological factors was as follows: two patients were taking thiazide diuretics, one estrogen contraceptive and one was on statins therapy, seven were diabetic. Six patients stated that one or both of their parents have had HLD, but were not able to provide precise data about the form of HLP, its duration, intensity and outcome, which (with inability to perform genetic investigation) was not enough to diagnose familial HLP. The incidence and distribution of hyperlipidemic disorders are presented in Table 1; the prevalence of examined parameters is presented in in the Figure 1.

Table 1. The incidence and distribution of hyperlipidemic disorders

Type of hyperlipidemia	No of patients: 24
Hypercholesterolemia	8 (33%)
Moderate	3
Severe	5
Hypertriglyceridemia	16 (67%)
Moderate	7
Severe	9
Transient (normalized at discharge)	11 (46%)
Persistent (one month after discharge)	8 (33%)
Lethal outcome	5 (21%)

Out of 10 patients with GS>3 seven had HLP, out of 10 patients with organ failure six had HLP, out of 17 patients treated in ICU 12 had HLP, out of 14 patients with local complications 10 had HLP and out of six patients that died five had HLP (Fig. 2).

The correlation between the duration of HLP (transient or persistent) and severity, course and outcome of AP is presented in the Figure 3. The analysis of correlation between the severity of HLP and severity, course and outcome of AP revealed similar pattern (Table 2).

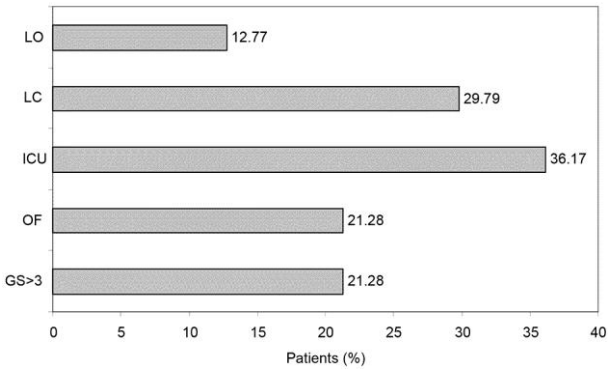

Fig. 1. The prevalence of examined parameters.
LO, lethal outcome; LC, local complications; ICU, intensive care unit treatment; OF, organ failure; GS, Glasgow score.

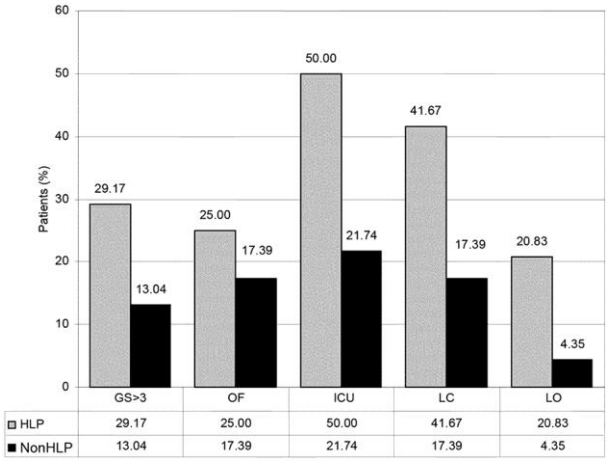

Fig 2. Correlation between lipid status and severity, course and outcome of acute pancreatitis.
HLP, patients with hyperlipidemia; NonHLP, patients without hyperlipidemia; GS, Glasgow score; OF, organ failure; ICU, intensive care unit treatment; LC, local complications; LO, lethal outcome.

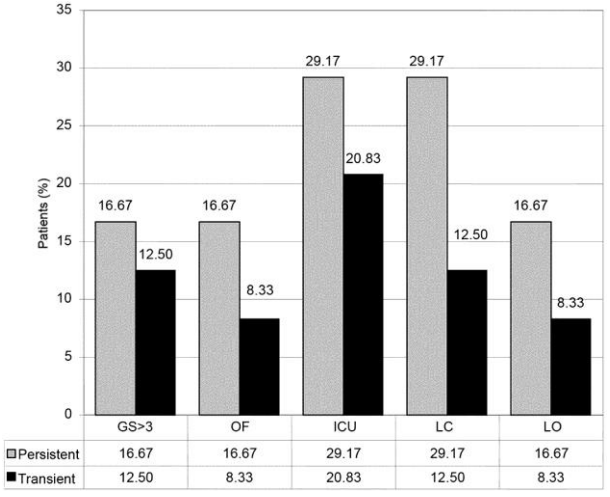

Fig. 3. The correlation between the duration of transient or persistent hyperlipidemia and severity, course and outcome of acute pancreatitis
GS, Glasgow score; OF, organ failure; ICU, intensive care unit treatment; LC, local complications; LO, lethal outcome.

Table 2. The incidence and distribution of hyperlipidemic disorders

	Hypercholesterolemia		Overall	Hypertriglyceridemia	
	Moderate	*Severe*		*Moderate*	*Severe*
Glasgow score >3	0	2	2 : 5	2	3
Organ failure	1	1	2 : 4	1	3
Intensive care unit	1	3	4 : 8	3	5
Local complications	1	3	4 : 6	2	4
Lethal outcome	0	0	0 : 5	1	4

Discussion

The results of our clinical study revealed high incidence of HLP in 51% of examined AP patients with the prevalence of severe forms in more than half of these patients. Dominant lipid disorder was HTG, followed by hypercholesterolemia. HTG is rare, but well documented cause of severe AP. In experimental model, infusion of triglycerides induces significant histopathological changes of pancreas tissue including oedema and hemorrhage, similar to AP [9]. Also, HLP deteriorates the course of experimental AP (both oedematous and necrotizing) [5, 10], while in human population with the history of AP exogenous lipids intake induces HLP with acute abdominal pain [7]. Reportedly, HTG may cause respiratory failure in patients with AP [11]. The serum triglyceride level (STL) that may induce AP or significantly influence its severity and course is not strictly determined yet. As reported by some authors, HTG-induced AP rarely develops with STL lower than 20 mmol/L [6]. Nevertheless, some reports state that STL higher than 11.3 mmol/L may initiate AP episode and that its reduction prevents further inflammation episodes [12]. It has also been reported that HTG can increase the pancreas damage during AP and predispose the transition from oedematous to necrotizing AP if STL exceeds 5.65 mmol/L [13]. STL exceeds 20 mmol/L almost exclusively in patients with genetic lipid disorder (familial HTG) and in these patients the settings of AP may induce severe pain and lead to a state called "hyperlipidemic abdominal crisis".

HTG is considered the third most frequent cause of AP, after alcohol and gallstones [6, 12]. The incidence of lipid abnormalities in AP patients varies from 3.8 to 39% [6, 7]. However, secondary lipid metabolism disorders (especially mild to moderate) are most common in alcohol-induced AP and in diabetic, pregnant and obese patients [12]. However, in spite clear correlation, it may still be difficult to differentiate between mild to moderate HLP as secondary comorbidity in AP from severe HTG that primarily induces AP, particularly in patients with hereditary HLP. Also, the influence of HLP on AP evolution is still unclear, despite well documented association between high serum triglyceride levels and some molecular mechanisms of pancreas acinar cells damage. It has been reported that HTG independently influences the severity and deteriorates necrotizing AP [14, 15]. On the other hand, some reports state that HLP does not influence the outcome of AP [2, 6, 16]. The results of our study clearly showed that patients with HLP, especially HTG, had more severe AP, higher incidence of complications and poorer outcome compared to normolipemic patients. Although this clearly indicates that HLP (HTG) worsened AP in our patients, it is reported that, in reverse, AP may induce HTG making this correlation a sort of a HTG-AP "circulus vitiosus" which may be difficult to cease [17].

Based on literature and our data from presented study, the administration of additional, specific hypolipidemic treatment (beside ordinary therapy for AP which is mandatory) would seem beneficial in patients with AP and HLP. Its goal would be maximal possible reduction of STL since it is reported that reduction of STL under 500 mg/dL [12], 1000 mg/dL [2] or 2000 mg/dL [18] may prevent abdominal pain and AP episode relapse. Although STL and serum chylomicrone levels rapidly decrease while fasting, targeted hypolipidemic therapy would accelerate plasma lipoproteins clearance. It is also well documented that dietary therapy combined with exercise and body weight loss facilitates the treatment and prevents inflammation relapse [2, 19]. The choice of hypolipidemic treatment is individual and depends on type and intensity of HLP and current disease/patient status. It includes many options, such as plasmapheresis, lipoprotein apheresis, insulin, heparin, purified apoC-II, penta-association therapy (hemofiltration and TG adsorption, statins and/or fibrates). However, despite the reasonable amount of evidence there is still a lack of agreement on routine use of these therapeutic variables. Nevertheless, many authors agree that maximal efforts should be made to prevent further hyperlipidemic AP episodes by achieving a permanent reduction of serum lipid levels using long-term medication (statins, fibrates, niacin), adequate dietary treatment (restriction of alcohol, fat and carbohydrate intake, enough antioxidants, vitamin, mineral and protein intake, fish oil supplements) and successful control of secondary aggravating factors and comorbidities (diabetes, obesity, hypothyroidism).

Conclusion

Since the incidence of HLP in patients with AP may be quite high, it should be considered and treated by a clinician as a separate serious problem, both when being a cause and a concomitant disorder. Hypolipidemic therapy should be administered both in urgent AP settings and as a long-term treatment aimed to prevent inflammation recurrence by successful persistent serum lipid levels control.

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