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Comparison between oral and enteral tube refeeding in hyperlipidemic acute pancreatitis

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Abstract. – OBJECTIVE: Hyperlipidemic acute pancreatitis (HLAP) remains one of the major digestive emergencies with increasing health risks. Oral refeeding tolerant (ORT) and enteral tube feeding tolerant (ETFT) are commonly used for nutritional management in HLAP. However, the differences between ORT and ETFT are yet to be characterized.

PATIENTS AND METHODS: This study included consecutive patients admitted to the Ordos Central Hospital between January 2019 and April 2023, with predefined inclusion criteria.

RESULTS: A total of 335 HLAP patients were recruited according to the inclusion criteria. 268 patients were diagnosed with moderately severe acute pancreatitis (MSAP), of which 193 were in the OFT group and 75 in the ETFT group. In the ETFT group, abdominal pain and abdominal distension were significantly higher than that in the OFT group. No significant result was identified in the laboratory data. However, the OFT group showed a higher hospitalization and cost, as well as exocrine insufficiency and newly onset diabetes, than the ETFT group.

CONCLUSIONS: Based on the incidence of HLAP retrieved in this study, MSAP is the major type with increasing clinical value. From the nutritional management sense, patients who received OFT showed higher hospitalization and cost, as well as lower exocrine insufficiency and newly onset diabetes.

Key Words:

Hyperlipidemic acute pancreatitis, Oral refeeding tolerant, Enteral tube feeding tolerant, Moderately severe acute pancreatitis.

Introduction

Acute Pancreatitis (AP) is a common disease that occurs in the digestive system and can lead to local damage, systemic inflammation syndromes and, in severe cases, multi-organ failure[1]. Some clinical features were distinct amongst different types of AP, such as age, sex, and disease severity. There are several major causes of AP, including gallstones, excess alcohol consumption, and hypertriglyceridemia[2]. In fact, the incidence of hyperlipidemic acute pancreatitis (HLAP) is currently rising from 13% to 25.6% and features higher morbidity and mortality[3-5].

According to the Atlanta classification from the Acute Pancreatitis Classification Working Group[6], acute pancreatitis can be divided into three groups: mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP). The diagnosis of MSAP and SAP requires both imaging features and clinical evidence.

Nutrition therapy serves as one of the keys to the treatment of acute pancreatitis. Enteral nutrition remains the primary pattern, including oral refeeding and enteral refeeding tubes.

In this study, we aim to highlight the potential value of diverse refeeding patterns. MSAP and SAP were retrospectively analyzed with the clinical features of each HLAP and the difference between MSAP and SAP between various refeeding patterns.

Patients and Methods

Research Subjects

This was a retrospective cohort study that was conducted in the Department of General Surgery. The study was approved by the Institutional Review Board of Ordos Central Hospital. Informed consent from individuals was waived due to the retrospective, observational, and anonymous nature of the study. The study included consecutive patients admitted to the Ordos Central Hospital between January 2019 and April 2022. Information was collected manually by physicians.

Inclusion Criteria

Patients diagnosed with AP after admission were selected in this study. The diagnosis of AP was strictly in accordance with the 2012 revised

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Atlanta classification[6] and confirmed by any two or more of the following criteria: (1) abdominal pain consistent with AP (acute onset of a persistent, severe epigastric pain, often radiating to the back); (2) serum amylase and/or lipase activity at least three times higher than the upper limit of normal; and (3) characteristic findings of AP on contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) or transabdominal ultrasonography.

Patients had concurrent hypertriglyceridemia [serum triglyceride (TG) levels ≥1,000 mg/dl (11.3 mmol/L)]; or serum TG levels between 500-1,000 mg/dl (5.65-11.3 mmol/L) with chylous serum.

Patients meeting any of the following criteria were excluded: (1) have or had pancreatic malignancies; (2) concurrent immune diseases; (3) incomplete clinical data or received midway; (4) chronic pancreatitis.

Research Method

The included patients with HLAP were divided into three categories according to severity[6]: mild acute pancreatitis, moderate to severe acute pancreatitis, and severe acute pancreatitis.

These moderate to severe HLAPs were categorized into two groups based on the nutrition pathways: The oral refeeding tolerant (ORT) group and the enteral tube feeding tolerant (ETFT) group. ORT group were patients without nausea or vomiting, and oral enteral nutrition was provided immediately after the disappearance of abdominal pain and bloating. ORT group can have either a low-fat solid diet or a pure liquid diet. ETFT group were patients who did not tolerate oral feeding attempts. They were unable to consume most of their diet due to a recurrence of abdominal pain and bloating symptoms after ingestion of a liquid diet. Therefore, the ETFT group required increased analgesic doses and antiemetics, or developed vomiting and required nutrition via a nasogastric or nasojejunal tube feeding.

Timing of initiation of enteral nutrition: relief of abdominal pain, bloating, and triglycerides below 5.6 mmol/L.

Clinical Data Collection

General information

Patient data collected included gender, age, pancreatitis etiology, history of hypertension, diabetes, drinking, acute pancreatitis, antibiotic use, fever, abdominal pain, abdominal distension, nausea/vomiting, and nutritional style. In addition, the following laboratory data was collected at admission: white blood cell, red blood cell, hemoglobin and platelet counts; alanine aminotransferase, aspartate aminotransferase, and albumin, creatinine, sodium ions, calcium ions, blood amylase, blood lipase, triglyceride, total cholesterol, coagulation zymogen, and fibrinogen.

Clinical outcomes

Economic index: length of hospital stays and expenses; patients developed complications: exocrine insufficiency and new-onset diabetes. Follow-up was determined within 12 months of the onset of HLAP.

Statistical Analysis

SPSS 25.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analyses, and measurement data with normal distribution are shown as means ± standard deviations. Comparisons between the two groups were performed by an independent samples *t*-test, and a comparison of measurement data that did not conform to a normal distribution was performed by the Mann-Whitney U test. A Chi-square test or Fisher's exact test was used to compare the enumeration data between two groups. Differences were considered statistically significant when $p<0.05$.

Results

A total of 1,340 patients with AP diagnosis were initially randomized, after monitoring. 1005 patients were excluded from the analysis for not meeting the requirements of the study protocol (Figure 1). Of the 335 HLAP, 268 MSAP patients were included in the study, 193 in the OFT group, and 75 in the ETFT group.

General data comparisons between the ORT and the ETFT groups showed interesting findings. Out of a total of 268 patients, 220 (82%) patients were males, the median age was 40 years, and there were no significant differences in sex and age between the ORT and the ETFT groups. No statistically significant differences were found on the following variables: history of hypertension, diabetes mellitus, alcohol consumption, acute pancreatitis, antibiotics, fever, and nausea/vomiting. We found in the ETFT group, abdominal pain and abdominal distension were significantly higher than that in the OFT group (Table I).

Comparison of laboratory data among the OFT and the ETFT groups also yielded intriguing findings. There were no significant differences in the white blood cell, red blood cell,

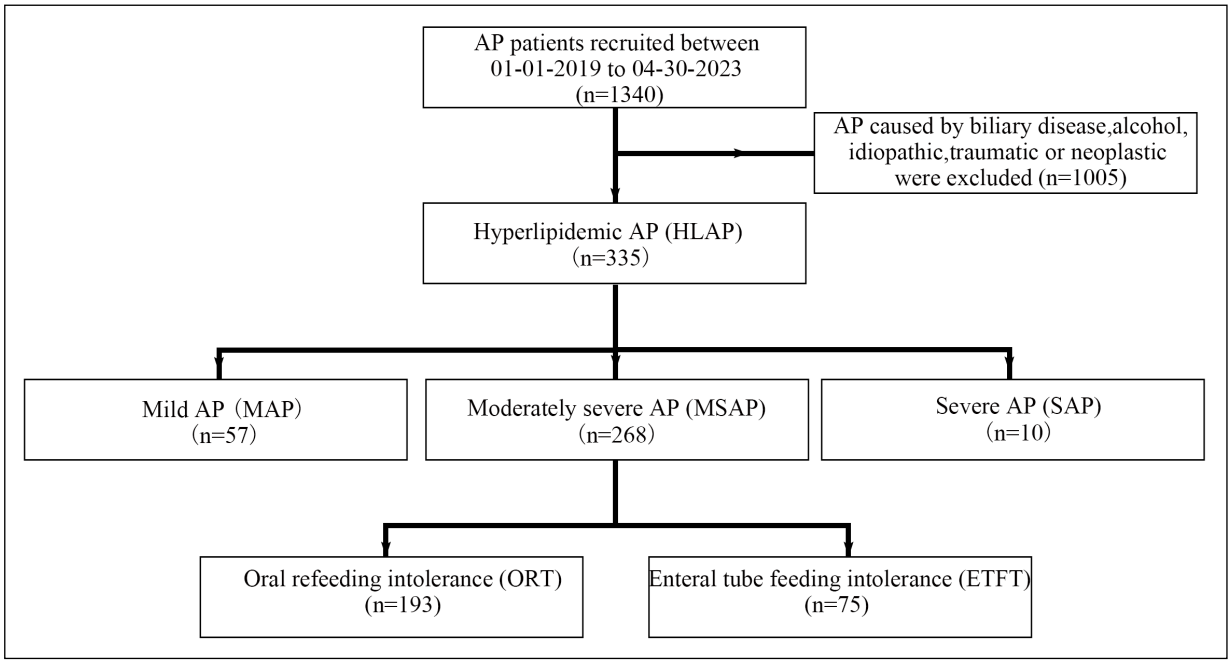

Figure 1. Flowchart of recruited hyperlipidemic acute pancreatitis (HLAP).

hemoglobin, platelet counts, alanine aminotransferase, aspartate aminotransferase, creatinine, calcium ion, blood amylase, blood lipase, total cholesterol, triglyceride, prothrombin, and fibrinogen levels between the OFT and the ETFT Groups (Table II).

Comparisons of the economic index and complications between groups were the last area compared. Regarding hospitalization and cost, they were higher in the OFT group than in the ETFT group, and the differences were statistically significant. There were also significant differences in complications (exocrine insufficiency and new-onset diabetes) between the OFT and the ETFT groups (Table III).

Discussion

Acute pancreatitis is one of the most commonly diagnosed diseases in the digestive system, with clinical outcomes closely associated with various causes and severity. Hyperlipidemia is the third most commonly diagnosed cause of

Table I. Comparison of general data of oral refeeding tolerance (ORT) and enteral tube feeding tolerance (ETFT) groups.

	Total (n=268)	ORT (n=193)	ETFT (n=75)	p
Gender	268	193	75	0.719
Male	220	159	61	-
Female	48	34	14	-
Age				0.544
30-39 years old	105	78	27	
40-49 years old	93	62	31	
Hypertension	59 (22%)	40	17	0.727
Diabetes mellitus	92 (34%)	65	27	0.719
Alcoholism	84 (31%)	53	31	0.028
History of acute pancreatitis	138 (52%)	95	43	0.233
Antibiotic therapy	109 (41%)	75	34	0.333
Fever	6 (2%)	3	3	0.354
Abdominal pain	265 (87%)	163	72	0.001
Abdominal distension	220 (82%)	150	70	0.003
Nausea/vomiting	125 (47%)	85	40	0.171

Table II. Comparison of laboratory data between ORT and ETFT groups.

	ORT	ETFT	*p*
Number	193	75	
WBC (10^9/l)	12.9±5.0	11.6±4.3	0.042
RBC (10^{12}/l)	5.1±0.6	5.0±0.5.	0.480
Hgb (10^{12}/l)	161.3±19.1	160.7±19.7	0.838
PLT (10^9/l)	219.3±60.5	214.5±60.1	0.562
ALT (u/l)	38.9±31.8	38.4±27.9	0.918
AST (u/l)	37.8±25.3	33.5±20.8	0.533
Cr (umol/l)	62.2±29.2	64.1±22.9	0.587
Ca^{2+} (mmol/l)	2.2±0.2	2.1±0.3	0.345
LPS (u/l)	250.4±231.6	260.6±237.8	0.760
AMS (u/l)	238.5±248.8	263.2±269.6	0.495
TC (mmol/l)	9.4±3.5	9.7±4.2	0.497
TG (mmol/l)	19.7±12.5	17.8±13.5	0.282
PT (s)	11.7±2.1	11.7±1.0	0.916
FIB (g/l)	4.0±2.7	4.2±1.9	0.536

WBC: white blood cells; RBC: red blood cells; Hgb: hemoglobin; PLT: platelet; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Cr: Creatinine; Ca^{2+}: calcium ion; LPS: blood lipase; AMS: blood amylase; TC: total cholesterol; TG: triglyceride; PT: prothrombin; FIB: fibrinogen.

Table III. Comparison of results of ORT and ETFT groups.

	ORT (n=193)	ETFT (n=75)	*p*
Economic index			
Hospitalization (days)	10.1±4.75	14.0±7.3	<0.001
Cost	13,252±9,311	19,279±13,021	<0.001
Complications			
Exocrine insufficiency	25	21	0.03
Newly onset diabetes	23	18	0.014

acute pancreatitis. HLAP is one of the major types of acute pancreatitis, accounting for 33% of all diagnosed acute pancreatitis cases[7]. Other causes include obesity, metabolism syndrome, diabetes, and cardiovascular disease[8].

Our study showed that HLAP may account for 25% of all acute pancreatitis, with incidence ranking second, featuring a younger median age, higher severity, increased recurrence, and untypical clinical manifestation. It may be associated with local diet, habits, and health status.

According to the Atlanta classification, acute pancreatitis can be divided into mild, moderate, and severe types. Around 80% of acute pancreatitis was mild, with 20% eventually developing into moderate or severe types, showing tissue necrosis and/or multiple organ failure[9]. Ding et al reported that around 85% of HLAP were classified as moderately severe acute pancreatitis (MSAP), with 1.9% as mild acute pancreatitis and 13.4% in severe type. Our study reported that 80% of included patients were diagnosed with MSAP. However, the association between severity, etiology and region remains largely unknown.

Both MSAP and SAP were extensively discussed in the classification of acute pancreatitis by international consensus. MSAP is characterized by transient organ failure (resolves within 48 hours) and/or local complications (for example, peripancreatic collection) or systemic complications (for example, exacerbation of coronary artery disease). SAP is characterized by persistent organ failure (longer than 48 hours) and multiple organ failure. Of note, SAP patients with early presentation of persistent organ failure are associated with a mortality near 50%[10]. Practically, a diagnosis of MSAP is based on the exclusion of MAP and SAP, with images, complications, and organ failure serving as evidence but without therapy.

Nutritional management has been essential to therapy strategy in acute pancreatitis. "Pancreatic rest" has served as a key in old models; however, nutritional management remains largely excluded[11].

Nonetheless, mounting evidence[11,12] shows the benefits of early oral and enteral feeding, as it is closely associated with significantly reduced mortality rate and multiple organ failure. Additionally, early enteral feeding enhances the gut contractile force and provides sufficient blood supply to maintain the structural integrity of epithelial cells[13]. Therefore, enteral nutrition could reduce the incidence of infection, multiple organ failure, and mortality rates, and may contribute to decreased in-hospital stays[14,15]. Although the proper point for oral or enteral feeding remains disputed, most of researchers[16] agree that it should take place 24 to 48 hours after admission. According to this study, the standard of oral or enteral feeding, which includes decreased abdominal pain or bloating, shows that TG is less than 5.6 mmol/L. In fact, most patients received oral or enteral feeding at approximately 48 to 72 hours. However, early nutritional support may not be fully beneficial to the treatment of HLAP as the management may prolong the metabolism of TG.

MSAP is the most common type of HLAP. This study compared the difference between oral and enteral refeeding in MSAP, showing distinct variables, such as in-hospital stay, increased costs, functional failure in excretion, and new-onset diabetes. Excretion functional failure and new-onset diabetes were identified as key variables associated with acute pancreatitis that can result in poor quality of life and a high risk of mortality[17-19].

Conclusions

Based on the incidence of HLAP retrieved in this study, MSAP is the major type with increasing clinical value. From the nutritional management sense, patients who received OFT showed higher hospitalization and cost, as well as exocrine insufficiency and newly onset diabetes, than the ETFT group.

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Conflict of Interest
All authors declare no conflict of interest.

Authors' Contributions
ER-XIA CHEN and XI CAO conceived of the study, performed the statistical analysis, and drafted the manuscript. ZHAN-FEI SHE, JIAN-HUA TONG and GENG CHE supervised the study, performed the statistical analysis and drafted the manuscript. All authors read and approved the final manuscript.

Ethics Approval
This study was reviewed and approved by the Ethical Review Committee of Ordos Central Hospital (No. 202312).

Informed Consent
Not applicable.

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