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Research Article

Early Oral Refeeding and Selection of Initial Diet in Mild Acute Pancreatitis

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1. Abstract

1.1. Background/Objectives: When and how to initiate oral reefeding in patients with mild acute pancreatitis (AP) is still an important issue. The aim of this study was to evaluate the efficacy of early oral reefeding in these patients.

1.2. Methods: This is a singl ecenter, prospective, randomized controlled trial. Patients with mild biliary acute pancreatitis who admitted to our hospital were included. The patients were separated into two different main groups: early oral reefeding (EORF) and routine oral reefeding (RORF). These main two groups were divided into three subgroups according to initial dietary regimen (liquid, soft and solid diet). After the comparison according to mean pain index, pain index after initial meal, length of hospitalization, inflammation and need for antibiotics and painkiller drugs between two main groups, subgroups were compared according to same parameters also.

1.3. Results: There were 49 patients in EORF group and 49 patients in RORF group. In EORF group, mean hospitalization length, mean pain index and need for antibiotics were seen significantly lower (p values in order <0.001, 0.003, 0.009). Pain index after first meal after hospitalization was lower in RORF group (p<0.001). Subgroups were compared according to same parameters and there were no significant difference.

1.4. Conclusion: The patient, who suffered mild acute pancreatitis, may eat first routine meal, regardless of the severity of the pain and without waiting for pancreatitis to recovery.. The onset of bolus presence is the impedance dropped to 90% of the nadir; the offset of bolus presence was the return to 50% of the impedance baseline.

2. Key words: Acute pancreatitis; Oral reefeding; Pain index

3. Introduction

Acute pancreatitis is an acute inflammatory disease of the pancreas affecting peripancreatic tissues and other organs as well. It starts with intracellular release and premature activation of digestive enzymes, leading to injury in pancreatic acinar cells [1]. While 80% of the patients with AP have a mild episode, severe pancreatitis is seen in 20% of the cases. Main goals of AP treatment includes providing adequate nutritional support and positive nitrogen balance, avoiding iatrogenic complications such as over nutrition, taking control of inflammatory response and protecting normal body functions [2, 3]. Nutrition is important to reverse the catabolic process. Parenteral nutrition should be applied only in severe, acute or prolonged pancreatitis if nutritional support is mandatory when patient is unable to tolerate oral food intake. Enteral nutrition is preferred over parenteral nutrition in mild AP [4]. Beneficial effects of early enteral nutrition in mild AP have been reported in literature and further studies are continuing to confirm these results. Studies have shown that enteral nutrition with immunonutrition may be useful in prevention of gut-origin sepsis. Pancreatic secretion can play a role to maintain gastrointestinal microbial balance by having antimicrobial features and supporting the bactericidal effects of some antimicrobial drugs [5]. The decision to start oral reefeding is traditionally based on resolution of abdominal pain and normalization of the pancreatic enzymes. Contrary to

this, some recent studies have suggested that normalization of the pancreatic enzymes is not obligatory to decide when to start enteral nutrition [6]. In patients with AP, the choice of initial diet is an important issue also. Usually, a low-fat liquid diet as is preferred as initial diet in mild AP. Discharge was decided when patient tolerates solid diet [3]. Time to start oral reefing and choice of initial diet in patients with AP is important because of their effects on recurrence of the abdominal pain and hospitalization time. Although there are some studies about this issue, the results are inconclusive. The aim of this study is to evaluate the role of early oral reefeding (EORF), routine oral reefeding (RORF) and the effect of initial dietary regimen (liquid, soft and solid diet) on the course of the disease, mortality and morbidity both during the hospitalization period and up to 30 days following discharge.

4. Materials and Methods

4.1. Study design and setting

This trial was a single center, prospective, randomized controlled study comparing the effects of EORF, RORF and initial dietary regimen on the clinical outcomes of patients with mild biliary AP. The study protocol was approved by the IRB (Ethics and Human Research) of our institution and all patients completed a written informed consent before enrolment.

4.2. Inclusion and exclusion criteria

Patients who were admitted to the Gastroenterology Clinic of Mersin University Hospital with the diagnosis of AP between December 2011 and December 2013 were evaluated for enrolment in our study. The inclusion criteria were as follows: (1) age older than 18 years; (2) onset of acute abdominal pain accompanied with elevated serum levels of amylase and/or lipase , overall at least 3-fold higher than the upper limit measure of the reference range and radiological evidence of AP; (3) mild biliary AP according to Atlanta criteria. Exclusion criteria were the following: (1) age 18 years or younger; (2) moderate/severe pancreatitis according to Atlanta criteria; (3) non biliary acute pancreatitis; (4) having pancreatic fistula, pancreatic ascites or pancreatic pseudocyst; (4) patients who do not speak Turkish. Early stopping criteria were as follows: (1) development of acute abdomen; (2) development of multiorgan failure; (3) development of sepsis; (4) development of ileus; (5) death.

4.3. Study Protocol

A total of 98 patients were included in the study. They were randomized as EORF group (n=49) which includes patients who were started reefeding at first meal time after admission and RORF group (n=49) which includes patients who started reefeding after clinical improvement and normalization of the laboratory results. Both groups were divided into three subgroups according to the initial dietary regimen. Liquid diet was defined as regimen 1 (850 kcal; 75% carbohydrates, 12% protein and 13% fat), soft diet was defined as regimen 2 (1600 kcal; 63% carbohydrates, 15% protein and 22% fat) and solid diet was defined as regimen 3 (1600 kcal; 48% carbohydrates, 17% protein and 35% fat) (**Figure 1**). Age, gender, body mass index (BMI), laboratory results, Ranson and APACHE scores, hospitalization length, mean pain index, pain score after initial enteral nutrition, feeding intolerance, need for analgesics and antibiotics of the patients were recorded. Total meperidine dose of each patient was recorded also. Patients were evaluated for local complications with abdominal ultrasonography, morbidity and mortality 30 days after discharge. After two main groups were compared with each other, subgroups were compared also. Turkish version of the brief pain inventory was used to determine pain scores [7, 8]. Pain assessments were done after each meal (six times a day). Daily pain indexes of each patient were calculated as mean values of these measurements. Mean pain index were calculated mean value of these daily pain indexes during hospitalization were calculated.

4.4. Statistical Analysis

It was tested by the Shapiro Wilks test whether the parameters were complied with normal distribution, or not. The mean and standard deviation were used as descriptive statistics for the continuous variables in the group which complied with the normal distribution, whereas the median and percentage were used in the group without normal distribution. It was given the number and percentage values for the categorical parameters. The Student's t test was used to test the difference of means between two groups for the parameters with normal distribution and Mann -Whitney U test was used to test the difference of means between two groups, for the parameters without normal distribution. For comparison of the three sub-groups, the ANOVA test was used for parameters with normal distribution, whereas the Kruskal-Wallis test was used for parameters without normal distribution. Chi-square test was used for the categorical parameters to analyses the relationship between the groups. Statistical significance was $p < 0.05$.

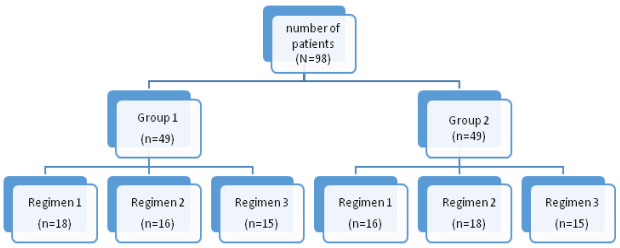

Figure 1: Divisions of groups and subgroups.

5. Results

Baseline characteristics of the patients in the two main groups were shown in Table1. Mean age of the all patients included in this study was 54.9 years. While 47.5% of the patients were male, 52.5% of them were female. In 73% of the patients, the etiology of pancreatitis was biliary disease. Less need for antibiotics in was observed in EORF group compared to RORF group. 2.1% of the patients in EORF group and 18.4% of the patients in RORF group needed for antibiotics which was statistically significant (p=0.009). This data revealed that EORF reduced infection risk together with decreasing CRP levels. When groups were compared regarding mean pain indexes, lower mean pain indexes were found in EORF group compared to RORF group (EORF group: 4.4±0.54 points, RORF group: 5.8±0.75 points, P=0.003) although higher dose of analgesics were used in RORF group (p=0.044). Despite that, pain score after initial enteral nutrition was lower in RORF group (EORF group: 5.4±0.85 points, RORF group: 3.9±1.03 points, P<0.001) (**Table 2**). If we look at the mean pain indexes at 24th hour, 48th hour and 72nd hour of the groups, 24th hour mean pain indexes of EORF group were lower than RORF group (p<0.001). While feeding intolerance was seen in 3 patients in EORF group, no patient in ROFR group (p=0.083) (**Table 2**).Mean hospitalization length was 3.89±0.69 days in EORF group compared to 4.93±0.77 days in RORF group (p<0.001). When we look at the serum CRP levels at 24th hour, 48th hour and 72nd hour of the groups, CRP levels were higher and elevated faster in RORF group and it was statistically significant (p<0.05) (**Table 1**, **Figure 3**).

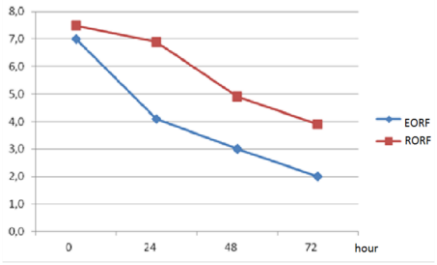

Figure 2: Mean pain indexes at admission time, 24th hour, 48th hour and 72nd hour of hospitalization. (mean pain index at admission was 7.0±0.55 in EORF group and 7.5±0.25 in RORF group, p=0.290; at 24th hour was 4.1±0.20 in EORF group and 6.9±0.15 in RORF group, p<0.001).

Table 1: Baseline characteristics of the patients in the two main groups.

	EORF	RORF	P
Patients (Male/Female)	49 (25/24)	49 (22/27)	0.307
Age, median (range), yr	53 (25-88)	56 (27-86)	0.582
Etiology, n (%)			
Biliary			
37 (79.2%)			
35 (71.4%)			
0.259			
Alcohol	10 (20.8%)	14 (28.6%)	0.482
BMI (Body Mass Index)	27±4.4	26±3.8	0.395
Serum Amylase, IU/L			
1571±457			
1199±487			
0.241			
Serum Lipase , IU/L	2956±468	3289±635	0.25
White Blood Cell Count, x 10^9/L	11486 ±991	11295± 642	0.293
Hematocrit	0.36±0.08	0.38±0.07	0.44
CRP	22.3±6.4	37.1±17.4	0,354
Creatinin (mg/dL)	0,76±0.24	0,82±0.22	0.214
APACHE 2 Score, Mean±SD	3.9±3.2	3.2±2.9	0.195
Ranson-0 Score, Mean± SD	1.07±0.9	0.95±0.7	0.149
LDL, Mean±SD	101.9±28.6	107.9±32.7	0.376
Triglyceride level±SD	153.7±32.6	192.0±36.5	0.154

Table 2: Results of EORF and RORF groups.

	EORF	RORF	
Need for antibiotics (n)	1(%2.1)	9(%18.4)	P=0.009
Mean pain index (VAS)	4.4±0.54	5.8±0.75	P=0.003
Pain score after first meal (VAS)	5.4±0.85	3.9±1.03	P<0.001
Length of hospitalization (day)	3.89±0.69	4.93±0.77	P<0.001
Total meperidine dose, mean	181.1±128 mg	346.6±186.4 mg	P=0.044
Mortality (n)	0	0	
Feeding intolerance (n)	3	1	P=0.190

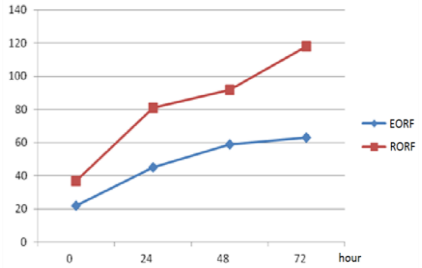

Figure 3: CRP levels were higher and elevated faster in RORF group and it was statistically significant (p<0.05).

After comparison of two main groups, subgroups according to initial dietary regimens were compared also. Subgroups of EORF group were compared with each other regarding hospitalization length, mean pain index and pain score after initial enteral nutrition (**Table 3**) and there were no significant difference between subgroups (group 1a: regimen 1, group 1b:regimen 2, group 1c:regimen 3). Subgroups of RORF group were also

compared with each other regarding hospitalization length, mean pain index and pain score after initial enteral nutrition (**Table 4**) and there were again no significant difference between subgroups (group 2a: regimen 1, group 2b:regimen 2, group 2c:regimen 3). It was observed that initial dietary regimen did not influence the severity of pain and hospitalization length in patients with mild AP. In this study, none of the patients developed sepsis, acute abdomen, multiorgan failure, complications requiring surgery or death.

Table 3: Mean serum CRP levels at admission time, 24th hour, 48th hour and 72nd hour.

	EORF Mean±SD	RORF Mean±SD	p value
CRP at admission	22.3±6.4	37.1±17.4	0.354
CRP 24th hour	45.2±22.8	81.4±36.8	**0.036**
CRP 48th hour	59.6±36.4	92.6±50.4	**0.008**
CRP 72th hour	63.9±56.4	118.5±60.2	**0.017**

Table 4: Comparison of group 1a, group 1b, group 1c.

	Group 1a	Group 1b	Group 1c	P değeri
Mean pain index (VAS)	4.33±0.48	4.50±0.51	4.50±0.65	P=0.613
Pain score after first meal (VAS)	5.44±0.70	5.75±1.06	5.21±0.69	P=0.386
Length of hospitalization (day)	3.80±0.75	4.00±0.73	3.78±0.57	P=0.723
Total meperidine dose, (mean)	158.3±146 mg	210±113 mg	175±123 mg	P=0.245

Table 5: Comparison of group 2a, group 2b, group 2c.

	Group 2a	Group 2b	Group 2c	p value
Mean pain index (VAS)	4.93±0.77	5.65±0.73	5.90±0.77	P=0.900
Pain score after first meal (VAS)	4.37±1.20	3.94±0.93	3.46±0.83	P=0.085
Length of hospitalization (day)	5.18±0.75	4.88±0.75	4.73±0.79	P=0.245
Total meperidine dose, (mean)	359±194 mg	300±136 mg	380±229	P=0,280

6. Discussion

Studies have shown that early oral reefeding reduces gut-origin sepsis and makes antimicrobial effects against various microorganisms by increasing pancreatic secretion in patients with mild AP [5, 9-11]. In accordance with this data, we observed better outcomes in EORF group in point of risk of infection and need for antibiotics. In a study with 149 patients which was carried out by Juan li et al in 2009, early oral reefeding group had shorter hospitalization length compared to routine reefeding group [10]. In a similar randomized controlled study which was conducted by Guniella E.Eckerwall et al also demonstrated that oral feeding on admission for mild acute pancreatitis was associated with a significant decrease in length of stay from 6 to 4 days (p = 0.047) compared with withholding oral food and fluids [9]. In this regard, our study seems to be support the results of these studies. When and how to initiate oral refeeding in mild AP is still an important issue. Many clinicians advocate that the decision to recommence oral refeeding is based on resolution of abdominal pain and normalization of laboratory findings. Traditionally, oral refeeding starts with liquid diet and continue with soft and solid diet if patient tolerates well. However, there are no clinical evidence about this issue [11, 12]. There a few studies which recommends soft or solid diet as initial dietary regimen. The major benefits from early feeding appear to be effective only if feeding is commenced within the first 48 hours following admission, [13-60] and the current recommendation based on a 2010 meta-analysis of 32 RCTs is to commence oral feeding at the time of admission if tolerated or within the first 24 hours [13,14]. Finally, a low-fat diet was shown to be preferable to clear fluids on admission for mild acute pancreatitis owing to a higher caloric intake with no associated adverse effects [9,15]. There is no evidence to suggest that a low-fat diet is preferable to a regular dietE.Sathiaraj et al. [16] reported that hospitalization length in soft diet group was shorter than liquid diet group, whereas there was no statistically significant difference between groups in terms of recurrence of pain [15]. Similarly, a study which was published in 2010 by Moares et al. [16] revealed that patients in solid diet group had shorter hospitalization time [16]. Our findings in this study revealed that initial dietary regimen did not affect severity of pain and hospitalization length. On the other hand, severity of pain and need for analgesics in EORF group decreased gradually probably because of reduction in inflammatory response no matter how severe the initial pain is. Early nutrition has also shown that it reduces the length of hospital stay **(Table 2)**. We did not observed mortality within 30 days.EORF in patients with mild acute pancreatitis reduces abdominal pain attacks and hence the need for pain relief; we have shown that the laboratory findings including inflammatory markers are normalized more rapidly, thereby reducing the length of hospital stay and antibiotic requirement. This controlled, randomized clinical trial confirmed the effectiveness and feasibility of EORF in patients with mild AP. Routine oral feeding should be started immediately in patients with mild acute pancreatitis and oral feeding should be continued unless the patient's clinic worsens or if there is no severe abdominal pain to the extent that meperidine is unresponsive. As a result, the patient who suffered mild acute pancreatitis may eat first routine meal, regardless of the severity of the pain and without waiting for pancreatitis to recovery.

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