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OBSERVATION

Oral refeeding in mild acute pancreatitis: An old challenge

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Abstract

Although the idea that pancreas rest has long been considered as a very relevant topic in acute pancreatitis (AP) therapy, the right time and type of diet to be offered to patients recovering from an acute attack are a great challenge to clinicians who treat this condition. Fortunately, the last decade was noted for several trials looking for the best answer to the question: "when and how to start oral refeeding in AP?" It is well known that 80% of patients present with mild disease characterized by usually uncomplicated clinical course are managed with pancreatic rest through nil per oral; while the use of specific nutritional intervention is an exception. Therefore, mild AP has been the most investigated form of AP and researchers have tried different kind of meals to offer calories and reduce costs by shortening hospitalization time. Usually in mild AP, the oral refeeding is introduced between the first 3 d and 7 d after hospitalization but, the type of diet and patients' tolerance have been scrutinized in detail with mixed results. Although 20% to 25% have pain recurrence requiring nutritional support and greater time of hospitalization, most patients seem to tolerate oral refeeding well. We propose analyzing the most recent investigations of this matter and their conclusions to develop a better understanding of the management of AP.

Key words: Acute pancreatitis; Oral refeeding; Nutrition; Treatment; Diet

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INTRODUCTION

Patients recovering from acute pancreatitis (AP) have been a great challenge for gastroenterologists with issues concerning the timing and type of diet to be offered without risk of increasing gland stimuli and worsening pancreas inflammation. The thought that as long as unfed they could be maintained through nil per oral was based on the idea that pancreas rest was considered an essential strategy in the treatment. This assumption has been taken up for years although there is, until now, little hard scientific basis to support it. It is conceivable that many patients with even more severe episodes of AP might eat quite early in the course of their disease, with no deleterious effects. In fact, nowadays there are no sufficient data to make clear this postulate. Moreover, this hypothesis was based only in physiological research. Until now no general consensus has been established about the type of diet and the appropriate time when it should be offered to patients convalescing from AP. An important aim in dealing with AP patients is to find a better way of managing oral food reintroduction. Since 80% of patients have mild AP, such patients have been more frequently investi-

gated. Pancreatic rest through nil per oral was always considered necessary in AP while the general rule suggested starting oral refeeding 3 d to 7 d after patients were hospitalized[1,2]. In general, oral intake of small amounts of calories have been usually considered the better strategy to start oral refeeding, once the clinical symptoms and signs of AP are absent, when the patients recover appetite and do not have nausea, vomiting or abdominal pain with normal bowel sounds[1,3]. Therefore, the traditional way to deal with this challenge during hospitalization was starting oral intake with clear liquids (CLD), since they do not exert relevant stimulatory effects on pancreatic exocrine secretion. A low-fat diet would be allowed to those who tolerate an initial trial[3]. Lipids can stimulate pancreatic secretion and clinicians have in mind that patients recovering from mild AP, eating a low-fat diet, have reduced exocrine pancreatic secretion as well as cholecystokinin (CCK) production. Therefore, potentially deleterious effects on the inflamed pancreas would occur, but there is little scientific evidence supporting this concept[4]. Although this approach is usually assumed, it is only based on clinical experience. New trials would be necessary to define amore appropriated diet to oral refeeding in patients recovering from AP.

REFEEDING IN AP

In 1997, Lévy *et al*[5], in a multivariate multicenter prospective study, tried to analyze the frequency and risk factors of recurrent pain during oral refeeding in 116 patients with mild AP. The conclusion was that pain relapse occurred in 20% of the patients and was more common in patients with necrotizing pancreatitis who had longer periods of pain. This survey seems to suggest that we would be able to predict high-risk patients who have pain recurrence during oral refeeding and could be considered a first step in pain relapse prevention. They also noticed that pain relapse frequency was not modified significantly in any of the therapeutic procedures adopted. However, in another evaluation, Chebli *et al*[6] studied 130 patients with mild AP and observed that during the oral refeeding period, 24.6% of patients had pain relapse, more frequently on days 1 (68.8%) and 2 (28%) and observed that it was related to higher serum levels of lipase on the day before refeeding, higher serum levels of C-reactive protein on the fourth day as well as peripancreatic fluid collections ($P < 0.01$). Pain relapse increased hospital stay and overall costs of disease treatment. Petrov *et al*[7] in a literature review, (cited in Cochrane Central Register of Controlled Trials, EMBASE, and MEDLINE) as well as the conclusions of abstracts of major gastroenterological meetings, taking into account that outcome measures studied were the incidence of pain relapse and length of hospitalization (LOH), pointed that only three studies met the inclusion criteria. They concluded that sixty (22%) of 274 patients had pain relapse during the course of AP and in 78.3% it occurred within 48 h after starting oral refeeding. All three studies found a difference in scores of severity in patients who had or had not pain relapse and found a significant increase in the LOH in those whose pain reappeared after oral refeeding. Therefore it becomes clear that, in these patients, there is an increased cost of treatment. Jacobson *et al*[8] developed a prospective randomized trial comparing CLD *vs* low-fat solid diet (LFSD) as the initial meal in mild AP. They randomized two similar groups with mild AP and hypothesized that initiating oral nutrition with LFSD after mild AP would be well-tolerated and would result in a shorter LOH. Their final conclusion was that starting oral nutrition after mild AP with a LFSD appeared to be safe and provided more calories than a CLD, but did not result in a shorter LOH. On the other hand, Reber[4] considered that earlier discharge was not an advantage and suggested a flaw in trial design, because he found it intuitively obvious that at least 1 d of hospitalization would have been saved in those who had begun with solid food. Moreover, Reber[4] posed two interesting questions: whether offering solid food to patients with AP can be done safely, does the nutrient composition (in particular, the fat content) of the diet affect the clinical response; and is it more relevant to feed such patients with a low rather than a higher fat content that might be more palatable? Meanwhile, Sathiaraj *et al*[9] compared two groups of mild AP patients who, as their initial meal had a soft diet or a clear liquid diet. They observed a statistically significant decrease in the LOH (total and post-refeeding) of a median 2 d in patients receiving a soft diet ($P < 0.001$) but no significant difference for refeeding interruption due to pain, was observed between the two groups, and patients who started on a soft diet consumed much more calories and fats on study day 1 ($P < 0.001$). The researchers conclusion was that oral refeeding with a soft diet in patients with mild AP can be considered safe and can result in shorter LOH. Studies of the best feeding option has come from comparisons between CLD and LFSD. Different kinds of diets have been tried but no one study was ambitious enough to investigate the tolerance of a full solid diet as the initial meal in AP. In 2010, Moraes *et al*[10] conducted an investigation to try to demonstrate whether or not a heavier diet could be dangerous given the evidence of previous studies. They observed through a prospective, randomized, controlled double blind clinical trial that oral refeeding, with a full solid diet in mild AP, was well tolerated by most patients and resulted in a shorter LOH among patients without abdominal pain relapse. Therefore, employing this strategy would save health care resources. It was observed that a full solid diet may be more palatable and a cost-saving alternative for the dietary management of patients recovering from mild AP. The authors also called attention to the fact that their findings may not be applied to patients with severe AP, since only those with mild AP were evaluated. As far as we are concerned, this is a highly relevant contribution to the optimal dietary approach to oral refeeding in mild AP but further clinical trials are necessary to investigate other strategies to prevent pain relapse during oral refeeding in patients with AP. It is well known that a 20% intolerance can be seen in AP, regardless of the type of

initial oral refeeding diet.

After analyzing the data in recent studies reviewed above, we can state that in patients with mild AP, the nutrient composition and the physical features of meals do not appear to change the clinical course of disease. Hence, a very interesting question arose: would we be able to match the interesting clinical data to those found in physiological studies[11,12] that show slower pancreatic response and higher pancreatic enzyme output in response to a high-fat solid diet with greater caloric loads? It is possible that the injured pancreas can have an attenuated response to feeding stimuli. So, we can speculate that the basal and stimulated pancreatic enzyme secretion, in particular pancreatic secretory response to CCK, may be woken markedly early, after the onset of AP, as have been shown in experimental studies[13,14]. Evidence allows us to conclude that in human pancreatitis the injured pancreas may be less responsive to stimulation by food than previously considered[15,16].

In the last two decades we noticed that several investigations tried to test the tolerance to food stimulation of the inflamed gland after an episode of mild AP. Initially on a longer fasting period followed by an early oral refeeding with clear liquid and a low fat diet. Moreover, the evidence that a full solid meal can be used in such circumstances with better tolerance, demonstrated that increased nutritious calories and a reduction in therapy costs can occur. However, the findings of Moraes *et al*[10] lead us to suppose that we have now found the answer to an old question. A full solid diet is well tolerated by the majority of patients and results in a shorter length of hospital stay without abdominal pain relapse, thereby saving health care resources. Petrov[17] pointed out in Moraes study that the rate of feeding intolerance was around 20%, regardless of the type of initial diet used for oral refeeding and this was unacceptable both from the perspective of patient's quality of life and the cost of treatment. However, this rate of intolerance was observed also in other trials[5,6] and it seems a rule in oral refeeding of patients with mild AP.

CONCLUSION

In summary, identifying patients who are at high risk of developing pain recurrence during oral refeeding due to more intense or persistent pancreatic inflammation on the day before refeeding (for example, those patients presenting with a substantially increased serum lipase concentration and high level of C-reactive protein)[6], might allow a timely implementation of more specific therapeutic measures for this subgroup of patients such as nasojejunal tube feeding. Thus further clinical investigations are necessary to improve the identification of these subgroup patients and to establish an adequate strategy to prevent their pain relapse. To the best of our knowledge it seems that when considering full solid diet refeeding, we do not need to be afraid of "wakening the sleeping tiger. " The in-hospital time can be, saving costs.

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