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Oral Refeeding in Acute Pancreatitis

When and How Should it be Restarted?

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Introduction

Traditionally, refeeding in acute pancreatitis (AP) has been initiated when serum levels of pancreatic enzymes are decreasing, intestinal peristalsis is present, and patients are free from abdominal pain and fever. Oral intake has usually been started with clear liquids followed by solid low-fat meals with increasing caloric content over a period of three to six days in order to minimize pancreatic stimulation and the risk for abdominal pain and AP relapse [1]. A concern that refeeding will lead to cholecystokinin release, stimulation of exocrine pancreatic secretion, and aggravation of pancreatitis has been the theoretical basis of the traditional "nil by mouth" management in the early phase of AP. However, this concept has been challenged in a number of recently published studies investigating either the optimal time for refeeding [2,3] or the optimal schedule [4–7].

Recent guidelines and technical reviews have recommended early oral feeding in mild (interstitial) AP [8–10]. In patients with predicted severe or necrotizing AP, hospital stay is typically prolonged, and patients are often intolerant to oral feeding for a longer period of time. In these latter groups of patients, establishing a definite diagnosis of severe or necrotizing AP usually occurs between three and five days after initial presentation, a time when nasogastric or nasojejunal feeding is recommended to maintain the gut-mucosal barrier and to prevent infection of necrosis.

In this chapter, the following points are addressed: what is the optimal timing of oral refeeding in AP, how must the reintroduction of oral intake be scheduled, and what are the predictors of oral feeding intolerance in AP patients? As already mentioned, patients with predicted severe AP used to have more prolonged hospital stay, multiorgan failure and intensive care requirements, and hence oral refeeding in this group of patients does not constitute the main problem as nutritional requirements are supplemented mainly with enteral nutrition via the nasogastric or nasojejunal route.

What is the Optimal Timing of Refeeding in AP?

Optimal time of refeeding in AP has been investigated in several trials over the years. The traditional approach is to start oral refeeding after relief of abdominal pain and once serum levels of pancreatic enzymes return to normal. Several studies have questioned this approach. In a prospective and randomized trial our group compared two different protocols of refeeding and two different schedules for refeeding [11]. Four groups of patients with AP were defined according to the refeeding protocol (Table 11.1). The primary outcome of the study was length of hospital stay (LOHS); in addition, gastrointestinal symptoms after refeeding were evaluated. We did not find any significant difference in tolerance or gastrointestinal symptoms when comparing initiation of refeeding early, as soon as bowel sounds were present, or at standard time; when bowel sounds were present, there was no abdominal pain, no fever, decreasing serum lipase levels, and blood leukocyte counts had decreased to below 15×10^9/l. However, we observed a significant reduction in LOHS by two days in the early refeeding group. It seems therefore that refeeding after bowel sounds are present is a safe approach and well tolerated for patients with mild AP. Similar findings were reported from a Chinese randomized clinical trial, where refeeding started once patients felt hungry resulted in shorter LOHS compared to refeeding started at routine times, without any significant difference in adverse gastrointestinal events [12]. A German multicenter trial was unable to demonstrate any difference in LOHS when comparing initiation of refeeding in mild AP at the time self-selected by patients or when serum lipase levels were below twice

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Table 11.1 Oral refeeding protocols after acute pancreatitis.

Protocol	Time of refeeding	Refeeding schedule
Standard time and stepwise schedule	Standard[a]	Stepwise increase from a liquid 1200 kcal/day diet, to a soft 1500 kcal/day diet and a solid 1800 kcal/day diet over at least three days
Early time and stepwise schedule	Early[b]	
Standard time and direct schedule	Standard[a]	Initial solid diet containing 1800 kcal/day
Early time and direct schedule	Early[b]	

[a] Once the following criteria are fulfilled: bowel sounds are present, no abdominal pain, no fever, no leukocytosis, and decreasing serum pancreatic enzyme levels.
[b] Once bowel sounds are present and pain in controlled with non-opioid analgesics.

the upper limit of normal [3]. Eckerwall et al. [2] compared two protocols of oral refeeding in mild AP: immediate oral feeding ad libitum and traditional management by initial fasting followed by stepwise reintroduction of oral intake. LOHS was significantly shorter in the early refeeding group (4 vs. 6 days; $P < 0.05$). However, this study does not allow differentiation of the individual importance of early reintroduction of refeeding and rapid step-up protocol. All studies together clearly demonstrate that normalization of pancreatic enzyme levels is not a prerequisite to restart feeding. Early refeeding may shorten LOHS, but this was not consistently observed in all studies. The different definitions used for early and standard time for refeeding may explain this discrepancy to some extent.

In our center, oral refeeding after AP is started as soon as bowel sounds are present and abdominal pain is controlled with non-opioid analgesics.

How Should Oral Refeeding be Scheduled?

The initial meal given to patients with AP is considered to be important in determining whether reintroduction of oral intake is tolerated. Patients following the conventional stepwise refeeding protocol are traditionally started on a hypocaloric clear liquid diet and, if this first meal is well tolerated, soft diet (modified in texture, and in caloric and fat content) and solid low-fat diet are introduced in a stepwise manner until the patient can tolerate a normal oral diet [13].

In the study performed by our group [11], a protocol for refeeding with a solid low-fat diet (about 1800 kcal, 19 g of fat) versus standard stepwise increasing caloric diet over three days was evaluated (see Table 11.1). We found that a solid low-fat diet from the start was similarly tolerated compared to stepwise increasing caloric intake, and it was associated with a shorter LOHS if associated with early refeeding.

Different protocols for refeeding in subjects with mild AP have been investigated in five previous randomized clinical trials [2,4–7]. Jacobson et al. [5] compared a clear liquid diet (588 kcal, 2 g of fat per day) to a low-caloric, low-fat diet (1200 kcal, 35 g of fat per day) in patients with mild AP and showed no difference in tolerance or LOHS. Moraes et al. [6] performed a study with three treatment arms comparing a hypocaloric clear liquid diet, an intermediate hypocaloric soft diet (both around 250 kcal, 2 and 4 g of fat, respectively) and a full solid diet (around 1200 kcal, 30 g fat per day) in patients with mild AP. No differences in pain relapse rates or LOHS between the three treatment arms were found. Sathiaraj et al. [7] compared refeeding with a clear liquid diet (458 kcal, 11 g of fat) to a soft diet (1040 kcal, 20 g fat per day) in patients with mild AP. LOHS was significantly reduced in the soft diet group. Finally, Rajkumar et al. [4] investigated clear liquid diet compared to soft diet. Total and post-refeeding LOHS was shorter in the soft diet group. None of the previously published randomized clinical trials observed any increased risk of refeeding intolerance or other adverse events related to the more aggressive refeeding protocols [2,4,6,7].

What are the Predictors of Oral Feeding Intolerance in AP Patients?

There is significant concern about the relapse of gastrointestinal symptoms and pancreatitis following oral refeeding after AP since, the burden of oral feeding intolerance can be high. Some studies have shown that patients with oral feeding intolerance have significantly longer length of hospitalization [14–16], while others have demonstrated a reduced quality of life during hospitalization [17]. There is also evidence suggesting that these patients are at increased risk of early readmission if they are discharged with ongoing gastrointestinal symptoms, or are unable to tolerate a full diet at discharge [18].

A recent systematic review analyzed the current body of evidence and the incidence and predictors of oral feeding intolerance [19]. By evaluating 2024 patients in 22 studies these authors showed a global incidence of oral feeding intolerance of 16% (Table 11.2) [2–6,11,12,14–17,20–29]. The study found no relationship between the risk of developing oral feeding intolerance and age, sex, duration of symptoms before hospital admission, or etiology of AP. However, patients with blood lipase levels prior to refeeding of more than 2.5 times the upper limit of normal and those with (peri)pancreatic collections and pleural effusions were

Table 11.2 Characteristics of studies included in systematic review.

Author	Year	Setting	Study design	Total no. of AP patients included	No. of AP patients included in meta-analysis	Age, mean	Sex, no. (%)		Etiology, no. (%)		
							Male	Female	Biliary	Alcohol	Other
Bakker et al. [21]	2014	Netherlands	Multicenter randomized controlled trial	205	104	65	59 (57)	45 (43)	56 (54)	23 (22)	25 (24)
Chebli et al. [15]	2005	Brazil	Multicenter prospective observational study	130	130	47	67 (52)	63 (48)	60 (46)	42 (32)	28 (22)
Ciok et al. [27]	2003	Poland	Prospective observational study	214	214	46	102 (48)	112 (52)	106 (50)	62 (29)	46 (21)
Eckerwall et al. [28]	2006	Sweden	Retrospective observational study	99	99	60	64 (65)	35 (35)	31 (31)	30 (30)	38 (38)
Eckerwall et al. [2]	2007	Sweden	Randomized controlled trial	60	30	52	14 (47)	16 (53)	14 (47)	5 (17)	11 (37)
Francisco et al. [14]	2012	Spain	Retrospective observational study	232	232	74	122 (53)	110 (47)	150 (65)	25 (11)	57 (24)
Jacobson et al. [5]	2007	USA	Randomized controlled trial	121	66	47	34 (52)	32 (48)	15 (23)	19 (29)	32 (48)
Lariño-Noia et al. [14]	2014	Spain	Randomized controlled trial	72	17	69	8 (47)	9 (53)	9 (53)	3 (18)	5 (29)
Levy et al. [16]	1997	France	Multicenter prospective observational study	116	116	51	74 (64)	42 (36)	54 (47)	36 (31)	26 (22)
Levy et al. [26]	2004	France	Multicenter nonrandomized trial	23	—	51	15 (65)	8 (35)	7 (30)	11 (48)	5 (22)
Li et al. [12]	2013	China	Randomized controlled trial	149	74	49	47 (64)	27 (36)	37 (50)	19 (26)	18 (24)
Moraes et al. [6]	2010	Brazil	Randomized controlled trial	210	70	48	33 (47)	37 (53)	32 (46)	16 (23)	22 (31)
Pandey et al. [20]	2004	India	Randomized controlled trial	28	15	45	6 (40)	9 (60)	5 (33)	7 (47)	3 (20)
Pendharkar et al. [17]	2015	New Zealand	Prospective observational study	131	131	51	62 (47)	69 (53)	61 (46)	39 (30)	31 (24)
Petrov et al. [24]	2013	New Zealand	Randomized controlled trial	35	—	54	18 (51)	17 (49)	20 (57)	8 (23)	7 (20)
Pupelis et al. [25]	2006	Latvia	Nonrandomized trial	29	—	52	21 (72)	8 (28)	11 (38)	18 (62)	—
Qin & Qiu [22]	2002	China	Randomized controlled trial	204	99	57	65 (66)	34 (34)	—	—	—
Rajkumar et al. [4]	2013	India	Randomized controlled trial	60	30	36	28 (93)	2 (7)	2 (7)	27 (90)	1 (3)
Ren et al. [29]	2015	China	Retrospective observational study	323	—	—	—	—	—	—	—
Sathiaraj et al. [7]	2008	India	Randomized controlled trial	101	52	39	44 (85)	8 (15)	9 (17)	25 (48)	18 (35)
Teich et al. [3]	2010	Germany	Multicenter randomized controlled trial	143	—	47	50 (35)	93 (65)	43 (30)	64 (45)	36 (25)
Zhao et al. [23]	2015	China	Randomized controlled trial	138	71	48	43 (61)	28 (39)	16 (22)	14 (20)	41 (58)

at increased risk of developing oral feeding intolerance [19]. However, daily monitoring of serum lipase levels is not currently recommended in clinical practice and is associated with additional time and financial costs. Furthermore, the impact of monitoring serum lipase levels on risk of developing oral feeding intolerance has not been shown in other studies [11]. On the other hand, the practical significance of (peri)pancreatic collections as potential predictors of oral feeding intolerance is limited (given the need for early CT imaging, which is not routinely conducted prior to oral refeeding), and its presence leads to categorization of the episode of AP as moderately severe (and not mild) according to the Revised Atlanta Classification [30].

Moreover, it is important to keep in mind that many patients experience gastrointestinal symptoms after refeeding. In the study published by our group, up to 53% of all patients experienced gastrointestinal symptoms after refeeding. These were mainly meteorism and postprandial fullness of mild degree that only led to refeeding cessation in three cases. Abdominal pain was registered in 21 of 72 (29%) patients, but was severe enough to interrupt refeeding in only 4 of 72 (5.6%) cases (two of whom had signs of relapse of AP) [11].

Summary and Recommendations

The most recent and robust evidence supports early oral refeeding in mild AP. It is recommended that patients with AP should initially be kept nil by mouth after admission, while initial fluid resuscitation and intravenous analgesia is being administered. Once intestinal peristalsis recovers, as demonstrated by the presence of bowel sounds, initiation of refeeding is safe and generally well tolerated. A stepwise increase of caloric and fat content is usually not needed, but it should be considered in some patients, mainly in those with moderate or severe AP.

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