ORIGINAL ARTICLE

Immediate feeding tolerance in patients with mild acute biliary pancreatitis

Tolerancia a la alimentación inmediata en los pacientes con pancreatitis biliar leve

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Abstract

Background: *Mild acute pancreatitis is defined as pancreatic edema, without organic failure and without local complications. Its management consists in three basic elements: hydration, analgesia and fasting. Start refeeding when the patient haven't pain and referring hungry, but exact time for this is not previously documented.* **Objective:** *To determine the tolerance to immediate oral feeding (8 hours after the start of management) compared to early feeding (48 hours) in patients with mild acute biliary pancreatitis.* **Method:** *Included all patient with mild acute biliary pancreatitis, and they were randomized in to two groups: A) early oral feeding (n = 30) and B) immediate oral feeding (n = 29). They were evaluated by a third blind observer (not involved in the study) for documented symptoms like nausea, vomiting, reactivation of abdominal pain, systemic inflammatory response syndrome, food tolerance and hospital stay.* **Results:** *There were no significant differences between both groups in the clinical data or in the biochemical studies. The hospital stay was significantly less in the group B (5.4 vs. 7.8 days; p < 0.003).* **Conclusion:** *Immediate oral feeding is well tolerated and secure in patients with mild acute biliary pancreatitis.*

Keywords: *Feeding. Abdominal pain. Acute biliary pancreatitis. Systemic inflammatory response syndrome.*

Resumen

Antecedentes: *La pancreatitis aguda leve es una inflamación local del páncreas sin complicaciones locales ni falla orgánica. Su manejo consiste en tres elementos básicos: hidratación, analgesia y ayuno. La realimentación se inicia cuando el paciente no tiene dolor y refiere apetito, pero el momento exacto para iniciarla no está previamente documentado.* **Objetivo:** *Determinar la tolerancia a la alimentación oral inmediata (8 horas posterior al inicio del manejo) en comparación con la alimentación temprana (48 horas) en los pacientes con pancreatitis aguda biliar leve.* **Método:** *Se incluyeron pacientes con pancreatitis aguda biliar leve y se aleatorizaron en dos grupos: A) alimentación temprana a las 48 horas (30 pacientes) y B) alimentación inmediata a las 8 horas de inicio del manejo (29 pacientes). Fueron evaluados por un tercer observador ciego (no involucrado en el estudio) para documentar síntomas como náusea, vómito, reactivación del dolor abdominal, síndrome de respuesta inflamatoria sistémica, tolerancia alimentaria y estancia hospitalaria.* **Resultados:** *No se encontraron diferencias significativas entre los grupos en cuanto a datos clínicos y bioquímicos. La estancia hospitalaria disminuyó significativamente en el grupo B (5.4 vs. 7.8 días; p < 0.003).* **Conclusión:** *La alimentación inmediata en las primeras 8 horas del manejo de los pacientes con pancreatitis aguda biliar leve es bien tolerada y segura, y reduce la estancia hospitalaria.*

Palabras clave: *Alimentación. Dolor abdominal. Pancreatitis biliar aguda. Respuesta inflamatoria.*

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Introduction

Mild acute pancreatitis is defined as edema of the pancreatic gland without organ failure or local complications[1], and its management consists of three basic elements: hydration, analgesia and temporary bowel rest[2-7].

The bowel rest concept assumes decrease in inflammation, pain, and pancreatic enzymes secretion in the parenchyma and peripancreatic tissue, mainly to prevent pancreatitis reactivation. Different studies have shown, when comparing patients on fasting against early oral feeding initiation, that there are no significant differences in pancreatitis reactivation[7-11]. Early feeding has also been shown to induce a stronger immune response, which reduces infectious processes (bacteremia, pneumonia and necrosis infection in severe pancreatitis) and overall mortality[12,13].

Despite the above, the exact time for refeeding to be started has not been defined; therefore, the purpose of this study was to evaluate tolerance and disease reactivation when oral feeding is started immediately (8 hours after having started hospital management) in patients with mild acute biliary pancreatitis (MABP) in comparison with early initiation (48 hours after having started management).

Method

Randomized, controlled, double-blind study carried out at "Dr. Ignacio Morones Prieto" Central Hospital. Patients older than 15 years, of both genders, diagnosed with MABP, classified < 3 according to the Ranson scale, < 8 on APACHE II and < 2 on the BISAP scale, were included[1,14,15]. All patients had liver and bile duct ultrasound available to verify the etiology. Patients with pancreatitis of non-biliary etiology, severe pancreatitis, high risk of choledolithiasis or cholangitis were excluded. Patients remained blinded to the study hypothesis all the time.

Patients were randomly assigned to two groups (simple randomization with a computer-generated random number table using the R package program, in strata of four): A) early refeeding 48 hours after hospital management was started, and B) immediate refeeding at 8 hours from hospital management start. The oral food that was used for oral route to be started was a standard polymer formula (Enterex Diabetic®, Pisa Pharmaceutical), calculated at basal requirements (25 kcal/kg of weight).

White blood cells (WBC) and C-reactive protein were determined at admission and at 8-24 and 48 hours.

All patients had the same initial management, with parenteral fluid resuscitation with Hartmann solution at 15 mL/kg/h for the first 8 hours, with the infusion rate necessary to obtain a 0.5 mL/kg/h diuresis then being evaluated. A proton pump inhibitor was used at a 40 mg/24 h i.v. dose; for analgesia, metamizole at a 2 g/6 h i.v. dose and ketorolac at a 30 mg/8 h i.v. dose; and as prokinetic-antiemetic, metoclopramide at a 10 mg/8 h i.v. dose.

In both groups, food tolerance was determined by an observer blinded to the patient group: if the patient met the criteria for absence of pain, nausea or vomiting, and was hungry at the time the diet was offered and also tolerated it without showing data consistent with systemic inflammatory response or pain recurrence, feeding tolerance was determined to exist.

All patients underwent cholecystectomy with intraoperative cholangiography after pancreatitis resolution, with resolution of the disease being determined at the time the patient tolerated the oral route. Patients were discharged 24 hours after surgery. Hospital stay was considered as the time elapsed from admission to discharge.

The sample size was calculated under the assumption of p1 = 10% and p2 = 30%, with a power of 80% and a two-tailed 95% confidence interval, with n = 25 patients per group being obtained[5].

Statistical analysis was carried out with JMP statistical package, version 8 (SAS Institute Inc., Cary, NC, USA), using Student's t-test for numerical variables with normal distribution or Mann Whitney's U-test in other cases. Categorical variables were analyzed with the chi-square test or Fischer's exact test, with a p-value < 0.05 being regarded as statistical significance.

The present work was authorized by the hospital ethics committee (Registry 07-15), and informed consent was obtained from all patients for being included in the study.

Results

Thirty patients were included in the early feeding group (A), and 29 patients in the immediate feeding group (B). Table 1 shows the baseline characteristics of each group. As it can be observed, there are no significant differences between the study groups, and thus they were considered to be comparable.

Table 1. Study groups baseline values

	Early feeding (n = 30)	Immediate feeding (n = 29)	p
Age (years)	38 (18-89)	37 (20-49)	0.946
Gender (males: females)	5:25	3:26	0.302
BMI	26.96 ± 4.15	26.35 ± 4.41	0.586
Onset of symptoms (h)	44.4 (4-144)	31.10 (4-96)	0.172
WBC (10^3/μL)	8.9 ± 4.3	8.3 ± 3.99	0.547
Amylase at admission (U/L)	1357 ± 689	1523 ± 587	0.102
Lipase (U/L)	945 ± 358	1024 ± 315	0.119
Baseline VAS	5.9 (2-10)	5.7 (0-10)	0.785
Ranson	1.37	1.3	0.276
APACHE II	4.73 ± 2.59	4.65 ± 3.16	0.917
BISAP	0.36	0.17	0.287

BMI: body mass index; VAS: visual analogue scale for pain; WBC: white blood cells.

Table 2. Patients who did not tolerate feeding

	Early feeding (n = 30)	%	Immediate feeding (n = 29)	%	p
Nausea/vomiting	0	0	0	0	NS
Abdominal pain	5	16.66	3	10.33	0.091
Systemic inflammatory response	0	0	0	0	NS
Organ failure	0	0	0	0	NS
Total	5	16.66	3	10.33	0.091

NS: Non-significant.

Abdominal pain evaluated with the visual analogue scale for pain showed no differences at 0, 8 and 48 hours: 5.9 ± 2.35, 5.7 ± 2.58 and 2.2 ± 2.1 for group A vs. 5.7 ± 2.58, 2.17 ± 2.0 and 0.13 ± 0.35 for group B.

WBC count at feeding initiation was 10.72 ± 4.3 x 10^3/mL in group A and 10.85 ± 3.99 x 10^3/mL in group B, with no significant difference (p = 0.905). At 48 hours, the values were 9.03 ± 6.37 x 10^3/mL in group A and 7.71 ± 2.42 x 10^3/mL in group B, with no significant difference (p = 0.143).

C-reactive protein measured at admission was 4.24 ± 5.85 mg/dL in group A and 3.52 ± 4.4 mg/dL in group B, and at 48 hours, it was 3.71 ± 5.33 and 2.05 ± 2.99, respectively, with no significant differences between both measurements. There were no cases with inflammatory response or organ failure during hospital stay in either of the groups.

There were eight patients (13.5%) who failed to tolerate the oral route: five in group A (16%) and three in group B (10.3%), with no statistically significant difference (p = 0.4) (Table 2).

We found statistical difference in hospital stay in favor of immediate feeding in comparison with early feeding: 2.39 vs. 3 days (p = 0.0001) and 5.4 vs. 7.8 days, respectively (p < 0.0003) (Fig. 1).

Patients were followed for 30 days and there were two readmissions in the early feeding group, both for residual choledocholithiasis, which was resolved by endoscopic retrograde cholangiopancreatography. No pancreatitis local complications were documented.

Discussion

The purpose of fasting, in traditional and essential acute pancreatitis management, has been the “rest of

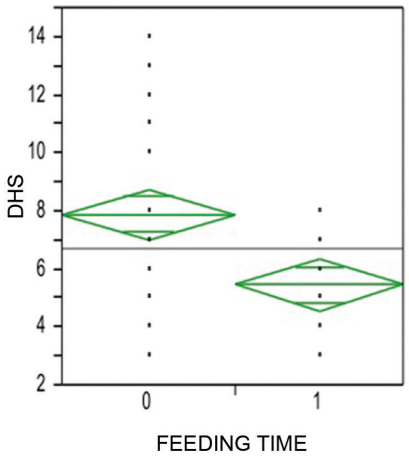

Figure 1. *Days of hospital stay (DHS). The median, 95% confidence interval, and limits are indicated.*

the pancreatic gland" to avoid enzyme secretion in response to cholecystokinin stimuli and minimize stress of the gland, with the purpose to decrease self-digestion and tissue damage exacerbation[8]. Although initial fasting is standardized and is generally well tolerated in patients with mild acute pancreatitis, the time needed until refeeding the patient to prevent disease reactivation or exacerbation has been poorly studied in randomized clinical trials. Current studies suggest that, in acute pancreatitis, the secretion of zymogens in response to food is decreased, which has allowed to assess an increasingly earlier refeeding initiation, once the first phase of treatment has started with hydration and analgesia, even without complete reduction of inflammatory parameters, as Niederau et al.[16] have shown in their study.

In this work, we found homogeneous groups with regard to baseline characteristics, with no differences in severity scales, and all patients received the same treatment, which is why the results could not be explained by imbalances in this possible confounding factor.

In previous studies, such as that by Mendes et al.[11], pain reactivation during early feeding is reported to be likely to occur in up to 19% of cases, although in this work, only 13.5% of patients experienced refeeding failure because they continued with abdominal pain, without a statistically significant difference, and we had no patients in whom pain was reactivated, which suggests nutritional intake safety when initiated within the first 8 hours of having started pancreatitis management.

The results obtained with the measurement of indirect acute phase reactants, such as WBC and C-reactive protein, did not report significant differences when both groups were compared, in their baseline measurements and at 48 hours, but they showed a tendency towards having lower counts in the immediate feeding group. This is consistent with the observations reported by Petrov et al.[17], who suggest that early feeding plays an immunomodulatory role that attenuates the inflammatory response in patients with severe pancreatitis[13,17].

Only a limited number of studies in pancreatitis have evaluated the impact of enteral feeding on pancreatic tissue. Sahin et al.[18] compared early oral vs. parenteral nutrition in acute pancreatitis and reported fewer histopathological changes in pancreatic tissue in orally-fed rats, which is explained by the hypothesis that oral feeding stimulates the production of enteral hormones (cholecystokinin, motilin and serotonin), and this produces fewer effects on pancreatic inflammatory process, as well as a trophic effect on pancreatic tissue, which increases pancreatic blood flow and intestinal motility.

Even so, we cannot be categorical with our study by mentioning that immediate feeding accelerates the period in which pancreatitis subsides; we can only observe that there is no further reactivation of pain and that there are no harmful effects on disease recovery.

The rationale in favor of immediate feeding has allowed us to intervene patients with MABP earlier and have a hospital stay almost 2 days shorter.

In conclusion, our study shows that immediate feeding established 8 hours after having started the management of a patient with MABP is well tolerated, safe, does not negatively affect disease evolution and allows to reduce hospital stay. As for pain, it occurred more frequently with early feeding, which is why studies including a larger sample size would have little chance of demonstrating or reversing the result; however, carrying out studies such as the present one in different age populations and with other factors, such as obesity and hospital management, is recommended.

Conflicts of interest

The authors declare that there are no conflicts of interest relevant to this research protocol.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures that were

followed adhered to the ethical standards of the responsible committee for experimentation on human beings and were in agreement with the World Medical Association and the Declaration of Helsinki.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

References

1. Banks P, Bollen T, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis - 2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62:102-11.
2. Working group IAP/APA. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13:e1-15.
3. Tenner S, Baillie J, DeWitt J, Vege SS; American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013;218:1-16.
4. Fisher JM, Gardner TB. The "golden hours" of management in acute pancreatitis. Am J Gastroenterol. 2012;107:1146-50.
5. Cebrián JG, Bello-Camara MP, Rodríguez-Tanez JC, Fernandez-Ruiz A. Analgesia y sedación en la pancreatitis aguda. Med Intensiva. 2003;27(2):118-30.
6. Jiménez Murillo L, Montero Pérez FJ. Medicina de urgencias y emergencias. Guía diagnóstica y protocolos de actuación. 4ª ed. Barcelona: Elsevier; 2010.
7. Spanier B, Bruno M, Mathus-Vliegen VM. Enteral nutrition and acute pancreatitis: a review. Gastroenterol Res Pract. 2011;2011:857949.
8. Eckerwall GE, Tingstedt BB, Bergenzaun PE, Andersson RG. Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery. Clin Nutr. 2007;26:758-63.
9. Teich N, Aghdassi A, Fischer J, Walz B, Caca K, Wallochny T, et al. Optimal timing of oral refeeding in mild acute pancreatitis. Pancreas. 2010;39:1088-92.
10. Li J, Xue GJ, Liu YL, Javed MA, Zhao XL, Wan MH, et al. Early oral refeeding wisdom in patients with mild acute pancreatitis. Pancreas. 2013;42:88-91.
11. Moraes JM, Felga GE, Chebli LA, Franco MB, Gomes CA, Gaburri PD, et al. A full solid diet as the initial meal in mild acute pancreatitis is safe and result in shorter length of hospitalization: results from a prospective, randomized, controlled, double-blind clinical trial. J Clin Gastroenterol. 2010;44:517-22.
12. Bakker OJ, van Santvoort HC, van Brunschot S, Ahmed Ali U, Besselink MG, Boermeester MA, et al. Pancreatitis, very early compared with normal start of enteral feeding (PYTHON trial): design and rationale of randomized controlled multicenter trial. Trials. 2011;12:73.
13. Eatock F, Chong P, Menezes N, Murray L, McKay CJ, Carter CR, et al. A randomized study of early nasogastric versus nasojejunal feeding in severe acute pancreatitis. Am J Gastroenterol. 2005;100:432-9.
14. Papachristou GI, Muddana V, Yadav D, O'Connell M, Sanders MK, Slivka A, et al. Comparison of BISAP, Ranson's, APACHE II, and CTSI Scores in predicting organ failure, complication, and mortality in acute pancreatitis. Am J Gastroenterol. 2010;105:435-41.
15. Maraví-Poma E, Patchen Dellinger E, Forsmark CE, Layer P, Lévy P, Shimosegawa T, et al. Clasificación internacional y mutidisciplinaria de la pancreatitis aguda: edición española 2013. Med Intensiva. 2014;38:211-7.
16. Niederau C, Niederau M, Luthen R, Strohmeyer G, Ferrell LD, Grendell JH. Pancreatic exocrine secretion in acute experimental pancreatitis. Gastroenterology. 1990;99:1120-7.
17. Petrov M, Windsor J. Nutritional management of acute pancreatitis: the concept of "gut rousing". Curr Opin Clin Metab Care. 2013;16:557-63.
18. Sahin M, Ozer S, Vatansev C, Aköz M, Vatansev H, Aksoy F, et al. The impact of oral feeding on the severity of acute pancreatitis. Am J Surg. 1999;178:394-8.