Digestive Diseases and Sciences (2022) 67:2535–2542
https://doi.org/10.1007/s10620-021-06992-6

ORIGINAL ARTICLE

Hunger-Based Versus Conventional Oral Feeding in Moderate and Severe Acute Pancreatitis: A Randomized Controlled Trial

Ashwin Rai[1] · Amaranathan Anandhi[1] · Sathasivam Sureshkumar[1] · Vikram Kate[1]

Received: 6 February 2021 / Accepted: 7 April 2021 / Published online: 30 April 2021

Abstract

Background The length of hospitalization is prolonged in patients with acute pancreatitis due to delay in feeding. The present study aimed at evaluating hunger-based early feeding for its efficacy in reducing length of hospitalisation.

Aims and Methods This was a parallel arm superiority randomized control trial. Patients with moderate and severe acute pancreatitis were randomised into hunger-based feeding and conventional feeding groups. Patients in hunger-based feeding group commenced feeding once they felt hungry and in conventional feeding group after normalization of biochemical parameters and resolution of symptoms. Patients were followed up till their discharge and were analyzed for length of hospitalisation, fasting duration, feed intolerance, incidence of infective morbidities and invasive procedures.

Results Hunger-based feeding and conventional feeding group included 56 and 54 patients, respectively. Hunger-based feeding led to a decrease in length of hospitalization (6.3 days in hunger-based feeding vs 7.3 days in conventional feeding group, $P=0.041$) and fasting duration (1.6 days in hunger-based feeding vs 2.7 days in conventional feeding group, $P=0.001$).The incidence of feed intolerance ($P=0.098$), infective morbidities and invasive non-surgical procedures were similar in both the groups.

Conclusion Hunger-based feeding significantly reduces length of hospitalization and fasting duration in cases of moderate and severe acute pancreatitis without any significant rise in the incidence of complications.
Registration number of Clinical Trails Registry India CTRI/2019/01/017,144.

Keywords Feeding in pancreatitis · Hunger-based feeding · Acute pancreatitis · Enteral nutrition

Introduction

Acute pancreatitis is one of the leading causes of hospitalization and contributes to a significant global disease burden. The global incidence of this disease is between 4.9 and 73.4 cases per 100,000 people worldwide [1]. Mortality rates can go up to 10–30% in cases of severe acute pancreatitis [2]. Moderately severe and severe acute pancreatitis leads to 40–50% systemic inflammatory and septic complications and up to 30% mortality [3]. Hence, management of septic complications and prevention of multi-organ failure forms an important aspect of treatment of acute pancreatitis. Nutrition forms a cornerstone in the management of acute pancreatitis. The maintenance of gut barrier is one of the most important function of enteral feeding in cases of acute pancreatitis. A dysfunctional gut barrier is responsible for infective complications in pancreas and also starts the cascade of systemic inflammatory response which can ultimately lead to multi organ failure.

Infected pancreatic necrosis causes mortality in 15% of the patients [4]. Around 33% of pancreatic infections take place in the first 24 h and 75% between first 48 to 96 h.[5] Hence, maintenance of gut barrier integrity is a major goal in the early phase management, which can be taken care of with enteral nutrition [6]. Enteral feeding prevents the atrophic changes in the gut lining as the uptake of nutrients in the intestinal cells comes directly from the intestinal lumen and also facilitates intestinal. These actions prevent intestinal bacterial overgrowth and increased gut permeability, hence decreasing the subsequent bacterial translocation and septic complications.

The conventional management protocols for acute pancreatitis advocated bowel rest in the form of being nil per

✉ Vikram Kate
drvikramkate@gmail.com

[1] Department of Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry 605006, India

oral (NPO) for managing patients in the acute stage [7, 8]. This was advocated in order to avoid pancreatic stimulation and facilitate pancreatic rest. But subsequent research studies have found out that putting patients on diet restrictions subjected them to negative energy balance and exacerbates the inflammatory response induced catabolism. It also leads to increased bacterial translocation and adds to morbidity and mortality [9, 10]. Hence, providing adequate enteral nutrition in the early stages of pancreatitis can help tackle these complications.

Reports in literature encouraged early feeding without any rise in morbidity. Naso-gastric feeding (NGF), when compared with nil per oral (NPO) regimen, showed reduction in the length of hospitalization, days with pain, need for opiates and risk of feed intolerance [11]. Naso-enteric tube feeding within 24 h when compared to oral diet initiated 72 h after presentation did not increase the rate of major infections or mortality [12]. Early feeding decreased the length of hospital stay without increasing the incidence of feed intolerance [13, 14]. These studies proved that early oral feeding was safe, feasible and lead to better patient outcomes. Another study assessing early soft diet versus clear liquid diet in patients with mild acute pancreatitis showed decrease in length of hospitalization without any increase in feed intolerance in the patients receiving soft diet as a initial feed [15].

Although NGF, immediate early feed, early feeding at 24 h and at 72 h have shown benefit in patients with acute pancreatitis, hunger-based oral feeding in pancreatitis is a relatively new concept. The idea of hunger-based feeding is based on the physiology of hunger and the fact that subjective feelings of hunger reflects recovery of GIT. A recent study showed that hunger-based early oral re-feeding was safe and decreased fasting time period and length of hospital stay [16]. The present study was carried out to determine the efficacy of hunger-based oral feed vs. conventional oral feed, in patients with moderately severe and severe acute pancreatitis.

Methodology

Study Design and Setting

The study was a parallel arm superiority randomized control trial conducted from November 2017 to December 2019 at tertiary care hospital. The study was approved by the Institute Ethics Committee (IEC) (IEC number- JIP/IEC/2018/047).

Patient Selection

All patients more than 18 years of age, with a diagnosis of moderately severe and severe acute pancreatitis (according to modified Atlanta classification 2012) were included in the study [17]. Patients who had traumatic pancreatitis, pancreatitis after endoscopic retrograde cholangio-pancreaticography (ERCP), malignancy of the pancreas or biliary tree, non-pancreatic infection or sepsis caused by a second disease, pancreatitis diagnosed during surgery, medical history of immune deficiency, patients presenting with shock, intubated patients, patients referred from other hospitals after initial management and patients with naso-jejunal tube in situ were excluded from the study.

Sample Size

Sample size was estimated to be 56 in each group based on detecting expected difference of 2 days in hospital stay between the 2 groups [16]. Calculations were done based on OpenEpi software with 95% confidence limits and 90% power. Assuming 15% loss to follow up, the final sample size was calculated to be 65 in each group.

Outcome Measures

Primary outcome measure was the length of hospitalization (LOH) which was measured from the day of admission till the day of discharge. In case of a delay in discharge due to logistic reasons, the day of decision to discharge was considered as the day of discharge [18]. Secondary outcome measures were reduction in the fasting duration, feed intolerance, morbidities and invasive non-surgical procedures. Fasting duration was measured from the day of onset of abdominal pain till the day when oral feeds were resumed [16]. Feed intolerance was defined as occurrence of pain abdomen and/or nausea and/or vomiting and/or abdominal distention after taking the first feed till the patient's discharge [13, 16]. Invasive non-surgical procedures which were analyzed were aspiration of acute peri-pancreatic fluid collection and walled off necrosis (APFC/WON), pigtail placement, pleural fluid aspiration, ascitic fluid aspiration, ERCP and stone removal and chest tube placements. Morbidities which were analyzed were sepsis, infected pancreatic collections, pleural effusion, pneumonia, ascites and pancreatic necrosis.

Study Procedure

Stratified permuted block randomization was done using computer program with randomly selected block sizes of 4 and 6 [14]. Allocation concealment was carried out the by

serially numbered opaque sealed envelope (SNOSE). The principal investigator was blinded to feeding regimen. The sealed envelope was opened by the nursing staff before allotment of the subject to a group. The subjects were allocated into two treatment groups; Group 1—Hunger-based feed group (HBF) and Group 2—Conventional feed group (CF).

Patients in HBF group were commenced on oral feeding once they felt hungry regardless of the pain abdomen, and laboratory parameters and patients were observed for the tolerance of the feed. The feeds were gradually escalated from clear liquids to semisolids and then solid feeds, as tolerated by the patient [16]. In the event of feed intolerance, feeds were withdrawn and restarted once patient felt hungry. Ryle's tube was put in patients with vomiting, and once it subsided, the Ryle's tube was removed, and the patient was started on oral feeds. Patients in the CF group received oral feeding as per the conventional standard protocol which allowed oral feeds to be started once the pain abdomen reduced and vomiting and nausea resolved. The feeds were gradually escalated from clear liquids to semisolids and then solid feeds, as tolerated by the patient [16]. Patients in both the groups were followed up till their discharge. The data regarding the primary and secondary outcomes were tabulated and analyzed.

Statistical Analysis

Analysis was done using SPSS version 19.0. The descriptive statistics included frequencies, proportions and percentages for categorical variables and the continuous variables were analyzed and explained in terms of mean, standard deviation and median. In the inferential statistics Chi-square test or Fisher's exact test was carried out to find out the difference between proportions for gender, presence of co-morbidities, presence of moderate or severe pancreatitis, feed intolerance, presence of infective morbidities and invasive procedures between the groups. Mann–Whitney U test was used to analyse the mean difference for LOH, age, BMI, mean fasting duration, mean amylase level, etc. All the analysis was done as per modified intention-to-treat (mITT) analysis. Patients on ventilator support and too sick to start oral feeds who ultimately succumbed to the severe nature of the disease were not randomized, and they were analyzed as per mITT analysis. The results were explained for any significant difference found for continuous variables between HBF group and CF group at the 95% significance level along with 95% confidence intervals wherever required and applicable and $P < 0.05$ was considered significant between the test groups. Power of the study was 90%.

Results

Enrollment and Baseline Characteristics of the Patients

A total of 110 patients were included in the study with 56 patients in HBF group and 54 patients in CF group. The schematic representation of the study is shown in Fig. 1. There were 3 subjects in HBF group and 4 subjects in CF group following randomization who did not receive their allocated intervention as they were too sick to start oral feeds, on ventilator support, and ultimately succumbed due to the severe nature of disease. As 3 patients in the HBF group and 4 patients in the CF group did not receive the allocated intervention, a modified intention-to-treat (mITT) analysis was carried out. As the recruitment number of 56 was achieved in the study arm (following the adjustment for attrition rate) and the overall statistical significance was achieved, further recruitment was stopped on the advice of the statistical consultant.

The demographic parameters like age, comorbidities and Body Mass Index (BMI) were similar in both the groups without any significant difference (Table 1). However, there was a significant difference in gender distribution ($P = 0.010$). Alcohol intake was the major cause of pancreatitis in both the groups with 96% patients in HBF group and 87% patients in CF group. The distribution of aetiology was similar in both the groups ($P = 0.128$).The severity of pancreatitis was also similar in both the groups ($P = 0.232$). Both the groups were similar in mean amylase value ($P = 0.390$) and TLC ($P = 0.110$).

Primary Outcome Measures

Mean LOH (SD) in HBF group was 6.3 ± 3.5 days and that in CF group was 7.3 ± 3.4 days. The mean difference of LOH between the 2 groups was 1.04 days with (95% CI, 0.44–2.3; $P = 0.041$) (Table 2). Box plot graph for the length of hospitalization in days is depicted for both the groups in Fig. 2.

Secondary Outcome Measures

Mean duration of fasting (SD) was 1.6 ± 0.9 days and 2.7 ± 0.7 days, in HBF and CF group, respectively. Mean difference of fasting duration in the 2 groups was 1.13 days with (95% CI, 0.82–1.4; $P = 0.001$) (Table 2). Box plot graph for fasting duration in days is depicted for both the groups in Fig. 3. The incidence of feed intolerance was similar in both the groups ($P = 0.098$). (Table 2) Although,

Fig. 1 Schematic representation of study

Table 1 Demographic and clinical characteristics

	HBF group ($N=56$) n (%)	CF group ($N=54$) n (%)	p value
Age (Mean, SD)	38(10.3)	37.9(10.5)	0.154 [a]
Males	56(100)	48(88.9)	0.010[b]
Presence of comorbidities	12(21.4)	11(20.3)	0.545[b]
BMI (Mean, SD)	22.4(2.3)	22.3(2.6)	0.328 [a]
Aetiology			
Alcohol intake	54(96.4)	47(87.0)	0.128[b]
Gallstone disease	0 (0)	3(5.6)	0.073[b]
Idiopathic	2(3.6)	4(7.4)	0.375[b]
Moderately severe pancreatitis	44(78.6)	37(68.5)	0.232[b]
Severe pancreatitis	12(21.4)	17(31.5)	0.232[b]
Mean amylase level (SD)	755.1(721.9)	800.7(545.4)	0.387 [a]
TLC > 11, 000	27(48.2)	18(33.3)	0.113[b]

[a]Mann-Whitney U test

[b]Chi-square test/ Fisher's exact test

BMI body mass index, *CF* conventional feeding *HBF* hunger-based feeding, *SD* standard deviation, *TLC* total leukocyte count

Table 2 Primary and secondary outcome parameters

Clinical outcome parameters	HBF group (n = 56) n (%)	CF group (n = 54) n (%)	*p* value
Mean LOH (SD)	6.3(3.5)	7.3(3.4)	0.041[b]
Feed intolerance	24(42.9)	15(27.8)	0.098[a]
Mean fasting duration (SD)	1.6(0.9)	2.7(0.7)	< 0.001[b]

[a]Chi-square test

[b]Mann-Whitney U test

CF conventional feeding, *HBF* hunger-based feeding, *LOH* length of hospitalization, *SD* standard deviation

the feed intolerance in the HBF group was high at 42.9%, many of these patients had either transient pain in the abdomen, nausea and vomiting. In all of these patients after a brief period they could be started on oral feeding.

The incidence of morbidities were similar in both the groups which included; sepsis ($P = 0.270$), infected pancreatic collections/ pancreatic necrosis ($P = 0.648$), pleural effusion /pneumonia ($P = 0.478$), ascites ($P = 0.578$). 15 patients had pancreatic necrosis/infected collections with 7 in HBF group and 8 in CF group, 4 patients had sepsis with 1 in HBF group and 3 in CF group, 3 patients had ascites with 2 in HBF group and 1 in CF group, 17 patients had pleural effusion/pneumonia present with 10 in HBF group and 7 in CF group. (Table 3).

The number of invasive non-surgical procedures done were similar in both the groups, which included aspiration of APFC/WON ($P = 0.073$), pigtail placement ($P = 0.595$), pleural fluid aspiration ($P = 0.514$), ascitic fluid aspiration ($P = 0.212$), ERCP and stone removal ($P = 0.278$) and chest tube placements ($P = 0.329$). (Table 4).

Discussion

Treatment of acute pancreatitis continues to be a clinical challenge. The management of acute pancreatitis involves a multimodal approach with the aim of reducing infective morbidities, controlling sepsis, maintaining hemodynamic stability and providing proper nutrition to avoid a catabolic state. Contrary to previous practices and teachings which involved providing bowel rest and pancreatic rest by keeping patients nil per oral, newer practices, based on multiple clinical studies, involve early feeding preferably through oral route. The present study showed a significant decrease in LOH and fasting duration in HBF group as compared to CF group. Additionally, the feed intolerance was also similar in both the groups indicating that hunger-based early feeding in acute pancreatitis patients is well tolerated.

The conventional criteria for starting feeds in a patient of pancreatitis is based on the resolution of symptoms like abdominal pain, nausea, vomiting and normalization of biochemical parameters like amylase and lipase. Zhao et al. used an alternate approach based on presence of hunger to start feeds, irrespective of the resolution of clinical or biochemical parameters [16].

NGF, immediate early feeding, early feeding at 24 h and at 72 h have proven to be safe and feasible and have provided better patient outcomes.[11–13] But hunger-based

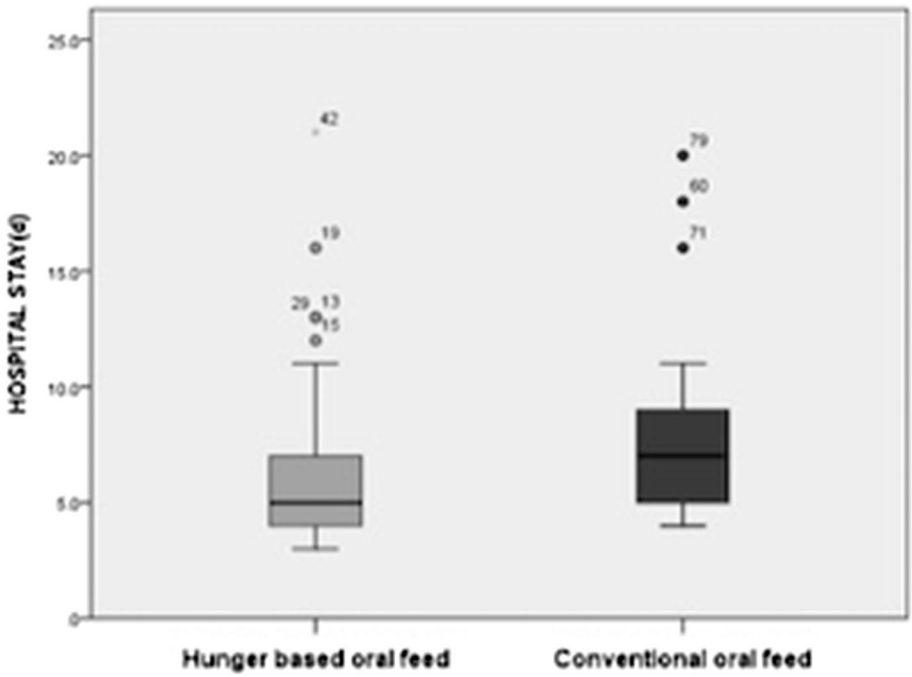

Fig. 2 Box plot graph for length of hospitalization in days in both the groups

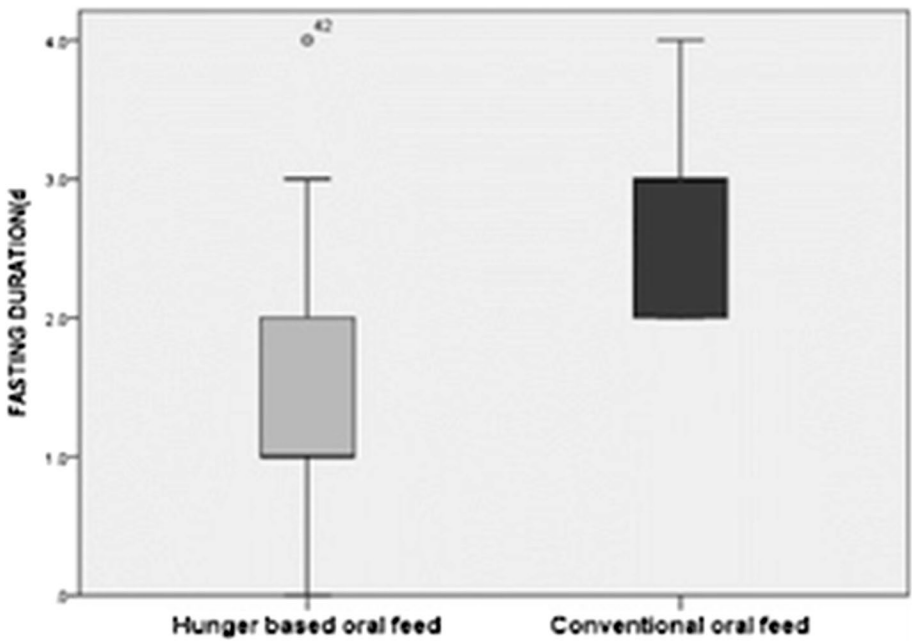

Fig. 3 Box plot graph for fasting duration in days in both the groups

Table 3 Comparison of various infective morbidities in HBF and CF groups (Secondary outcome parameter)

Morbidities	HBF group ($N=20$) n (%)	CF group ($N=19$) n (%)	p value
Infected collection/Pancreatic necrosis	7 (35)	8 (42.1)	0.648[a]
Sepsis	1 (5)	3 (15.7)	0.270[b]
Ascites	2 (10)	1 (5.2)	0.578[b]
Pneumonia/Pleural effusion	10 (50)	7 (36.8)	0.478[a]

[a]Chi-square test b-Fisher's exact test

CF conventional feeding, *HBF* hunger-based feeding

Table 4 Comparison of invasive procedures done in HBF and CF groups (Secondary outcome parameter)

Procedure	HBF group ($N=10$) n(%)	CF group ($N=9$) n(%)	p value[a]
Aspiration of APFC/WON	3(30)	0(0)	0.073
Pigtail placement	2(20)	1(11.1)	0.595
Pleural fluid spiration	3(30)	4(44.4)	0.514
Ascitic fluid aspiration	1(10)	3(33.3)	0.212
ERCP and stone removal	0(0)	1(11.1)	0.278
Chest tube placement	1(10)	0(0)	0.329

[a]Fisher's exact test

APFC acute peri-pancreatic fluid collection, *CF* conventional feeding, *ERCP* endoscopic retrograde cholangio-pancreaticography, *HBF* hunger-based feeding, *WON* walled off necrosis

early oral feeding in pancreatitis is a relatively new concept with only one such study done previously. In the present study, we used hunger-based early oral feeding in patients with moderate and severe acute pancreatitis in order to gain further insight into the safety and feasibility of early oral feeding based on hunger in cases of acute pancreatitis.

In the present study, the age distribution and the mean age of the hunger-based feeding group (HBF) and the conventional feeding group (CF) were similar to the study done by Bakker et al.[12] There was a male preponderance as the majority of the cases with acute pancreatitis in our institute were due to alcohol consumption. The prevalence of alcohol consumption is found to be significantly lower in females as compared to males in our region.

In the present study, the distribution of comorbidities, BMI, mean amylase level, TLC level, severity of pancreatitis and infective morbidities were similar in both the study groups. A similar trend was observed in previous studies too [12, 16]. In the present study, subjects in both the groups had alcohol consumption as the most common cause for pancreatitis with gallstone disease and other causes a distant second. However the study by Zhao et al. showed hyperlipidaemia as the most common cause and gallstone disease and alcohol consumption were the 2nd most common cause [16].

In the present study, the mean LOH was 6.3 days in HBF group and 7.3 days in CF group with a difference of 1.04 days. There were a few outliers in both the groups. This was due to prolonged treatment for infective

morbidities in those subjects, which included prolonged ventilator support and intensive care unit (ICU) stay, prolonged pigtail drainage, need for repeated pleural aspiration and prolonged duration of chest tube drainage. The shorter LOH was primarily due to shorter fasting duration in the HBF group which was analyzed as a separate secondary outcome. The mean LOH in the previous hunger-based early feeding study was found to be to be 13.7 days in HBF group and 15.7 days in the CF group with a mean difference of 2.1 days [16]. A study on early naso-gastric feeding reported a mean LOH of 8.4 days in HBF group and 10.2 days in CF group with a mean difference of 1.8 days [11]. The wide variation in the LOH in the various studies was because of the distribution of severity in those studies. The present study showed a mean fasting duration in HBF and CF group of 1.6 days and 2.7 days, respectively, with a mean difference in fasting duration of 1.1 days, fasting duration being less in HBF group. In the previous hunger-based early feeding study, the mean fasting duration in the HBF group was 8.3 days, and in the CF group, it was 10.5 days with a mean difference of 2.2 days [16]. It appeared that the shorter fasting duration in the HBF group translated into shorter LOH by almost the same duration in both the studies. This may suggest that subjective feelings of hunger reflected the recovery of GI dysfunction and indicated that patients were ready for a trial of food [16]. Another possible reason could be that hunger may indicate the physiological recovery of the GI system. It has also been documented that initiation of oral feeding, scheduled on hunger, may not lead to an increase in the pancreatic enzyme secretion, and maintain it under functional threshold [19, 20]. In the present study, a non-significant difference was seen in the 2 groups with respect to feed intolerance. Previous similar studies also didn't show any significant difference in the incidence of feed intolerance in the 2 groups [13, 14, 16]. Although, the feed intolerance in the HBF group was higher than that of CF group, many of these patients had either transient pain in the abdomen, nausea or vomiting and the patients could be started on oral feeding after a brief gap. The incidence of infective morbidities and non-surgical invasive procedures were similar in both the groups.

The strengths of the study are that this is one of the very few studies to determine the efficacy of hunger-based feeding in patients with moderate and severe pancreatitis. It had an adequate sample size to demonstrate the reduction of LOH in HBF group without any significant increase in the complications. The limitation of the study was that specialized diet like low fat diet and probiotics were not investigated in this study due to logistic reasons. Inclusion of the above parameters could have provided a better insight into the hunger-based feeding protocol for acute pancreatitis.

Conclusion

Hunger-based feeding in cases of moderate and severe acute pancreatitis showed a decrease in length of hospitalization and fasting duration without any significant rise in the incidence of feed intolerance or infective and septic complications or the number of invasive non-surgical procedures.

Acknowledgment The authors would like to thank Dr. Tanveer Rehman, Junior Resident, Department of Preventive and Social Medicine (PSM), Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India, for his help in the statistical analysis

Author's contribution A. Anandhi and Vikram Kate equally contributed to the conception and design of the research; Vikram Kate contributed to the design of the research; Ashwin Rai contributed to the acquisition and analysis of the data; A. Anandhi and S. Sureshkumar contributed to the interpretation of the data; and S. Sureshkumar and Ashwin Rai drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Declaration

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Yadav D, Lowenfels AB. Trends in the epidemiology of the first attack of acute pancreatitis: a systematic review. *Pancreas* 2006;33:323–330.
2. Working Party of the British Society of Gastroenterology, Association of Surgeons of Great Britain and Ireland, Pancreatic Society of Great Britain and Ireland, et al. UK guidelines for the management of acute pancreatitis. *Gut* 2005; 54 Suppl 3: iii1–9.
3. Luiten EJ, Hop WC, Lange JF et al. Controlled clinical trial of selective decontamination for the treatment of severe acute pancreatitis. *Ann Surg* 1995;222:57–65.
4. Rodriguez JR, Razo AO, Targarona J et al. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. *Ann Surg* 2008;247:294–299.
5. Wereszczynska-Siemiatkowska U, Swidnicka-Siergiejko A, Siemiatkowski A et al. Early enteral nutrition is superior to delayed enteral nutrition for the prevention of infected necrosis and mortality in acute pancreatitis. *Pancreas* 2013;42:640–646.
6. Capurso G, Zerboni G, Signoretti M et al. Role of the gut barrier in acute pancreatitis. *J Clin Gastroenterol* 2012;46:S46-51.
7. Singh VK, Moran RA, Afghani E et al. Treating acute pancreatitis: what's new? *Expert Rev Gastroenterol Hepatol* 2015;9:901–911.
8. Janisch NH, Gardner TB. Advances in management of acute pancreatitis. *Gastroenterol Clin North Am* 2016;45:1–8.
9. Fritz S, Hackert T, Hartwig W et al. Bacterial translocation and infected pancreatic necrosis in acute necrotizing pancreatitis derives from small bowel rather than from colon. *Am J Surg* 2010;200:111–117.

10. Petrov MS, Windsor JA. Nutritional management of acute pancreatitis: the concept of 'gut rousing.' *Curr Opin Clin Nutr Metab Care* 2013;16:557–563.
11. Kurti F, Xinxo S, Shpata V et al. Role of enteral feeding in mild to moderate acute pancreatitis. *Pancreatology* 2015;3:S62.
12. Bakker OJ, van Brunschot S, van Santvoort HC et al. Early versus on-demand nasoenteric tube feeding in acute pancreatitis. *N Engl J Med* 2014;371:1983–1993.
13. Lariño-Noia J, Lindkvist B, Iglesias-García J et al. Early and/or immediately full caloric diet versus standard refeeding in mild acute pancreatitis: A randomized open-label trial. *Pancreatology* 2014;14:167–173.
14. Eckerwall GE, Tingstedt BBÅ, Bergenzaun PE et al. Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery—A randomized clinical study. *Clin Nutr* 2007;26:758–763.
15. Rajkumar N, Karthikeyan VS, Ali SM et al. Clear liquid diet vs soft diet as the initial meal in patients with mild acute pancreatitis. *Nutr Clin Pract* 2013;28:365–370.
16. Zhao XL, Zhu SF, Xue GJ et al. Early oral refeeding based on hunger in moderate and severe acute pancreatitis: A prospective controlled, randomized clinical trial. *Nutrition* 2015;31:171–175.
17. Banks PA, Bollen TL, Dervenis C et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;62:102–111.
18. Waring J, Marshall F, Bishop S, et al. *Hospital discharge and patient safety: reviews of the literature*. NIHR Journals Library, https://www.ncbi.nlm.nih.gov/books/NBK259995/ (2014, accessed 15 March 2021).
19. McClave SA, Heyland DK. The physiologic response and associated clinical benefits from provision of early enteral nutrition. *Nutr Clin Pract Off Publ Am Soc Parenter Enter Nutr* 2009;24:305–315.
20. Al-Omran M, Albalawi ZH, Tashkandi MF, et al. Enteral versus parenteral nutrition for acute pancreatitis. *Cochrane Database Syst Rev* 2010; CD002837.