

## Original Research Article

# Effect of early enteral feeding on recovery profile in mild acute pancreatitis

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### ABSTRACT

**Background:** Acute pancreatitis is a pestilent disease with severity ranging from mild and self-limiting to a rapidly progressive illness leading to multi organ failure. Mild acute pancreatitis is inflammation of the pancreas with minimal remote organ involvement. Since the disturbance in the homeostasis is minimal, the treatment aims at supporting the native reparative processes of the body. One of the main supportive mechanisms is adequate nutritional supplementation. Gut barrier damage in the early phase of acute pancreatitis accounts for the bacterial translocation, initiation of sepsis, infected pancreatic necrosis and SIRS. Aim of the study was to determine the feasibility, advantages and disadvantages of early enteral nutrition in mild acute pancreatitis.

**Methods:** 40 patients taken consecutively from units which start enteral feeds before 48 hours (study group) were compared against 40 patients taken consecutively from units where patients will be kept fasting for 48 hours (control group) to determine whether early enteral feeding is better in determining the recovery in terms of duration of hospital stay, reduction in abdominal symptoms and use of analgesics.

**Results:** There was significant reduction in the duration of hospital stay ( $p=0.011$ ), intensity and duration of abdominal pain, need for analgesics, and risk of oral food intolerance in the study group.

**Conclusions:** Patients with mild acute pancreatitis can safely be started on early enteral feeds. It reduces gastro intestinal adverse effects, abdominal pain and need for analgesics and improves oral food tolerance causing shorter hospital stay.

**Keywords:** Abdominal pain, Analgesics, Early enteral feeds, Mild acute pancreatitis

### INTRODUCTION

Acute pancreatitis has been recognized since antiquity but the importance of pancreas and the severity of its inflammatory disorders were realized only in the middle of the 19<sup>th</sup> century.<sup>1,2</sup> In 1925 when Moynihan described acute pancreatitis as the most terrible of all calamities that occurs in connection with abdominal viscera.<sup>3,4</sup> At one end of the spectrum is the mild variety of acute pancreatitis, which invariably results in 'restitutio ad integrum' or spontaneous resolution of symptoms and requires supportive therapy only. At the other end is the

severe variety which requires aggressive resuscitative and, occasionally, surgical intervention. Because of this wide variation in clinical symptoms, the treatment requires a multidisciplinary approach. But even today with great technical advances in medical and surgical fields, acute pancreatitis remains a major cause of morbidity and mortality.<sup>5,6</sup>

Acute pancreatitis, a common disorder, has been noted to show an increase in the incidence by a factor of 10 in the past three decades. The reason for the increase is speculated to be increase in alcohol abuse and an improved ability to diagnose the disease.<sup>5,6</sup>

80% of cases are related to alcohol or biliary tract stone disease and the remaining 10% to metabolic factors, drugs and other conditions and 10% are idiopathic.<sup>3,6</sup> However the variation in the frequency of different forms of pancreatitis from source to source is quite marked and depends on country of origin and the population studied.

Mild acute pancreatitis is defined as inflammation of the pancreas with minimal remote organ involvement.<sup>7</sup> Since the disturbance in the homeostatic mechanism of the body is minimal, the treatment is aimed at supporting the native reparative processes of the body. One of the main supportive mechanisms is adequate and safe nutritional supplementation. Acute pancreatitis is a hyper metabolic state marked by increased energy expenditure, proteolysis, gluconeogenesis, and insulin resistance. Nutritional supplementation in acute pancreatitis is complicated by these diverse pathophysiologic derangements associated with the disease. In the past, patients with acute pancreatitis were not given any form of enteral nutrition, because it was believed that any stimulation of the exocrine pancreas would affect the disease course negatively. Now it is known that the pancreas is already at rest during pancreatitis, and restoring secretion would be a much more physiological strategy than resting the organ. Increasing evidence suggests that enteral feeding maintains the intestinal barrier function and prevents or reduces bacterial translocation from the gut. Furthermore, enteral nutrition eliminates some of the complications of parenteral nutrition such as catheter related sepsis, thrombosis, thrombophlebitis, catheter related embolism and pneumothorax. There is also a significant reduction in the incidence of stress induced hyperglycemia. The risk of adversely affecting humoral immunity, as seen with TPN, is not seen with enteral nutrition. Additionally, the cost of enteral nutrition is only 15% of the cost of TPN.<sup>8,9</sup> These findings along with the fact that enteral nutrition is clearly not harmful in acute pancreatitis make it an increasingly accepted treatment modality today.

### ***Aim and objective***

To determine the feasibility, advantages and disadvantages of early enteral nutrition in mild acute pancreatitis.

## **METHODS**

This was an observational prospective study during the period June 2018 to June 2019 was conducted in the Department of General Surgery in Government Medical College Kottayam including Patients who are admitted from Surgery causality of Government Medical College Kottayam with a diagnosis of mild acute pancreatitis.

Assuming the proportions in the study group and control group as 0.2 and 0.5 (with reference to Petrov et al clinical nutrition 2013), population risk difference that is 0.2 with 95% confidence interval and 2 sided test, sample

size required is 40 each  $N = z^2 \times pq / d^2$  Sample size is 80. (The data from medical records library for last one year has more than 100 mild acute pancreatitis, which supports the present study's sample size).<sup>10</sup>

Consecutive sampling was done in which every subject meeting the criteria is selected until the required sample size is achieved.

### ***Inclusion criteria***

Patients with BISAP score <2, serum creatinine  $\leq 2$  mg/dl, and mild acute pancreatitis (revised Atlanta classification 2012).<sup>11</sup>

### ***Exclusion criteria***

Patients with drug induced pancreatitis and post ERCP pancreatitis.

### ***Study variables***

Length of hospital stay, abdominal pain and need for IV analgesics and nausea and vomiting following early enteral feeds were the variables estimated.

### ***Study procedure***

This study was done in a group of 80 patients who were admitted from surgery casualty with a diagnosis of mild acute pancreatitis and meets all inclusion criteria. The patients were admitted under their corresponding units. Patients were duly informed regarding the study and after obtaining the consent, a 16 F gauge nasogastric Ryle's tube was inserted for all patients with acute pancreatitis. 40 patients were taken consecutively from units which start early enteral feeds (before 48 hours), this group will be the study group and 40 patients were taken consecutively from units where patients were kept fasting for 48 hours and this formed the control group. Then feeding patterns were initiated in the study group depending upon the severity of symptoms. Initiation of enteral feeding started with clear fluid in small quantity, and which was then increased in frequency. Then patients were given low fat liquid diet followed by semisolid diet and then solid diet which was low in fat. Patients in both groups were followed up till the day of discharge and patients were discharged when they had tolerance to oral food, no abdominal pain and no analgesics for the last 12 hours. Abdominal pain was analyzed using visual analogue scale (VAS). The VAS consisted of a 10 cm line with numbers from 0 to 10 at 1 cm increments, with 0 representing "no pain" and 10 "the worst possible pain". Patients were considered to have minimal or no pain if VAS was less than 2.

Data was analyzed using statistical package for social sciences (SPSS) version 16. Data variables including age and duration of hospital stay were expressed as mean  $\pm$  standard deviation (SD) and was analyzed using students

t test while all the remaining variables like gender, abdominal pain, analgesics use, nausea and vomiting were analyzed using chi square test.

**RESULTS**

Total 80 patients were enrolled in the study. Comparison of age of the patients between 2 groups were done using students t test and is expressed as mean with standard deviation (SD). There were no statistically significant difference between the 2 groups (Table 1).

The study population was predominantly male, with males constituting about 88% in the study group and 90% in the control group. This male predominance can be attributed to alcohol being the most common etiology (Table 2).

Regarding the primary outcome of the study, that is duration of hospital stay was significantly reduced in the study group (p=0.011). Analysis was done using students t test (Table 3).

**Table 1: Age distribution.**

Group	N	Mean age in years	Std. deviation	t	P value
Study	40	47.73	9.879	791	0.431
Control	40	46.03	9.330		

**Table 2: Gender distribution.**

Group		Gender		Total	$\chi^2$	P value
		Male	Female			
Group	Study group	Count	35	5	125	723
		% within group	87.5	12.5		
	Control group	Count	36	4		
		% within group	90.0	10.0		
Total	Count	71	9	80		
	% within group	88.8	11.3	100.0		

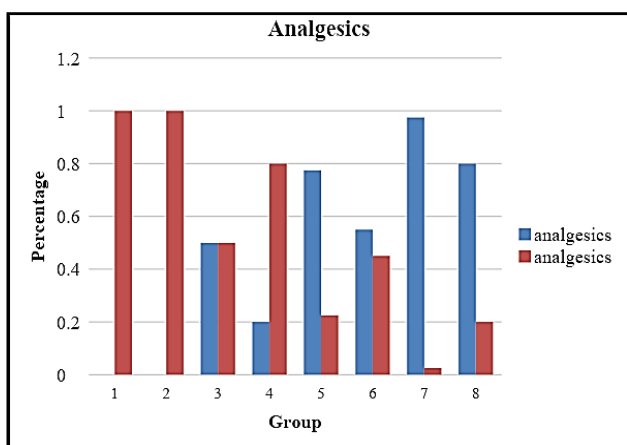
**Table 3: Duration of hospital stay in both group.**

Duration of hospital stay	Group	n	Mean	Std. deviation	t	P value
Duration of hospital stay	Study group	40	3.88	.648	2.611	0.011
	Control group	40	4.35	.949		

**Table 4: Comparison of abdominal pain in both groups.**

Abdominal pain		Abdominal pain		Total	$\chi^2$	P value
		No	Yes			
Day 1	Study group	Count	40	40	8.10	0.004
		%	100.0	100.0		
	Control group	Count	40	40		
		%	100.0	100.0		
Day 2	Study group	Count	20	20	4.59	0.032
		%	50.0	50.0		
	Control group	Count	8	32		
		%	20.0	80.0		
Day 3	Study group	Count	31	9	6.88	0.009
		%	77.5	22.5		
	Control group	Count	22	18		
		%	55.0	45.0		
Day 4	Study group	Count	39	1	6.88	0.009
		%	97.5	2.5		
	Control group	Count	32	8		
		%	80.0	20.0		

Secondary objectives of the study were to find out whether early enteral feeding resulted in decrease in the incidence of abdominal pain and gastro side effects. It was found that study group had significant reduction in the incidence of abdominal pain from day 1 to the successive days. Number of patients who had abdominal pain showed a gradual reduction over the days of hospital stay. All patients in the study group and control group had abdominal pain on the day of admission which gradually decreased to 20 on day 2, 9 on day 3 and 1 on day 4 in the study group and 31 on day 2, 18 on day 3 and 8 on day 4 with a significant p-value 0.004, 0.032 and 0.009 on days 2, 3 and 4 respectively. Abdominal pain was assessed using visual analogue scale (Table 4).

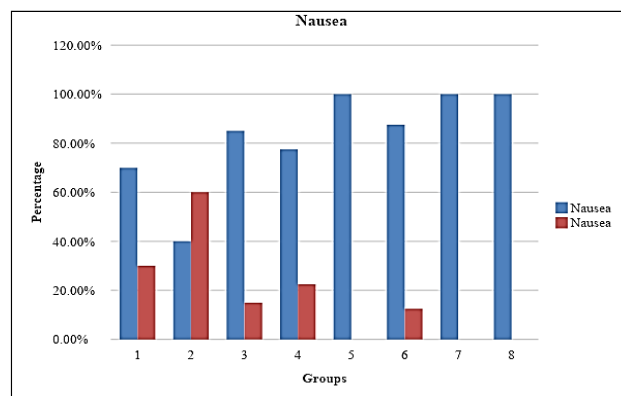


**Figure 1: Significant decrease in the consumption of analgesics over the days of hospital stay in the study group.**

Similar to abdominal pain, the use of analgesics also showed a significant reduction in the study group over the days of hospital admission. On the first day of admission, all patients in both groups required analgesics

which gradually decreased in both the groups but with more significant decrease in the study group with a p-value of 0.005, 0.033 and 0.013 on days 2, 3 and 4 respectively in the study group (Figure 1).

Apart from abdominal pain and use of intravenous analgesics, the other important secondary objectives were to find out whether early enteral feeding resulted in decrease in nausea and vomiting. Regarding nausea, though the number of patients who had nausea decreased from 12 on day 1st to 6 on day 2 and nil on day 3 and 4 in the study group while it was 24 on day 1, 9 on day 2, 5 on day 3 and nil on day 4 in the control group, p-value showed significant decrease only on day 1<sup>st</sup> (p=0.007) and day 3<sup>rd</sup> (p=0.021). On the second day though the number of patients with nausea decreased in the study group, it was not statistically significant (p=0.390) (Figure 2).



**Figure 2: Significant decrease in the occurrence of nausea in the study group on day 1<sup>st</sup> and 3<sup>rd</sup>. Though, the number of patients with nausea decreased in the study group on day 2<sup>nd</sup>, it was not statistically significant (p=0.390).**

**Table 5: Comparison of vomiting in both groups.**

Vomiting			Vomiting		Total	$\chi^2$	P value
			No	Yes			
Day 1	Study group	Count	36	4	40	0.000	0.000
		%	90.0	10.0	100.0		
	Control group	Count	36	4	40		
		%	90.0	10.0	100.0		
Day 2	Study group	Count	40	0	40	6.48	0.011
		%	100.0	0.0	100.0		
	Control group	Count	34	6	40		
		%	85.0	15.0	100.0		
Day 3	Study group	Count	40		40		
		%	100.0		100.0		
	Control group	Count	40		35		
		%	100.0		87.5		
Day 4	Study group	Count	40		40		
		%	100.0		100.0		
	Control group	Count	40		40		
		%	100.0		100.0		

Study group showed a significant decrease in vomiting over the days of hospital stay, where 4 patients had vomiting on the first day and nobody had over the remaining days of hospital stay ( $p=0.011$ ) (Table 5).

## DISCUSSION

The management of acute pancreatitis is in a state of constant change as our understanding of the intricate pathogenic mechanisms responsible for the disease evolves. Patients affected by acute pancreatitis exhibit a hyper catabolic state promoting nutritional deterioration. Consequently, acute pancreatitis is usually accompanied by increased resting energy requirements and reductions in protein mass. This persistently negative nitrogen balance results in loss of function and structural integrity of vital organs. Intestinal starvation impairs gut barrier and favors bacterial translocation. Hence extensive research has revealed the important role of nutritional support in the multidisciplinary treatment of acute pancreatitis and is very important in preventing serious complications and ensuring optimal recovery. Various techniques have been adopted for nutritional support in acute pancreatitis. According to the assumption that resting the pancreas by avoiding irritation and production of pancreatic digestive enzymes is beneficial in patients with pancreatitis, TPN was the standard route for providing exogenous nutrients since Feller et al reported decreased complication and mortality rates in patients supported with parenteral nutrition in 1974.<sup>12</sup> Another advantage of parenteral nutrition was that it could maintain lean body mass while avoiding adynamic ileus. But due to the emergence of complications such as catheter related sepsis, thrombosis, thrombophlebitis, catheter related embolism, pneumothorax, and adverse effect over humoral immunity, has now led to the newer increasingly accepted enteral nutrition.<sup>8,9</sup>

Now there are several evidence based data and international guidelines stating the importance of oral or enteral feeding in acute pancreatitis depending upon the grade of severity and also to start either oral or enteral nutrition in mild acute pancreatitis soon after admission.<sup>13</sup>

Patients in the study group did not vary much with respect to age ( $p=0.431$ ) and majority of the patients in both groups were male (study group- 35, control group- 36;  $p=0.723$ ).

The primary aim of the study was to find out the duration of hospital stay and it was found to be significantly reduced in the study group ( $p=0.011$ ). Our observation supports the outcome of study done by Vaughn et al which concluded that mild pancreatitis patients can be safely started on early enteral feeds and it showed lesser number of gastro intestinal adverse effects, better oral tolerance to feeds, lesser complications, and hence lesser duration of stay.<sup>14</sup> Similarly there was another study by Eckerwall et al which was a randomized clinical study and it concluded that immediate oral feeding in patients

with mild acute pancreatitis is safe and resulted in accelerated recovery without adverse gastro intestinal effects and reduced hospital stay.<sup>13</sup> Meta-analysis by Marik et al, and Mc Clave et al demonstrated that use of enteral nutrition in mild acute pancreatitis resulted in significant reduction in infections, complications other than infections, operative interventions and length of hospital stay as well as a decreasing trend toward organ failure.<sup>15,16</sup> The reason for shorter duration of hospital stay could be attributed to the fact that even small amounts of enteral nutrition may help to preserve intestinal epithelium and epithelial tight cell junctions, stimulating secretion of brush border enzymes, enhancing immune function and prevents bacterial translocation.<sup>14</sup>

Acute pancreatitis (AP) is a common digestive disease and the most frequent disorder of the pancreas. There has been a steady increase in the hospitalization rate for acute pancreatitis.

Over the last several decades. Given that two-thirds of the actual cost of treatment in AP is attributable to hospitalization, the consumption of healthcare resources could be significantly reduced by shortening the duration of the hospital stay. Efforts to reduce the length of hospital stay in patients with non-severe acute pancreatitis might prove to be particularly cost-effective as they represent up to 85% of all patients with acute pancreatitis. This forms the importance of present study. The usual criteria for hospital discharge of patients with non-severe acute pancreatitis are the resolution of pain and tolerance of oral refeeding. The conventional management of AP involves a nil per oral (NPO) regimen until the symptoms (pain) and signs (ileus) of AP have resolved. It is customary to commence oral intake with the resumption of clear oral fluids. If this is tolerated the patients are then offered oral food. However, this practice of staged reintroduction of feeding after a sustained period of NPO for AP is reported to be associated with pain relapses and prolonged hospitalization in at least a quarter of patients. It is suggested that this is sub-optimal, with considerable room for improvement using enteral feeding as early as possible after admission.<sup>12</sup> In addition, there are concerns that no feeding will increase the risk of complications as it will exacerbate intestinal dysfunction and result in protein deficiency within the first week due to the excessive rates of protein catabolism associated with the disease.

Management of nutrition in the setting of acute pancreatitis varies and can include oral, enteral, or parenteral nutrition. Most agree that maintenance of gut barrier function in mild acute pancreatitis is best achieved through the use of enteral rather than parenteral nutrition because, parenteral feeding carries numerous unfavourable side-effects such as atrophy and increased permeability of the gut mucosa. Furthermore, hypomotility of the gut, lack of peristalsis and stagnant bowel contents also cause significant changes in the intestinal micro flora causing adverse gut functioning in

patients with acute pancreatitis. Conversely, enteral feeding prevents the aforementioned atrophic changes as the uptake of nutrients in intestinal epithelial cells comes directly from the intestinal lumen and it increases the gut motility due to the hyper osmolarity of the nutrients. These pathophysiologic mechanisms protect against the overgrowth of abnormal intestinal flora and increase gut permeability, hence, potentially alleviating subsequent bacterial translocation.<sup>17</sup>

Characteristics of enteral nutrition that may affect gastrointestinal tolerance in patients with acute pancreatitis include the method of delivery (bolus vs. continuous), the formula (monomeric, oligomeric, polymeric, immune-modulating, fiber, or fiber free), and the delivery route (gastric vs. jejunal). Current literature supports the use of a polymeric formula delivered through either a gastric tube or a jejunal tube with as-needed adjustment to improve tolerance, which in turn influences morbidity and length of hospital stay. Early enteral nutrition, defined as the provision of nutrients within 48 hours of hospitalization, has been associated with reduced mortality and infections compared with delayed enteral nutrition which helps in reducing the duration of hospital stay.<sup>18</sup>

The secondary objective of our study was to evaluate whether early enteral feeding in acute pancreatitis resulted in decrease in abdominal symptoms like abdominal pain, nausea and vomiting. The study group was found to have significant decrease in abdominal pain which resulted in less consumption of analgesics and also a decreased incidence of other symptoms like nausea and vomiting. These results were in accordance with the randomized control study by Petrov et al where early nasogastric feeding reduced the intensity of abdominal pain, need for opiates and risk of oral food intolerance.<sup>10</sup>

Usually, the initial treatment of acute pancreatitis consists of a nil per oral (NPO) regimen and the administration of analgesics and ample intravenous fluids. The reason for maintaining the fasting state is the assumption that pancreatic stimulation by enteral feeding may aggravate pancreatic inflammation causing increased abdominal pain. But now this concept of “pancreatic rest” which was being followed over decades is debated. Moreover, it is also found out that, many patients when anorectic suffer increasing pain sensations and ileus-related nausea and vomiting. To date, there are substantial scientific proofs to say that nutritional support is a must in acute pancreatitis, not only for severe acute pancreatitis but also for mild grade and among different routes, enteral feeds are considered superior to parenteral nutrition.<sup>19</sup> The beneficial effects of enteral feeding on mucosal integrity and the prevention of bacterial overgrowth may well explain the superiority of enteral feeding over TPN. Enteral feeding significantly reduces the risk of infections, gastro intestinal adverse effects, need for opiates, lowers the need for surgical interventions, and

reduces oral food intolerance thus reducing the length of hospital stay.

The concept of “putting the pancreas to rest” assumes that pancreatic rest promotes healing and decreases pain, because it reduces the exocrine secretion and leakage of pancreatic juices in pancreas parenchyma and peri pancreatic tissue. The concept of pancreatic rest originates from the classic work of Ragins et al.<sup>20</sup> However, this concept of “putting the pancreas to rest” challenges the persistence of basal pancreatic exocrine secretion. The pancreatic exocrine secretion contains several components, among which only protein enzymes are held responsible for auto digestion of the gland which thus aggravates the inflammatory cascade. Hence supplementing nutrition via enteral feeds using accepted formulations to suppress protein enzyme output alone but with continued delivery of other components like bicarbonate and fluid volume output widely led to the acceptance of enteral feeds today.<sup>19</sup>

Several other studies also support these findings like study by Mc Clave et al where they compared the safety and efficacy of enteral feeds versus parenteral feeds in mild acute pancreatitis and found out the benefits of enteral feeds outstanding the other.<sup>16</sup>

According to another recent systematic review, it was found out that early feeding of patients hospitalized with acute pancreatitis does not appear to increase adverse events and might improve outcomes as well. Review included 11 randomized trials with 948 patients, all hospitalized with acute pancreatitis. The trials compared timing of feeding (early versus delayed feeding), feeding routes (oral, nasogastric, nasojejunal and oral or nasoenteric). Seven of the reviewed trials included patients with mild to moderate pancreatitis, and they concluded that early enteral feeding was associated with reduced length of stay, lower rates of gastrointestinal symptoms (feeding intolerance, nausea, vomiting, pain) with no increase in adverse events.<sup>6,7</sup> Also there is another RCT by Farooq et al which compared outcome between early enteral and total parenteral nutrition in patients with acute pancreatitis and found out that the mean length of hospital stay, the frequency of surgical intervention, complications and death were all significantly lower in early enteral nutrition group as compared to total parenteral nutrition group irrespective of patient’s age, gender and severity of pancreatitis.<sup>21</sup> Several meta-analysis like study by Bakkar et al found out that starting enteral feeding within 24 h after hospital admission, was associated with a reduction in complications and organ failure in acute pancreatitis.<sup>22</sup>

Regarding the starting of enteral feeds, optimal timing also plays an important role in the management of acute pancreatitis. Even though, the exact pathophysiologic mechanisms of bacterial infection in acute pancreatitis have not been elucidated. But it seems unequivocal that delaying enteral feeding increases the risk for pancreatic

necrosis and the development of multi organ failure in pancreatitis by increasing bacterial translocation and pathogen overgrowth, which can be detected in the very early phase of acute pancreatitis. In a multicenter study, Besselink et al demonstrated that bacteraemia can be detected as early as day 7 and that infected necrosis can be detected on average 26 days after hospital admission.<sup>23</sup> Early bacterial invasion may further worsen septicemia, making the patient even more susceptible to multi-organ failure, initiating a vicious cycle. Early enteral feeding may reduce or prevent bacterial translocation by maintaining the intestinal barrier. Hence, it is reasonable to start enteral feeding as early as possible.<sup>24</sup>

The American society for parenteral and enteral nutrition (ASPEN) and the society for critical care medicine (SCCM) suggested that patients with acute pancreatitis need frequent assessment by the nutrition support clinician, irrespective of their severity and in mild acute pancreatitis, patient diet should be started with oral feeds if tolerated and otherwise with enteral feeds within 7 days of admission. This also emphasize the need of nutritional requirement in mild acute pancreatitis because nutrition deprival can deteriorate the clinical status in patients with mild disease to severe disease. But there are only limited studies highlighting the importance of enteral feeds in mild acute pancreatitis. So additional clinical trials emphasizing clearly the benefits of early enteral feeds in mild acute pancreatitis with optimum feeding protocols and optimal timing is needed to minimize the heterogeneity in current feeding practice.<sup>14</sup>

### **Limitations**

The present study had few limitations like the impact of different etiological factors on the subsequent nutritional management has not been analysed. Secondly, additional outcome parameters like infectious complications, organ failure, rates of ICU admissions and mortality rates are not taken into consideration. Thirdly insights into the precise magnitude of all benefits of early feeding are limited. Fourthly it was an open label study and no blinding was done and lastly the study was limited to patients with mild acute pancreatitis only.

### **CONCLUSION**

Patients with mild acute pancreatitis can safely be started on early enteral feeds within 48 hours of hospital admission. Early feeding reduces gastro intestinal adverse effects, reduces abdominal pain and need for analgesics. It also improves oral food tolerance with reduced nausea and vomiting causing shorter hospital stay and thus reducing the economic burden also.

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