

Comparison of Outcome between Early Enteral and Total Parenteral Nutrition in Patients with Acute Pancreatitis

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ABSTRACT

Objective: To compare the outcome between early enteral and total parenteral nutrition in patients with acute pancreatitis.

Methods: This six months randomized controlled trial was carried out at Department of General Surgery, Unit-I, Sir Ganga Ram Hospital, Lahore study. A total of 234 patients of both genders, aged between 18-70 years presenting with acute pancreatitis were included in this study after taking written informed consent. These patients were randomly allocated into two treatment groups. Patients in Group A received early enteral nutrition while Group B received total parenteral nutrition. Need for surgical intervention, length of hospital stay and death was recorded. Patients presented with complications of acute pancreatitis like shock, pancreatic necrosis and pancreatic abscess and diabetic patients were not included in this study.

Results: The age of the patients ranged from 18 years to 70 years with a mean of 43.8 years. Majority (49.6%) of the patients belong to age group of 35-50 years. There were 152 (65.0%) male and 82 (35.0%) female. Among them, 39 (59.4%) patients had mild pancreatitis while 39 (16.7%) had moderate and 56 (23.9%) had severe pancreatitis. Both the study groups were comparable in terms of mean age ($p=0.764$), gender ($p=0.584$) and severity of pancreatitis ($p=0.786$). The mean length of hospital stay was significantly shorter with early enteral nutrition (14.7 vs. 17.7 days; $p=0.000$) as compared to total parenteral nutrition. This difference was significant across all age, gender and disease severity groups. The frequency of surgical intervention (28.2% vs. 82.9%; $p=0.000$) and death (15.4% vs. 45.3%; $p=0.000$) was significantly lower in early enteral nutrition group as compared to total parenteral nutrition group irrespective of patient's age, gender and severity of pancreatitis.

Conclusion: The mean length of hospital stay the frequency of surgical intervention 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.

Keywords: Acute pancreatitis; Early enteral nutrition; Total parenteral nutrition.

INTRODUCTION

Acute pancreatitis is an acute inflammatory condition which is thought to be due to triggering of enzymes within the pancreatic acinar cells, causing inflammation extending into the surrounding tissues. The two most common causative factors, contributing more than 80% of cases, are gallstones and alcohol abuse⁽¹⁾. Just a decade ago, treating a patient with acute pancreatitis looked rather straightforward for just about every resident: it meant IV fluids, suitable pain killers and a strict nil-by-mouth regimen for at least a couple of days. Nutritional support was, if at all, given via the parenteral route. The rationale after this regimen was the idea that any stimulus to

the inflamed gland must be eluded as it would worsen the disease⁽²⁾. However, during the past decade, there have been studies which prove safety of early enteral nutrition and challenge this idea of pancreatic rest. Doley et al. in 2009 showed that early enteral nutrition in patients with acute pancreatitis was equivalent to total parenteral nutrition in terms of need for surgical intervention (56.0% vs. 60.0%; $p=1.000$) and death (20.0% vs. 16.0%; $p=1.000$)⁽³⁾. Paiva et al. in 2010 observed no significant difference in length of hospital stay with early enteral nutrition (25.47 ± 5.55 vs. 22.25 ± 11.07 ; $p=0.320$) as compared to total parenteral nutrition⁽⁴⁾. The results of these two studies show that enteral feeding is at least as safe as total parenteral

nutrition in patients with acute pancreatitis. Wu et al. in 2013 documented that enteral nutrition was even better than total parenteral nutrition and was associated with lesser need for surgical intervention (22% vs. 80%; $p < .05$) and mortality (11% vs. 43%; $p < .05$)⁽⁵⁾. Moreover, enteral nutrition is much cheaper than total parenteral nutrition and is associated with much lesser systemic complications⁽⁶⁾. In the light of above evidence; early enteral nutrition can be a safer alternative in patients with acute pancreatitis. However, the most frequent cause of acute pancreatitis in Pakistani population is gallstones compared to alcoholism in Western society⁽⁷⁾. However, no such study had been conducted in local population previously. Therefore, this study undertake to compare outcome between early enteral and total parenteral nutrition in patients with acute pancreatitis.

MATERIALS AND METHODS

Operational definitions: *Acute pancreatitis:* Patients with clinical features of acute pancreatitis (like abdominal pain which radiated to back, fever, vomiting) confirmed on serum amylase level (>3 folds increase from baseline).

Early enteral feeding: It was established after passing a nasogastric tube within 24 hours of admission. Daily caloric requirement was calculated as 25 Kcal/kg/day. The calculated calories were provided in divided meals at 6-8 hours interval.

Outcome: It was evaluated in terms of length of hospital stay, measured in days from the day of admission till the day of discharge. Discharge criteria was pain free on oral analgesics and serum amylase level <30 units/liter.

Need for surgical intervention: Any surgical intervention required due to pancreatitis itself or its complications within 30 days of admission.

Mortality: It was the death of patient due to pancreatitis or its complications within 30 days of admission.

Sample Size: Sample size of 234 cases (117 in each group) was calculated with 80% power of test, 95% confidence level, taking expected hospital stay to be mean \pm sd 25.47 \pm 5.55 days after early enteral nutrition and 22.25 \pm 11.07 days after total parenteral nutrition in patients with acute pancreatitis⁽⁴⁾.

Data collection: Approval from Hospital's Ethical Review Board was taken. This randomized controlled trial was carried out at in General

Surgery Department, Unit-I, Sir Ganga Ram Hospital, Lahore. Duration of study was 6 months from 18/09/2014 to 17/03/2015. Patients of both aged between 18-70 years with acute pancreatitis as per operational definition and patients who signed informed written consent included in this study. However, patients presented with complications of acute pancreatitis like shock (on clinical examination), pancreatic necrosis and pancreatic abscess (as per abdominal ultrasound scan), who were known diabetics, foreign nationals and who refused to give written informed consent to participate in the study were excluded from study.

Total 234 patients meeting the inclusion criteria, presenting in the surgical outdoor and emergency departments of Sir Ganga Ram Hospital, Lahore were enrolled into this study. Detailed history and written informed consent was taken from each patient. The patients were randomly allocated into two groups by lottery method. Group-A was of early Enteral Nutrition while Group-B was of Total Parenteral Nutrition. Patients candidate for early enteral nutrition were passed Nasogastric (NG) tube and feeding was started as per operational definition. Need for surgical intervention, length of hospital stay and death was noted and recorded along with demographic data of the patient into the proforma. All the patients were managed by consultant in charge of the unit to eliminate bias. Confounding variables were controlled by exclusion.

Data analysis: All the collected data was entered and analyzed through SPSS version 20. Numerical variables; age and length of hospital stay were presented by mean \pm SD. Categorical variables i.e. gender, need for surgery and death have been presented by frequency and percentage. Independent sample t-test was used to compare mean length of hospital stay among groups taking p-value $\leq .05$ as significant. Chi-square was used to compare need for surgery and death among groups taking p-value $\leq .05$ as significant. Data was stratified for age, gender and severity of disease to address effect modifiers.

RESULTS

The age of the patients ranged from 18 years to 70 years with a mean of 43.79 \pm 12.16 years. Majority (n=116, 49.6%) of the patients were aged between 35-50 years. There were 152 (65.0%) male and 82 (35.0%) female patients in the study group. 139 (59.4%) patients had mild pancreatitis while 39

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(16.7%) had moderate and 56 (23.9%) had severe pancreatitis. Both the study groups were comparable in terms of mean age (p=0.764), gender (p=0.584) and severity of pancreatitis (p=0.786). All these findings have been summarized in Table 1. The mean length of hospital stay was significantly shorter with early enteral nutrition (14.69±4.46 vs. 17.76±3.74 days) as compared to total parenteral nutrition. This

difference was significant (p=0.000) across all age, gender and disease severity groups. The frequency of surgical intervention (28.2% vs. 82.9% p=0.000) and death (15.4% vs. 45.3%; p=0.000) was significantly lower in early enteral nutrition group as compared to total parenteral nutrition group irrespective of patient's age, gender and severity of pancreatitis (Table 1-3 and Figure 1).

Table 1: General characteristics of the study population

Characteristics	Overall	Early enteral nutrition (n=117)	Total parenteral nutrition (n=117)	p-value
Age (years)	43.79±12.16	44.03±12.43	43.56±11.93	0.764
Age groups				
<35 years	61 (26.1%)	31 (26.5%)	30 (25.6%)	0.901
35-50 years	116 (49.6%)	59 (50.4%)	57 (48.7%)	
>50 years	57 (24.4%)	27 (23.1%)	30 (25.6%)	
Gender				
Male	152 (65.0%)	78 (66.7%)	74 (63.2%)	0.584
Female	82 (35.0%)	39 (33.3%)	43 (36.8%)	
Severity				
Mild	139 (59.4%)	67 (57.3%)	72 (61.5%)	0.786
Moderate	39 (16.7%)	21 (17.9%)	18 (15.4%)	
Severe	56 (23.9%)	29 (24.8%)	27 (23.1%)	

Independent sample t-test and chi-square test, Observed difference was statistically insignificant

Table 2: Frequency of need for surgery among different pancreatitis severity groups.

Severity of pancreatitis	Study group		p-value ¹
	Early enteral nutrition (%)	Total parenteral nutrition (%)	
Mild	9 (13.4)	58 (80.6)	0.000
Moderate	9 (42.9)	15 (83.3)	0.010
Severe	15 (51.7)	24 (88.9)	0.003

¹p-value was calculated by chi-square test; p<0.05 was considered as significant.

Table 3: Frequency of mortality among different pancreatitis severity groups.

Severity of pancreatitis	Study group		p-value ¹
	Early enteral nutrition (%)	Total parenteral nutrition (%)	
Mild	7 (10.4)	29 (40.3)	0.000
Moderate	4 (19.0)	9 (50.0)	0.041
Severe	7 (24.1)	15 (55.6)	0.016

¹p-value was calculated by chi-square test; p<0.05 was considered as significant.

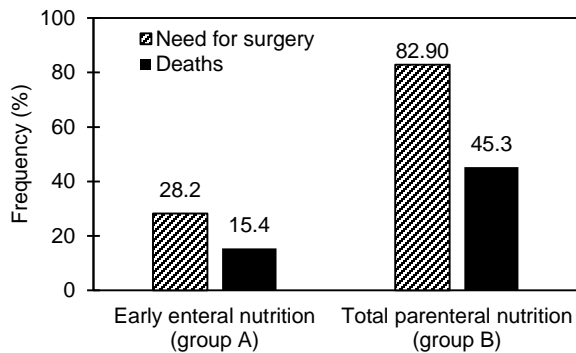
DISCUSSION

Acute pancreatitis is an inflammatory condition which is thought to be due to enzymatic activation in acinar cells which causes inflammation that extends towards tissues around them.

There is actually cell-signaling cycle which is thought to be initiated by bacterial infection (mostly by Gram negative organisms) The most probable source of this infection is through gastrointestinal system. Increased permeability of gut allows translocation of bacteria. Due to this,

macromolecules for examples bacteria, antigens and endotoxins from the gastrointestinal tract migrate to spleen, liver, pancreas, portal system and mesenteric lymph nodes. This whole migration process causes stimulation of circulatory neutrophils, granulocytes and macrophages, initiating release of pro-inflammatory cytokines, which ultimately, leads to inflammation. If this response is over-activated, it can start self-destructing process, although originally it acts as defense system for the host.

Figure 1: Frequency of need for surgery and deaths among both study groups.



There is release of inflammatory mediators in an unbalanced manner which may end up into the development of systemic inflammatory response syndrome (SIRS), infective pancreatic necrosis and resultantly multi-organ failure (MOF)⁽¹⁾. Just a decade ago, treatment of acute pancreatitis was straightforward, like giving IV fluids, adequate pain killers and putting patient on strict nil-by-mouth regime for a couple of days. Nutrition, if needed, was only given through parenteral route. The idea behind this pancreatic rest regime was to reduce any stimulus to inflamed pancreas which could further increase the condition⁽²⁾. However; during the past decade, there have been studies which prove safety of early enteral nutrition and challenge this idea of pancreatic rest. Pathogen overgrowth and translocation of bacteria can be determined in very early phases of acute pancreatitis. Besselink et al., in multicenter study, showed that bacteremia can be determined as early as on 7th day of acute pancreatitis. That is why; if translocation of bacteria is prevented by maintaining intestinal barrier through enteral feeds, convalescence from the disease would be enhanced. Based on this proposed mechanism, a number of studies compared the patient outcome

with early enteral versus total parenteral feeding and their results have challenged this traditional concept of pancreatic rest. Moreover, enteral nutrition is much cheaper than total parenteral nutrition and is associated with much lesser systemic complications⁽⁶⁾. Therefore, early enteral nutrition is now recommended management of such patients. However, the most frequent cause of acute pancreatitis in Pakistani population is gallstones (compared to alcoholism in western society)⁽⁷⁾ therefore, there was need to confirm the safety of early enteral nutrition in local population with AP before adopting it in routine practice. The age of the patients ranged from 18 years to 70 years with a mean of 43.79 ± 12.16 years in the present study. Iqbal et al. in 2015 (43 ± 11 years), Raza et al. in 2010 (44.68 ± 17.47 years) and Shah et al. in 2009 (42 ± 11 years) observed similar mean age among patients of acute pancreatitis in local population^(7,8,9). However, Pal et al. in 2012 reported comparatively higher mean age of 51.6 ± 14.6 years at Agha Khan University Hospital, Karachi⁽¹⁰⁾. Doley et al. 2009 reported much lower mean age of 38.4 ± 13.8 years in Indian such patients while Casas et al. in 2007 reported much higher mean age of 55.6 ± 15.6 years among Spanish population^(3,11). Majority ($n=116$, 49.6%) of the patients were aged between 35-50 years. A similarly higher proportion (50%) of patients in this age group was previously observed by Iqbal et al. (139,8). There were 152 (65.0%) male and 82 (35.0%) female patients in the study group giving a male: female ratio of 1.9:1. A similar male predominance was previously reported by Zhao et al. (1.8:1) and Wu et al. (1.7:1)^(5,12). Shah et al. and Petrov et al. reported much higher male: female ratio of 3:1 in Pakistani and Russian populations respectively^(9,13). These variations in age and gender distribution can be due to differences in environmental and etiological factors of AP among populations⁽⁷⁾. Both the study groups were comparable in terms of mean age ($p=0.764$), gender ($p=0.584$) and severity of pancreatitis ($p=0.786$). Thus randomization was effective and there was no inherent bias among the study groups. The mean length of hospital stay was significantly shorter with early enteral nutrition (14.69 ± 4.46 vs. 17.76 ± 3.74 days; $p=0.000$) as compared to total parenteral nutrition. This difference was significant across all age, gender and disease severity groups. A similar significant improvement in terms of length of hospital stay with early enteral feeding was observed previously

by Zhao et al. in 2015 (13.7±5.4 vs. 15.7±6.2 days; p=0.0398) (12). Paiva et al. in 2010 also observed no significant difference in length of hospital stay with early enteral nutrition (25.47±5.55 vs. 22.25±11.07; p=0.320) as compared to total parenteral nutrition proving early enteral nutrition to be at least equally safe⁽⁴⁾. The frequency of surgical intervention (28.2% vs. 82.9%; p=0.000) and death (15.4% vs. 45.3%; p=0.000) was significantly lower in early enteral nutrition group as compared to total parenteral nutrition group irrespective of patient's age, gender and severity of pancreatitis. A similar difference in the frequency of surgical intervention was previously reported by Modena et al. (25% vs. 88.4%; p<0.001), Wu et al. (22% vs. 80%; p<.05) and Casas et al. (0% vs. 2.7%; p<0.001)^(5,12,14). Doley et al. (56.0% vs. 60.0%; p=1.000) observed insignificant difference confirming early enteral nutrition to be at least as safe as total parenteral nutrition in terms of need for surgical intervention⁽³⁾. Similar difference in mortality was reported by Wu et al. (11% vs. 43%; p<.05), Modena et al. (5% vs. 35%; p=0.001) and Petrov et al. (5.71% vs. 34.29%; p<0.01)^(5,12,14). Doley et al. (20.0% vs. 16.0%; p=1.000) observed insignificant difference confirming early enteral nutrition to be at least as safe as total parenteral nutrition in terms of frequency of death⁽³⁾. The present study is first of its kind in local population and has found significant decrease in mean length of hospital stay (14.69±4.46 vs. 17.76±3.74 days; p=0.000), the frequency of surgical intervention (28.2% vs. 82.9%; p=0.000) and death (15.4% vs. 45.3%; p=0.000) with early enteral nutrition as compared to total parenteral nutrition in patients of acute pancreatitis irrespective of patient's age, gender and severity of pancreatitis. The results of the present study are in line with the similar studies in other populations and has confirmed the safety and supremacy of early enteral feeding in such patients. Early enteral feeding is much cheaper than total parenteral nutrition and is associated with much lesser systemic complications⁽⁶⁾, therefore it should be adopted in future practice in patients of acute pancreatitis.

CONCLUSION

The mean length of hospital stay, the frequency of surgical intervention 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.

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