Prospective Study To Evaluate The Outcome Of Early Enteral Nutrition In Severe Acute Pancreatitis

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Abstracts: **Background and Objectives**: Severe acute pancreatitis (SAP) affects the nutritional status of the patient. This prospective study was carried to assess the tolerance and outcome of early enteral nutrition via naso-jejunal feeding tube (NJFT).**Methods:** 30 patients of SAP were given enteral feeding via endoscopically inserted NJFT within 48 – 72 hours of admission. The volume of the feeds was increased as per tolerance. The patients who tolerated the feed (Group A) and those who did not tolerate (Group B) were followed up by biochemical parameters, amount and duration of feeding. The patient outcome noted and the results statistically analyzed. **Results:** 27 (90%) patients tolerated the feed, reached the goal feed volume and were subsequently started on oral feeds. No complication related to NJFT insertion was encountered. A significantly higher ICU stay (p=0.04) and number of complications (p = 0.048) was observed in Group B patients than in Group A. All nutritional parameters improved in patients in Group A with significant improvement in serum calcium, serum albumin and fasting blood glucose levels**. Conclusion:** Enteral nutrition is an economical and effective way to provide nutrition to patients with severe acute pancreatitis. The patients who tolerated feeds had less morbidity, mortality and hospital stay. [SIngla S et al NJIRM 2014; 5(3) :116-121]

Key Words: Acute Pancreatitis, Enteral Nutrition, Naso Jejunal Feeding.

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Introduction: Acute pancreatitis is a common disease with an incidence of 30-50/10000 inhabitants/year [1]. Mild acute pancreatitis is characterized by interstitial edema of the gland with minimal organ dysfunction. Severe acute pancreatitis is characterized by a severe systemic inflammatory response and often multiorgan failure with necrosis of the parenchyma. About one-thirds of the deaths occur in early phase of the disease [2], the chief cause being multiorgan failure while deaths occurring later than one week are due to septic complications. The mortality rises significantly when the spectrum of disease shifts from mild to severe form.

The effect of the disease on the nutritional status of the patient depends upon its severity. The majority of the patients (80%) have mild acute pancreatitis (APACHE-II < 8[2], Ranson's criteria < 3[3]) and is managed by "functional rest" of the small intestine for a short period, intravenous hydration and analgesia[2]. On the contrary, patients with severe acute pancreatitis (APACHE -II $\geq$ 8[2], Ranson criteria $\geq$ 3[3]) need long hospitalization and have increased complications and mortality rates. In these patients, nutritional support is expected to positively affect the course of the disease and affect the outcome.

Of the main nutritional agents, lipids more intensively stimulate pancreatic secretion while carbohydrates have the weakest stimulatory effect. Oligopeptides (dipeptides and tripeptides) seem to have even less stimulating action. Solutions of high osmolarity are more stimulating than solutions of low osmolarity.

The early infusion of oligopeptide solutions for enteral nutrition, distally to the proximal jejunum, has been shown to ensure adequate 'pancreatic rest'[4]. The complexity of the digestion procedure of various nutritive substances also significantly affects pancreatic secretion[5].

Even though the nutritional deficits are frequent in acute severe pancreatitis; nutrition, as a part of therapy, was neglected for a long time. Despite fears, that enteral nutritional may exacerbate acute pancreatitis, because of the known stimulatory effect of luminal nutrients on

trypsinogen synthesis, several randomized clinical trials have shown that the outcome is better and the cost is lower if enteral nutrition is used instead of total parenteral nutrition (TPN) [6].

The explanations are complex and are related to the fact that enteral nutrition avoids TPN complications and may prevent the progression of multi organ failure. It is also the most effective way of supporting intestinal metabolism. In our study, we have tried to assess the tolerance and outcome of early enteral nutrition via naso-jejunal feeding tube (NJFT) in predicted severe acute pancreatitis (SAP).

Material And Methods: The study was conducted from January 2010 to July 2011 in the Department of Surgery of Dayanand Medical College and Hospital, Ludhiana after obtaining approval from the ethical committee. It included patients admitted with the diagnosis of severe acute pancreatitis made on the basis of history, biochemical and radiological investigations with APACHE II Score $\geq$ 8 and Ranson's score $\geq$ 3. Patients aged < 20 and > 65 years, with acute pancreatitis due to trauma/ surgery/ cancer, with inflammatory bowel disease, stoma, short bowel, and chronic pancreatitis with exacerbation were excluded from the study.

All the selected patients were put nil orally with intravenous fluids, antibiotics and analgesics. Enteral feeding was given via naso-jejunal feeding tube inserted endoscopically. The goal of the study was to get the NJFT feeds started within 48-72 hours of admission. The feeds were started on the same day or the next day of NJFT insertion. Semi-elemental feeds were given to deliver about 1.5 gm proteins/kg/day. The volume of the feeds was small initially and gradually increased as the feed was tolerated. Oral feeds were tried when the bowel sounds returned and continued if tolerated. The patients who tolerated the feed were included in Group A and those who did not tolerate in Group B.

The patients were followed up by the biochemical parameters (Hb, TLC, blood glucose, total serum proteins, serum albumin); amount and duration of feeding, patient outcome on the days- 0, 2, 7 and 14 days post admission.
The subject was deemed to have reached the end point of study if the subject could not tolerate NJ

feed as evidenced by multiple episodes of vomiting/loose stools, abdominal pain or distension; if he/she started oral feeds and passed flatus/stools with biochemical tests returning to normal; undergoes intervention/surgery; there is tube malpositioning/patient non compliant/refusal to get the tube repositioned; dies during the course of study. Descriptive studies were used to display the results of the study. Chi-square test, t-test and coefficient of correlation were used to compare the outcome in the groups stratified

Result: A total of 30 patients were studied for the tolerance and outcome of early enteral nutrition in acute severe pancreatitis. The age of the patients varied from 23-65 years. The mean age was 46 years with the maximum number of patients in the age group of 51- 60 years. (n=9, 31%). Majority of the patients were males (n=26, 87%). Alcohol induced pancreatitis was the commonest cause of acute severe pancreatits (n=13, 43.34%) followed by gall stones (n=10, 33.33%) and miscellaneous causes (n=7, 23.33%) which included idiopathic, hyperlipidemia and hypercalcemia. All cases of alcohol induced pancreatitis were males whereas all the females had gallsone induced pancreatitis. Six males also had biliary pancreatitis.

Table 1: Severity Of Pancreatitis

APACHE II Score	Group A No.	%	Group B No.	%	TOTAL No.	%
8 - 12	16	59.25	2	66.67	18	60.0
12 – 16	6	22.22	0	00	6	20.0
➢ 16	5	18.50	1	33.33	6	20.0
Total	27	100	3	100	30	100
Mean	12.93		13		12.93	
SD	4.22		6.08		4.31	
P value	0.93					

The overall mean APACHE II score for the patients at admission was 12.93 with a standard deviation of 4.31 and score ranging from 8-26. No significant

difference in the APACHE II score was seen between the patients in Groups A and B. (Table 1)

The findings of patients in both the groups were correlated with the day of presentation. The mean day of presentation was 4.73 days with a standard deviation of 3.11 after the onset of abdominal pain. However it was found that patients who did not tolerate feed presented earlier at a mean of 2 days post abdominal pain. 70 % of the patients presented during first 5 days of onset of the disease, with remaining 20% during 6^{th} to 10^{th} day and 10% of the patients during 10^{th} to 15^{th} day of the onset of disease.

NJFT tolerance was assessed by nasogastric aspiration, abdominal distension, loose stools and abdominal pain. Out of 30 patients, 27 patients tolerated the feed, reached the goal feed volume and were subsequently started on oral feeds. 2 patients did not tolerate the feed as evidenced by abdominal pain, increased nasogastric aspiration and distension. 1 patient tolerated feeds after the 10^{th} day and was included in Group B (Group A included patients who tolerated early feed i.e. during 48-72 hours).

No complication related to NJFT insertion was encountered. No patient required a re-endoscopy to replace or reposition a displaced/pulled out NJFT. However, 5 patients experienced bouts of diarrhea which settled without altering the feeds. In 2 separate cases, feeds had to be withheld for a maximum of 12 hours due to abdominal distension/discomfort.

28 patients were started feeds within 48 hrs of NJFT insertion amongst whom, 26 (92.8%) fully tolerated the feeds. 2 patients got delayed till the third day out of whom one patient fully tolerated the feed on the third day. Both patients had a higher mean APACHE II score of 15.5 compared to <13 for the rest of the patients but the difference was not statistically significant (p = 0.08).

If there were no complications/ intolerance, the NJFT feeds were gradually increased and it reached the tube feeding goals within 2-3 days after initiation of the feeds. Most of the patients (n=19, 70%) in Group A were able to reach the tube feeding goal by the 4^{th} - 5^{th} day (mean: 4.52 days, range: 2-8 days). Only 4 patients of that group were delayed beyond the 5th day. There was no statistical difference in the APACHE II scores for the patients who reached the goal feed at different times. (Table 2)

Table 2 : Time taken to reach goal NJFT feed

Full Feed started Days	Group A No.	%	Group B No.	%	TOTAL No.	%	APACHE II Mean	SD
0	0	0	2	66.67	2	6.67	15	7.07
2 – 3	4	14.8	0	0	4	13.33	13.5	5.92
4 - 5	19	70.3	0	0	19	63.33	12.79	4.4
>5	4	14.8	1	33.33	5	16.67	12.2	2.28
Total	27	100	3	100	30	100		
Mean	4.52		3.33		4.40		P value: 0.07	
SD	1.34		5.77		2.01			
P value	0.16							

28 of the 30 patients of acute severe pancreatitis required ICU admission on presentation. Only 2 patients were stable enough to be considered for ward care. Of the 27 patients in Group A, the mean ICU stay was 6 days with a SD of 4.87 days (range: 0-23 days). Patients in Group B had a significantly higher ICU stay with an average of 12.67 days (p = 0.04).However, there was no statistically significant correlation between the duration of stay of the patients and the APACHE II score (p = 0.84).

The mean hospital stay of patients in our study was 15.50 days with a standard deviation of 10.61. The mean was slightly lower in Group A (mean: 5.15, SD: 7.15) than in group B (mean: 18.67, SD: 10.61) but the difference was not statistically significant (p = 0.20).

There was no statistically significant correlation between the duration of hospital stay of the patients and the APACHE II score (p = 0.91)

although there was a positive correlation between increase in the hospital stay and increasing APACHE II score.

Table 3 shows the complications encountered in the patients. The number of complications were significantly more in the Group B than in Group A (p = 0.048).

Table 3 : Complications Encountered

Complications	Group A (n=27)		Group B (n=3)		TOTAL (n=30)	
	No.	%	No.	%	No.	%
Nil	12	30	0	0	12	30
Acute fluid Collection	10	25	1	2.5	11	27.5
ARF	6	15	0	0	6	15
Central line sepsis	3	7.5	0	0	3	7.5
Sterile Necrosis	6	15	2	5	8	20
DKA	1	2.5	0	0	1	2.5
Infected Pancreatic crosis	1	2.5	0	0	1	2.5
UGI Bleed	2	5	0	0	2	5
Haemorrhoidal Bleed	1	2.5	0	0	1	2.5
UTI	1	2.5	0	0	1	2.5
Fungal Septicaemia	0	0	1	2.5	1	2.5
Splenic Vein ombosis	0	0	1	2.5	1	2.5
Respiratory Failure	3	7.5	1	2.5	4	10
Total	**34**		**6**		**40**	
p-value	**0.04826**		**0.04826**		**0.04826**	

All nutritional parameters (serum calcium, fasting blood sugars, creatinine, albumin, total proteins and total leucocyte count) improved in patients in Group A with significant improvement in serum calcium, serum albumin and fasting blood glucose levels. Group B patients showed improvement in the serum calcium, creatinine and fasting blood glucose levels but they were not statistically significant. Other parameters deteriorated in the patients in Group B (Table 4)

Table 4: Biochemical outcomes

Parameter	*No.*	*Day 0 Mean*	*Day 0 SD*	*Day 2 mean*	*Day 2 SD*	*Day 7 mean*	*Day 7 SD*	*Day 15 No.*	*Day 15 mean*	*Day 15 SD*	*P value 2 vs 7*	*P value 2 vs 15*
Calcium (mg/dl)												
Gp A	*27*	*7.27*	*1.54*	*7.17*	*1.16*	*8.19*	*0.86*	*14*	*8.37*	*0.83*	*0.039*	*0.039*
Gp B	*3*	*66.93*	*1.36*	*6.67*	*1.56*	*7.43*	*0.31*	*2*	*7.90*	*0.14*	*0.199*	*0.156*
Total	*30*	*7.24*	*1.50*	*7.12*	*1.19*	*8.11*	*0.85*	*16**	*8.31*	*0.79*	*0.006*	*0.007*
TLC (x 10^3/µl)												
Gp A	*27*	*15.16*	*5.51*	*14.04*	*6.96*	*15.91*	*5.83*	*14*	*12.46*	*4.39*	*0.15*	*0.21*
Gp B	*3*	*17.87*	*6.00*	*15.43*	*8.84*	*17.27*	*10.76*	*2*	*18.20*	*1.84*	*0.72*	*0.39*
Total	*30*	*15.43*	*5.51*	*14.18*	*7.00*	*16.05*	*6.22*	*16**	*13.18*	*4.56*	*0.15*	*0.32*
FBS (mg/dl)												
Gp A	*27*	*206.59*	*62.21*	*198.15*	*45.6*	*169.70*	*44.25*	*14*	*146.29*	*25.74*	*0.042*	*0.006*
Gp B	*3*	*254.67*	*206.16*	*144.33*	*38.8*	*179.67*	*122.93*	*2*	*100.50*	*2.12*	*0.206*	*0.064*
Total	*30*	*211.40*	*211.40*	*192.77*	*47.3*	*170.70*	*52.98*	*16**	*140.56*	*28.62*	*0.057*	*0.006*
S. Creatinine (mg/dl)												
Gp A	*27*	*2.45*	*3.35*	*1.74*	*2.03*	*1.36*	*1.72*	*14*	*1.37*	*1.54*	*0.22*	*0.27*

Gp B	*3*	*1.20*	*0.46*	*2.62*	*2.90*	*3.21*	*4.00*	*2*	*0.86*	*0.08*	*0.79*	*0.20*
Total	*30*	*2.32*	*3.20*	*1.83*	*2.08*	*1.54*	*2.02*	*16**	*1.31*	*1.45*	*0.30*	*0.18*
Total serum proteins (mg/dl)												
Gp A	*27*	*6.50*	*0.74*	*5.78*	*0.95*	*6.27*	*0.76*	*14*	*6.36*	*0.74*	*0.05*	*0.05*
Gp B	*3*	*6.70*	*1.42*	*5.27*	*0.86*	*3.80*	*0.92*	*2*	*4.25*	*0.35*	*0.05*	*0.11*
Total	*30*	*6.52*	*0.79*	*5.73*	*0.94*	*6.02*	*1.07*	*16**	*6.09*	*1.00*	*0.15*	*0.14*
Serum albumin (mg/dl)												
Gp A	*27*	*3.46*	*0.56*	*2.83*	*0.48*	*3.15*	*0.59*	*14*	*3.03*	*0.48*	*0.044*	*0.130*
Gp B	*3*	*3.83*	*0.83*	*2.77*	*0.35*	*1.97*	*0.57*	*2*	*2.75*	*0.21*	*0.47*	*0.988*
Total	*30*	*3.49*	*0.59*	*2.82*	*0.46*	*3.03*	*0.68*	*16**	*2.99*	*0.46*	*0.117*	*0.138*

All the patients of Group A were discharged in a satisfactory condition. Of these one developed infective pancreatic necrosis with collection which was drained percutaneously with a per cutaneous drain and was subsequently discharged. One patient in Group B expired after 8 days of admission. He was operated for pancreatic necrosectomy; but died of septic complications. The other two patients of Group B were discharged after prolonged hospitalization (23 and 27 days). The overall mortality rate was 3.45% which was significantly more in Group B (p = 0.0084). The rate of intervention was 6.67% which was also significantly more in Group B (p = 0.05).

Discussion: Of the 30 patients studied, the average age of patients in our study was 46.1 years with a range of 23-65 years; the results were concordant with the studies conducted by other authors [6,7]. The statistics showed a relative increase in the incidence of pancreatitis in the age group of 40-46 years which may be because it is the most common age for females to get symptomatic gallstones and males to have complications arising from increased alcohol consumption.

Our study showed a higher preponderance for male subjects (87%) which is not in concordance to other studies[6,7]. This increase can be due to the gender bias regarding treatment of the males that prevails in India, especially in the rural section of the Indian society.

Major group of the patients with acute severe pancreatitis were alcohol induced (43%) followed by gallstones (33%). Abou-Assi et al[6] showed 62% incidence of alcohol induced and 18% gallstone related pancreatitis. However Hegazi et al[7] stated biliary pancreatitis as the most common (47%) cause of pancreatitis. The difference can be due to higher rate of alcohol consumption among the males in northern India especially the strong, unpurified 'desi' locally manufactured alcohol which is readily available at a low price.

The overall mean APACHE II score at admission was 12.93. This was comparable with the severity of the disease in patients in other studies[7] (mean-14.4). The mean day of presentation in our study was 4.73 days after the onset of acute abdominal pain which was comparable to 5.1 days reported by Kumar et al[8]. Olah et al[9] excluded the patients who arrived 48-72 hours after the onset of the symptoms. This much delay is expected in a tertiary referral centre like ours resulting in a high mean "onset of symptoms to day of presentation time".

The patients in Group B arrived earlier at a mean of 2 days as compared to 4.93 days for the Group A patients. The earlier presentation could be due to a referral bias resulting in patients with more morbidity being referred to a tertiary care centre earlier than others. However, the association between the day of presentation and whether the patient accepted the feeds was not statistically significant.

There was a 90 % tolerance of feeds in our study which was comparable to the studies of other authors [6,7]. The average time between the admission and onset of NJFT feeds was 1.8 days for the patients in Group A. Similar observation has been reported by other authors[6,9]. The mean time taken to reach goal feed from initiation was 2.7 days (65 hours) which was comparable to studies from other authors[6,9,10].

The mean ICU stay of the patients in Group A was 6 days which was comparable to 8 days reported by

Eatock et al [10] Patients in Group B had a significantly higher ICU stay of average 12.67 days. This compares to that of Hegazi et al[7] who observed that ICU stay in patients who reached goal feed more than 12 days after onset of pancreatitis was significantly more (19 days) than patients who reached the goals feed earlier (9 days). The mean hospital stay for our study patients was 15.50 days which was comparable to the findings of other authors[6].

The mortality rate in our study (3.45%) was comparable to 4.1% by Eckerwall et al [11] and the rate of intervention (6.67%) was comparable to 7.7% by Abou-Assi et al [6].

Conclusion: Pancreatitis is a non bacterial inflammatory disease that results from intra-pancreatic activation, release and digestion of the organ by its enzymes. In acute pancreatitis, general supportive therapy includes correction of the fluid volume, electrolyte and glucose abnormalities; respiratory, cardiovascular and renal support as necessary. The decision whether to use parenteral or enteral route for nutritional support is controversial. The jejunal feeding does not stimulate pancreatic secretion as opposed to intragastric or intraduodenal feeding. It also restores and prevents morphological changes in the intestine associated with fasting. Significant improvement was observed in the patients who tolerated the NGFT feeds with lesser complications and duration of ICU stay. All nutritional parameters improved with significant improvement in serum calcium, serum albumin and fasting blood glucose levels. Moreover as compared to TPN enteral nutrition is an economical and effective way of providing nutrition to patients with severe acute pancreatitis.

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