Early Enteral Feeding Versus Total Parenteral Feeding After Surgery in Severe Acute Pancreatitis: An Evidence-Based Case Report

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ABSTRACT

Background**:** *Acute pancreatitis is a self-limiting inflammatory disease that in some cases may lead to severe acute pancreatitis. To prevent this development, multimodal management, including nutritional management, is used in treating acute pancreatitis patients. The controversy between parenteral and enteral feeding has led to major debate. This case report aims to assess which method has better outcomes based on multiple cases of organ failure, inflammatory response, and length of hospital stay.* ***Methods*****:** *A 46-year-old male presented to the Emergency Department of our hospital with acute abdominal pain, nausea, and vomiting, 12 h before admission. Based on physical and further examination, the patient was diagnosed with severe acute pancreatitis and underwent a necrotomy procedure. Articles from multiple databases were obtained and assessed using the Cochrane Collaboration Risk of Bias tool. The articles were analyzed using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and a forest plot model. Effect size quantification for continuous and categorical variables was analyzed using continuous and binary random effect models, respectively.* ***Results*****:** *Seven articles were obtained after exclusion and review. A total of 491 patients with acute/severe acute pancreatitis were assessed. These seven articles conclude that enteral nutrition has advantages over parenteral nutrition.* ***Conclusion*****:** *Our study concluded that early enteral feeding provides better clinical improvement, reduced lipase enzyme levels, and shortened length of hospital stay.*

Keywords*: acute pancreatitis, early enteral feeding, clinical improvement, length of stay, case report.*

INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas with various outcomes, ranging from self-limiting to severe acute pancreatitis (SAP).[1-3] The severity of acute pancreatitis can be grouped using a scoring system such as Ranson's Score, BISAP Score, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and Sequential Organ Failure Assessment score.[4] The incidence of AP is increasing worldwide. Moreover, biliary acute pancreatitis caused by alcohol is also increasing significantly.[5,6] Statistically, men and women have the same incidence rate of AP. Higher mortality rates are found in hospitalized AP patients with organ failure or necrotizing pancreatitis.[5,6]

Inflammation of the pancreatic gland is accompanied by abdominal pain and exocrine failure leading to decreased oral intake, which is frequently related to malnutrition.[7] To prevent malnutrition, reduce inflammation, and improve the outcome of AP, nutritional support plays an important role in AP management. The traditional theory of "pancreatic rest" is trusted and has been widely used.[8] By allowing the intestines to rest, the autodigestion process will stop, thereby reducing the inflammatory process in the pancreas.[9] Many studies show the superiority of enteral nutrition over parenteral nutrition. Enteral nutrition has been proven to maintain the intestinal mucosa's function and structure. Moreover, lower mortality, multiple organ failure, and infection rates have been found by giving enteral nutrition. Early enteral feeding within 48–72 h after the onset of AP is recommended.[4,10-12]

There is still much controversy concerning the benefits of enteral versus parenteral nutrition in AP. This, therefore, leads to the aim of this case report, which is to answer several questions:

1. Which methods of enteral versus parenteral nutrition can improve the clinical condition?
2. Which methods of enteral and parenteral nutrition can reduce pancreatic inflammation based on lipase enzyme levels?
3. Which feeding method will result in a shorter length of stay (LOS), enteral or parenteral nutrition?

CASE ILLUSTRATION

A 46-year-old male presented to the Emergency Department, Sumber Waras Hospital, West Jakarta, Indonesia, complaining of acute abdominal pain 12 h before admission with nausea and vomiting. Since his teenage years, the patient had been smoking around 1-2 packs per day. He had been an alcoholic for 13 years with a habit of drinking 5 shots of Chinese wine per day. He had poor nutritional habits with inadequate calorie intake. He had a history of epigastric pain for half a year. There was no history of diabetes or hypertension. Physical examination showed abdominal distention, reduced bowel sounds, and diffuse and rebound tenderness. On the day of admission, the patient's heart rate was 90 beats per minute, respiratory rate 22 breaths per minute, and visual analog scale (VAS) of 4–5. He was categorized as grade I obese according to the Asia-Pacific body mass index (BMI) classification. Laboratory findings on admission revealed elevated lipase serum and electrolyte imbalance. Two days before discharge, a blood glucose check showed high serum levels of glycated hemoglobin (HbA1c). An abdominal computed tomography (CT) scan showed edematous pancreatitis with signs of necrosis on the caput and cauda of the pancreas. The patient was diagnosed with SAP based on the Revised Atlanta Criteria.[13]

The preoperative diagnosis was general peritonitis caused by necrotic pancreatitis.

The patient underwent an emergency exploratory laparotomy and debridement-necrosectomy of the pancreatic head within 6 h after admission. Intraoperative findings included: black serous hemorrhagic necrotic-like fluid, about 200 mL; fibrin tissue around the duodenogastric area and necrotic tissue in the pancreatic head. The necrotomy of the pancreas was performed, and three drains were installed.

In the post-operative procedure, a clear yellowish residue with a volume of more than 125 mL was found in the nasogastric tube. Laboratory findings revealed leukocytosis, elevated urea, and creatinine. Several parameters were found to have decreased, such as the VAS score, which decreased to a score of 1–2, heart rate below 90 beats per minute, and a normal respiratory rate. One day after the surgery, the patient managed to flatus, and to defecate on the second post-operative day. However, a significant decrease in lipase enzyme was found. Nutrition was given parenterally immediately after surgery. Early enteral nutrition was given on day two of admission with clear fluids that were increased to milk/broth/juice on day four. Nutritional management of the patient is described in **Table 1**.

The acute kidney injury resolved on post-operative day 4. There were no incidences of sepsis, re-surgery, or mortality during the post-operative period. The pharmacologic prescriptions for the patient include Omeprazole IV 40 mg, Ondansetron IV 4 mg, Ketorolac IV 30 mg, Ciprofloxacin 2 × 200 mg and Meropenem 3 × 1 g IV, Metronidazole 3 × 500 mg IV, Paracetamol 3 × 1 g, and Novorapid flat 1.5 units/h. The patient was discharged on the twelfth post-operative day.

METHODS

Articles were collected from PubMed, ProQuest, Scopus, and Springer databases using the keywords "acute pancreatitis," "severe acute pancreatitis," "necrotic pancreatitis," "early enteral feeding," and "parenteral feeding." The Inclusion criteria in this report were patients with AP who use early enteral feeding as the main nutritional intervention. AP was diagnosed according

Table 1. Daily Nutritional Management

Post-Operative Day (POD)	Nutrition Prescription
POD-0, Jan 14, 2023	Parenteral formula 1000 mL/24 h
POD-1, Jan 15, 2023	Parenteral formula 1440 mL/24 h Clear liquid 6 × 50 mL
POD-2, Jan 16, 2023	Parenteral formula 1440 mL/24 h Clear liquid 6 × 50 mL
POD-3, Jan 17, 2023	Parenteral formula 1440 mL /24 h Clear liquid 6 × 50 mL
POD-4, Jan 18 2023	Parenteral formula 1440 mL/24 h Milk/broth/juice 6 × 50 mL
POD-5, Jan 19, 2023	Parenteral formula 1000 mL/24 h Enteral formula 3× 15 mL/h (3 h, then stop for 1 h) If residue < 100 mL, enteral formula 6 × 50 mL
POD-6, Jan 20, 2023	Parenteral formula 1000 mL/24 h Enteral formula 3 × 15 mL/h (3 h, then stop for 1 h) If residue < 100 mL, enteral formula 6 × 50 mL
POD-7, Jan 21, 2023	Parenteral formula 1000 mL/24 h Enteral formula 3 × 15 mL/h (3 h, then stop for 1 h) If residue < 100 mL, Peptamen 6 × 50 mL
POD-8, Jan 22, 2023	Parenteral formula 1000/24 h Enteral formula 3 × 15 mL/h (3 h, then stop for 1 h) If residue < 100 mL, Peptamen 6 × 50 mL
POD-9, Jan 23, 2023	Parenteral formula 500 mL/24 h Enteral formula 6 × 50 mL Sugar-free rice flour porridge without coconut milk 2 × 1/2 portion Extra fruit juice 1 × 100 kcal Nasogastric tube was removed
POD-10, Jan 24, 2023	Parenteral formula was stopped Enteral formula 6 × 50 mL Sugar-free rice flour porridge without coconut milk 3 × 1 portion + steamed egg white Extra fruit juice 1 × 100 kcal
POD-11, Jan 25, 2023	Porridge with minced meat and vegetables + steam white egg 1 portion + coconut oil 1 tsp (960 kcal) Enteral formula 3 × 100 kcal Fruit juice 2 × 50 kcal

1 portion = 300 kcal

to the Revised Atlanta Criteria. Early enteral feeding is defined as providing enteral nutrition within 3 days after surgery for AP.

The main outcomes were improvement in clinical condition and inflammatory parameters (lipase enzyme), and reduced length of hospital stay. Clinical conditions were determined by the proportion of infection, organ failure, mortality incidence, and other clinical parameters such as the visual analog scale (VAS), systemic inflammatory response syndrome (SIRS), and intestinal motility. Only randomized controlled trial (RCT) studies that met the inclusion criteria were used in this report. Exclusion criteria were studies that did not use English and had no full text available. The selected articles were then assessed based on the Cochrane Collaboration Risk of Bias tool.[14]

Analysis and quality assessment were conducted using Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines, and the interpretation was carried out using a forest plot model. Effect size quantification was carried out based on standardized mean difference (SMD) for continuous variables using a continuous random effect model (Der Simonian–Laird).[15] For categorical variables, effect size was quantified based on log relative risk (RR) using a binary random effect model (Der Simonian–Laird).[15]

RESULTS

Using keywords, 101 articles were found. After duplicates were removed, 38 articles were obtained. Based on the title and abstract, 21 articles were excluded. Of the remaining 17 articles, 3 full texts were not acquired, leaving 14 articles to be reviewed. Applying the exclusion criteria, 7 more articles were excluded. Finally, only 7 articles were included in this report: Petrov et al.,[6] Casas et al.,[17] Doley et al.,[18] Hui et al.,[19] Noor et al.,[20] Horibe et al.,[21] and Farooq et al.[22]

A total of 247 subjects with AP/SAP were in the intervention group, and 244 subjects were in the control group. There was no significant baseline difference between the two groups. The control group used total parenteral nutrition or delayed enteral

nutrition as a comparison of management. All studies conduct an intention-to-treat (ITT) analysis, except Petrov et al.[6] Detailed studies are shown in **Table 2**.

Table 2. Study Description

No.	Author (Year)	Country	Subject	Analysis	Intervention	Number of subjects	control	Number of subjects	Main outcome (Intervention against Control)
1	Petrov et al. (2006)[16]	Russia	Severe acute pancreatitis	PP	Total enteral nutrition	35	Total parenteral nutrition	34	Clinical improvement >, CRP =
2	Casas et al. (2007)[17]	Spain	Severe acute pancreatitis	ITT	Total enteral nutrition	11	Total parenteral nutrition	11	Clinical improvement >, LOS =
3	Doley et al. (2009)[18]	India	Severe acute pancreatitis	ITT	Total enteral nutrition	25	Total parenteral nutrition	25	Clinical improvement =, CRP =, LOS =
4	Hui et al. (2019)[19]	China	Severe acute pancreatitis	ITT	Total enteral nutrition	16	Total parenteral nutrition	14	Clinical improvement >, CRP >
5	Noor et al. (2016)[20]	Pakistan	Severe acute pancreatitis	ITT	Early enteral nutrition	30	Delayed enteral nutrition	30	LOS >
6	Horibe et al. (2020)[21]	Japan	Acute pancreatitis	ITT	Early enteral nutrition	13	Delayed enteral nutrition	13	LOS >
7	Farooq et al. (2017)[22]	India	Acute pancreatitis	ITT	Early enteral nutrition	117	Total parenteral nutrition	117	Clinical improvement >, LOS >

*PP, per protocol; ITT, intention to treat; CRP, C-reactive protein; LOS, length of stay; >, significantly better; =, no significant difference; <, significantly worse.

Bias of included trials was assessed according to the Cochrane Collaboration Risk of Bias tool. Blinding of personnel and participants had the highest risk of bias. Studies from Petros et al., Hui et al., and Farooq et al. were graded as being of the highest quality. Details of the bias assessment are shown in **Table 3**.

The five studies shown in **Figure 1** include clinical condition outcomes. Two studies (Doley et al., Hui et al.) did not show a significantly better clinical condition after the intervention period between the two groups. RR (95% confidence interval) was 0.427 (0.249 to 0.606), $P < 0.001$. Clinical improvement was significantly higher in the intervention group. Heterogeneity was $I^2 = 68.93\%$ and $P = 0.012$, showing significant heterogeneity (**Figure 1**).

Table 3. Quality Assessment

	Petrov et al. (2006)[16]	Casas et al. (2007)[17]	Doley et al. (2009)[18]	Hui et al. (2019)[19]	Noor et al. (2016)[20]	Horibe et al. (2020)[21]	Farooq et al. (2017)[22]
Random sequence generation	+	+	+	+	+	+	+
Allocation concealment	+	+	+	+	+	+	–
Blinding of participants and personnel	–	–	–	–	–	–	+
Blinding of outcome Assessment	+	+	+	+	+	+	+
Incomplete outcome data	+	+	+	+	?	?	+
Selective reporting	+	+	+	+	?	?	+
Other bias	+	?	?	+	+	?	+

*Green represents low risk, red represents high risk, and yellow represents unclear risk (no evidence found).

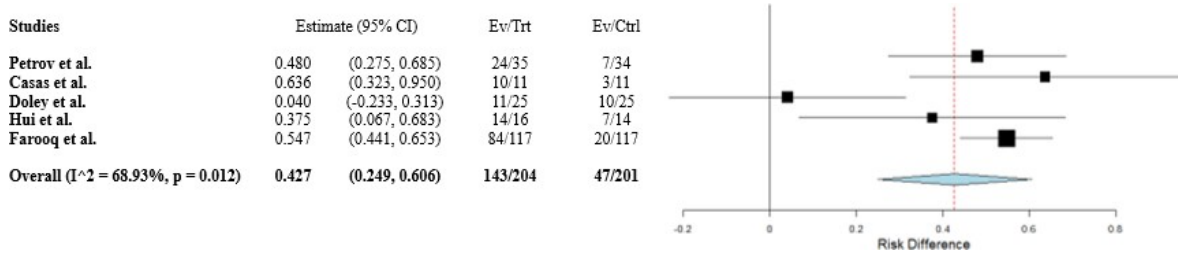

Figure 1. Results of clinical improvement using a forest plot.

The four studies in **Figure 2** include laboratory inflammatory outcomes. One study (Casas et al.) did not show a significant decrease in CRP (C-reactive protein) between the two groups after intervention. SMD (95% CI) was –9.569 (–18.973 to –0.615), $P = 0.046$. CRP level was significantly lower in the intervention group. Heterogeneity $I^2 = 97.55\%$ and $P < 0.001$, meaning there was significant heterogeneity (**Figure 2**).

The six studies in **Figure 3** include laboratory inflammatory outcomes. One study (Doley et al.) did not show a significant decrease in LOS in the intervention group. SMD (95% CI) was –3.139 (–5.831 to –0.448), $P = 0.022$. The LOS decreased significantly in the intervention group. Heterogeneity was $I^2 = 98.85\%$, and $P < 0.001$ was interpreted as significant heterogeneity (**Figure 3**).

DISCUSSION

Nutrition has a great impact on the management and recovery of AP. When the issue became controversial, new theories were proposed.[8,9] The majority of studies state that enteral nutrition outperforms the parenteral option. The meta-analysis of RCT studies included in this case report showed the superiority of early enteral nutrition therapy in all outcomes. The treatment of choice is currently enteral feeding within 3 days onset of AP.[4,10-12]

To analyze the clinical outcomes, parameters such as fewer infection incidences, organ failure, mortality rate, and other parameters were used. Petrov et al.[16] found a lower infection incidence in patients who received early enteral feeding ($P < 0.05$), as in our case, where there were no infection incidences. Wilson et al.[23] stated that SIRS may become a mortality predictor in AP. Although two criteria of SIRS[24] were fulfilled on the admission day, after intervention, the heart rate was successfully controlled below 90 beats per minute, and the respiratory rate was found to be within the normal range.

In addition, patients in this case may experience flatus on post-operative day one and defecate on post-operative day two. Sun et al.[25] further reported that early enteral nutrition had proven to enhance immunomodulating agents and maintain intestinal integrity, whereby a

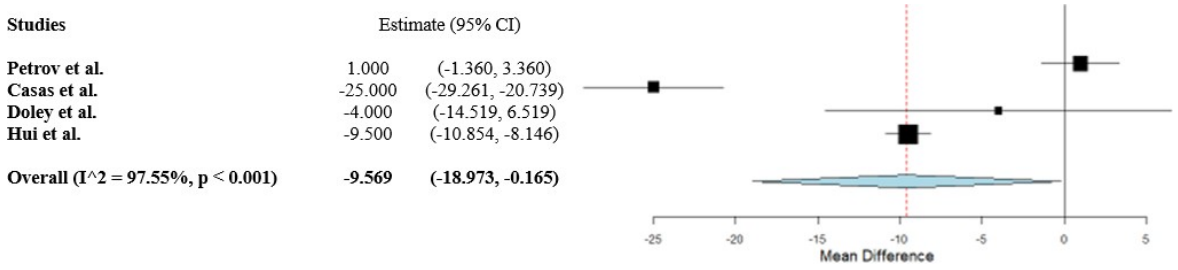

Figure 2. Results of inflammatory parameters (CRP) of the forest plot.

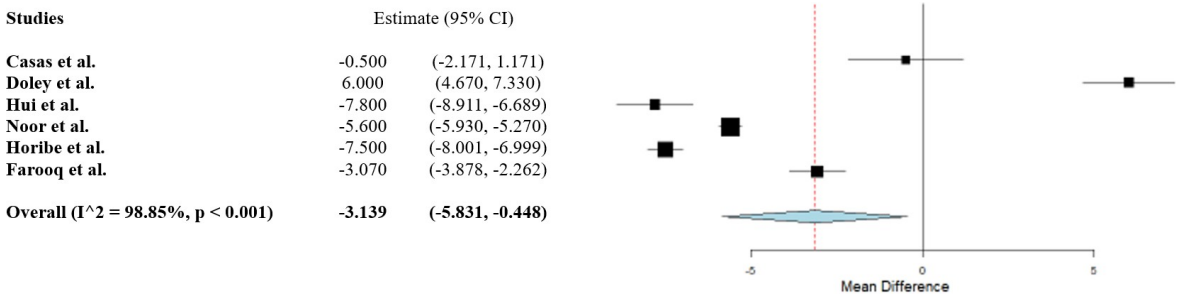

Figure 3. Results of length of stay using a forest plot.

lower incidence might be achieved. Of the five articles that evaluated clinical outcomes, Petrov et al.,[16] Hui et al.,[19] and Farooq et al.[22] revealed lower mortality rates with enteral feeding compared with parenteral feeding. Supported by Oláh et al.[26], enteral nutrition has statistically been proven to have more benefits than parenteral nutrition, and enteral nutrition can be administered safely even when complications occur.

Petrov et al.[16] and Hui et al.[19] stated that parenteral feeding caused more multiple organ failure incidences with *P* values of 0.02 and < 0.01, respectively. Our case supports the literature, with only a single case of organ failure (acute kidney failure) on the fourth post-operative day. This finding is supported by Schepers et al.,[27] who stated that 51% of organ failures in AP occurred in the first week of disease. Another study found that single or multiple organ failure will greatly affect the prognosis.[28]

Based on CRP as an inflammatory response, four articles include the difference between parenteral and enteral feeding. Hui et al.[19] and Noor et al.[20] both documented significant decreases in CRP in patients receiving enteral feeding. On the other hand, Petrov et al.[16] and Casas et al.[17] stated that there was no significant difference between enteral and parenteral feeding. In this case, pancreatic inflammation was assessed using

levels of the enzyme lipase as a surrogate marker of inflammatory activity. The lipase level in this case was 2400 U/L at baseline, which decreased to 68 U/L six days post-operatively. Normally, a threefold lipase elevation is maintained 7–14 days post-onset.[29] Our case showed shorter time to achieve lower lipase enzyme levels, reflecting a rapid fall in the pancreatic inflammation process.

Six out of the seven articles we found, namely Casas et al.,[17] Doley et al.,[18] Hui et al.,[19] Noor et al.,[20] Horibe et al.,[21] and Farooq et al.,[22] include LOS as one of the parameters useful in analyzing AP outcome. The mean LOS reported was 30.2 days, 42 days, 22.3 days, 10.8 days, 4 days, and 14.69 days, respectively. Furthermore, Hui et al.,[19], Noor et al.,[20] Horibe et al.,[21] and Farooq et al.[22] found significant differences, with enteral feeding patients showing shorter LOS than parenterally-fed patients. Our patients were discharged after 10 days as inpatients. A shorter LOS may result in lower medical costs,[20,30] and a longer LOS may increase the risk of hospital-acquired infection.[31]

The advantage of this evidence-based case report is that it involves only randomized controlled trials, so that the data obtained are rich and varied, with minimal confounding. Several limitations of our meta-analysis are noteworthy. First, there was statistical heterogeneity between the studies included. Second, the clinical improvement outcome may vary between studies. A large sample size with longer treatment follow-up would be beneficial. Third, we did not consider the effect of pharmacological treatment on the outcome. Furthermore, we did not account for quality and cost shortcomings, and further information, such as CRP and amylase enzyme levels, was not analyzed. Lipase enzyme levels as a surrogate for inflammation were examined instead.

CONCLUSION

We were able to respond to the question in this case report based on our case study and literature analysis.

1. Early enteral nutrition could lead to more significant clinical improvement, including with regard to the incidence, organ failure, mortality, and other post-surgery parameters of AP.
2. Early enteral nutrition could significantly lower lipase enzyme levels after surgery.
3. Early enteral nutrition could significantly shorten the length of hospital stay.

This report shows that early enteral nutrition can lead to better clinical improvement, lower inflammatory response, and shorter length of hospital stay than when treating by total parenteral nutrition. We therefore recommend using early enteral nutrition over total parenteral nutrition in post-surgery AP.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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