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Original Article

Total Parenteral Nutrition or Early Enteral Nutrition: Outcome and Economic Impact after Pancreatoduodenectomy

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Abstract

Background: Recent concept of enteral nutrition provision with good outcome gradually changes the current practice of postoperative management. But commercially available enteral formula is often costly, not affordable by native people, and often not tolerable. This study was carried out to compare the effect of total parenteral nutrition (TPN) versus early enteral nutrition (EEN) on postoperative outcomes and nutrition related cost after pancreatoduodenectomy.

Methods: Thirty patients who underwent pancreatoduodenectomy within one year in the Department of Hepatobiliary, Pancreatic & Liver Transplant Surgery, BSMMU included and categorized into two groups; EEN(n=15) group: enteral feeding made with indigenous food and TPN (n=15) group: only parenteral nutrition continued up to six/seven post-operative days (POD). In all the patients, biochemical parameter was measured on POD 1, 3, 7 & 14 for assessing primary end point (Nutritional condition, morbidity and mortality) and secondary end point (length of postoperative hospital stays, albumin requirement and nutrition related cost).

Results: EEN was shown to have a significant effect on reducing the overall complications rate (3/15 vs 10/15, $p<0.01^s$) and infectious complications rate (2/15 vs 7/15, $p<0.04^s$) compared with TPN . Additionally, EEN saved average 23 thousand taka (270 dollars) in costs compared to TPN for postoperative nutrition purpose. There were significant differences between TPN and EEN groups regarding mean duration of nutrition in EEN group 5.27±0.59 and in TPN group 9.73±4.28 days, time to start solid food (8.20±1.01 vs 12.87±4.50 days,$p<0.001^s$),albumin requirement (1.47±0.99 vs 3.40±1.68 unit, $p<o.oo1^s$), Inflammatory parameter and electrolyte imbalance (hypokalemic episode) significantly reduced at postoperative day 3 and day 7 in EEN group compare to TPN with less antibiotic and electrolyte support. Length of hospital stay is significantly longer in TPN in contrast to EEN (15.27±6.41 vs 10.47±2.10 days, p=0.001).There were no significant differences between TPN and EEN groups regarding mortality rate.

Conclusion: Blended meals prepared from locally available food may be considered as an alternate to commercially available enteral feeding formula after pancreatoduodenectomy. It reduces morbidity, electrolyte imbalance, albumin requirement and nutritional cost. Thus, ensure smooth postoperative recovery than TPN.

Key words: Total parenteral nutrition, Early enteral nutrition, Nasojejunal feeding.

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Introduction

After GIT surgery, the benefits of early enteral nutritional support are widely accepted[1]. study showed that early postoperative enteral nutrition (EN) enhanced immunocompetence, reduced clinical infection rates, and maintained gut structure and function, and it can potentially attenuate catabolic stress responses in patients after surgery[2] in various clinical settings because it is less expensive, safer, and maintains the nutritional, metabolic, immunological and barrier function of the intestines[3].Moreover,patients fed via EN after

abdominal surgery for trauma developed fewer septic complications than patients who received TPN [4].

Major stress like surgery, result in metabolic and physiologic changes and body responds to such stress by increasing its basal metabolic rate (BMR), using up its nitrogen stores and creating a negative nitrogen balance[5] increase in gluconeogenesis and acute phase proteins [6]. The body scavenges for the required nutrients but if it continued prolong periods of time could lead to adverse consequences. Perioperative nutritional supplementation, therefore, should stop the catabolic effects of such a high energy state. However, surgical stress result in increase intestinal permeability fourfold greater in some patients usually normalizing around postoperative day five[7-8]. and decrease in villous height, leading to malabsorption and an impaired ability of the gut to act as a barrier against endogenous bacteria and toxins [9].

Malnutrition following PD results in high post operative morbidity, mortality and hospital cost[10] , appropriate nutritional therapy is of great significance for post-operative rehabilitation following PD. Current clinical variation of nutrition provision following PD includes early enteral feeding through nasojejunal tube or jejunostomy tube or total parenteral nutrition with delayed enteral feeding[11]. But optimum route of nutritional provision continues to be debated[12].The European Society for Parenteral and Enteral Nutrition (ESPEN) recommended early enteral nutrition (EEN) should be routinely used in patients having gastrointestinal surgery for cancer including PD[13].The American Society for Parenteral and Enteral Nutrition (ASPEN) defines enteral nutrition (EN) as ‘‘nutrition provided through the gastrointestinal tract via a tube, catheter, or stoma that delivers nutrients distal to the oral cavity.’’ ASPEN defines parenteral nutrition (PN) as ‘‘the intravenous administration of nutrition, either via central or peripheral line[11].

EEN is economic than TPN as influence of EN on adverse events and savings from reduced hospital length of stay[14].Compared to PN, EN savings from reduced adverse event risks average nearly $1500 per patient; savings from reduced hospital length of stay amount to nearly $2500 per patient. Shifting 10% of parenterally treated adult patients in the U.S. to EN would save $35 million annually due to reduced adverse events and another $57 million due to shorter hospital stays[15].

This article reports the results of a case control study designed to compare the efficacy of postoperative EN and TPN in PD patients with objective to determine whether EN reduces major postoperative complications, mortality, or cost in such patients.

Materials and Methods

The protocol of the study was approved by the ethical committees and IRB board and informed consent was obtained from each of the patients. This is a case-controlled prospective study. The study includes patients (n=30) that underwent pancreato-duodenectomy surgery in different units of the Department of Surgery of Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2020 to December 2020.

Patients were categorized into two groups, EEN and TPN. In group EEN (n=15), a nasojejunal (NJ) feeding tube was inserted during operation to start enteral feeding on 2nd POD. Blended formulated diet was prepared from indigenous food (rice gruel, dal, egg white, soybean oil, table salt and coconut water, 1kcal/ml). NJ Feeding was started with 25 ml/ 2hourly and a total10 feeds were given with flushing with 25 ml coconut water after each administration. Incremental increase in daily 25ml/2 hourly in the subsequent PODs until reached 150 ml/2 hourly (>1500kcal through enteral route).Additional fluid and calorie requirement were calculated and provided with intravenous fluid to maintain standard fluid (25-40 ml/kg/day), electrolytes and energy requirement (25-40 kcal/kg/day). Removal of NJ tube was done on 7th PODs and oral soft diet allowed. The patient who developed abdominal cramps, bloating and loose motion after initiating the formula food managed either temporary stoppage or start TPN. In TPN ,Kabiven administrared through CV line. Outcome recorded postoperatively up to hospital stay. Post-operatively, biochemical parameter measured on PODs 1, 3, 7 and 14.

Data was documented in a data collection sheet and then compiled systematically, computed, analyzed with software (SPSS 26) and compared between the two groups. Data are stated as mean ±SD and percentage. Statistical analysis was done using the unpaired t test and Chi square (χ^2) test. P value 0.05 or less were leveled as significant.

Results

Patient Baseline Data

During the 12-month period, 30 patients identified as potentially eligible for the study and were purposely assigned to the EEN EN (n = 15) and TPN (n = 15). No patients were lost to follow-up. The 2 groups were similar regarding demographic data, nutritional status, and diagnosis (Table I).

Primary Endpoint Analysis

Surgical morbidity significantly lower in EEN than TPN (3/15 vs 10/15, p=0.01). Among them wound infection rate is less in EEN (2/15 vs 7/15, p=0.04) But biliary leakage and pancreatic fistula are almost similar in both groups as its more technical than nutritional. 2 patients need relaparotomy and 2 mortality in TPN (statistically not significant) (Fiqure 1)

Mean duration of enteral nutrition in EEN group 5.27±0.59 and total parenteral nutrition in TPN group 9.73±4.28. In the TPN group, parenteral nutrition was infused in all cases through a central venous catheter. Slightly earlier resumption of oral diet in EEN group than TPN TPN ut significantly earlier starting of solid food without complications in EEN group than TPN group. Postoperative 1st day of flatus passage are almost similar (2.60±0.51 vs 3.27±1.39 th day, p<0.091^{ns}) but first bowel movement are significantly earlier in EEN group than TPN group (5.13±1.13 vs 8.40±1.45 th day, p<0.001^{s}) (Table II)

Patients in the EN group started with 300 kcal/d through enteral route which incrementally increased to 1550 kcal/d on 7th POD, remaining required calorie given through parenteral intravenous fluid.Average 1500 kcal/d was given in the TPN group, no calorie through enteral route.

Table I : *Comparison of patient's demography between two groups*

variable	Route of Nutrition		p value
	EEN(n=15)	TPN (n=15)	
Age (Years)			
Mean ± SD	52.80±11.25	54.20±11.16	0.735^{ns}
Sex			
Male	9 (60.0)	10 (66.7)	0.705^{ns}
Female	6 (40.0)	5 (33.3)	
BMI (kg/m^2)			
Mean ± SD	21.71±2.08	21.47±1.96	0.754^{ns}
Comorbidity			
DM	2 (13.3)	2 (13.3)	1.000^{ns}
HTN	3 (20.0)	4 (26.7)	0.666^{ns}
Other co-morbidity	5 (33.3)	6 (40.0)	0.705^{ns}
Diagnosis			
Periampullary carcinoma	9 (60.0)	10 (66.7)	0.705^{ns}
Carcinoma head of pancreas	4 (26.7)	3 (20.0)	0.666^{ns}
Distal CBD growth	2 (13.3)	2 (13.3)	1.000^{ns}
Peoperative biliary decompression			
Yes	7 (46.7)	6 (40.0)	0.713^{ns}
No	8 (53.3)	9 (60.0)	
Yes	7 (46.7)	6 (40.0)	0.713^{ns}

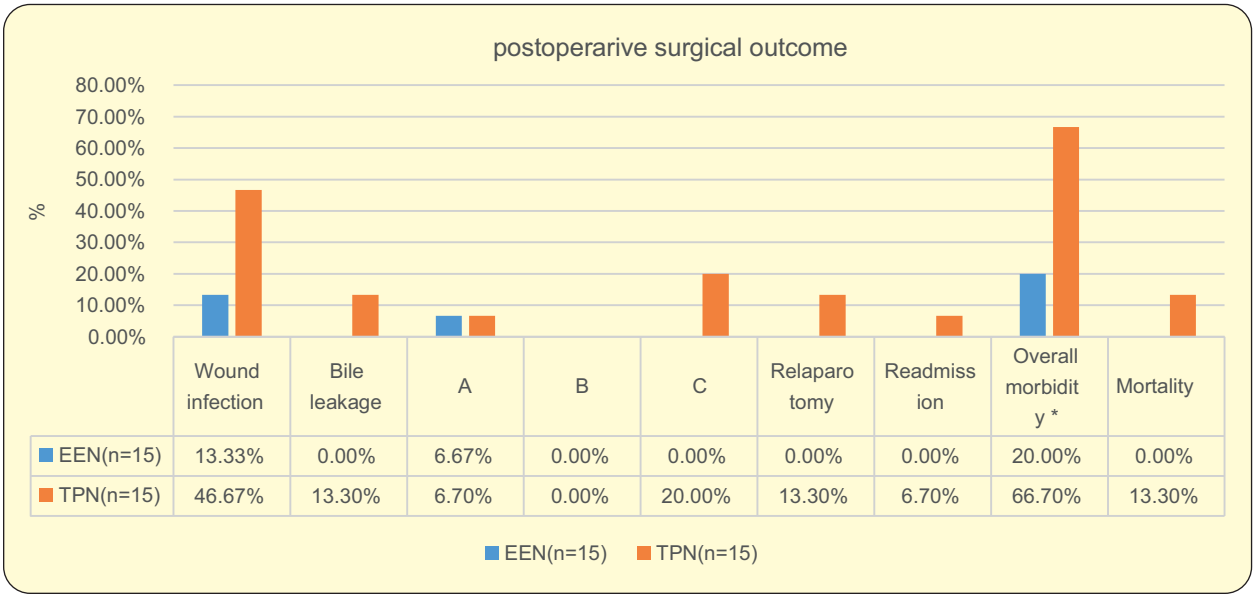

Figure 1: *Comparison of post-operative outcome between two groups*

Secondary Endpoint Analysis

Albumin transfusion rate is significantly low in EEN than TPN (1.47±0.99 vs 3.40±1.68 unit, p<o.oo1[s]) 100ml of 20 % albumin (1 unit)) (Table 3) with sustained improvement in EEN from POD 2 (Fiqure 2). Inflammatory parameter and electrolyte imbalance (hypokalemic episode) significantly reduced at postoperative day 3 and day 7 in EEN group compare to TPN (Fiqure 3 &4) with less antibiotic and electrolyte support. As more complication in TPN , length of hospital stay is significantly longer in TPN in contrast to EEN (15.27±6.41 vs 10.47±2.10 days, p=0.001) (Table II). But nutrition related cost (preparation of formula feed from indigenous food plus intravenous fluid in EEN and kaviben in TPN) is significantly less in amount in contrast to TPN . (5982.67±684.49 vs 29055.67±13035.95 BDT, p=<0.001[s]) (Table III)

Table-II : *Difference in postoperative Resumption of normal oral intake between two groups*

Parameter	Group		P value
	EEN(n=15) Mean±SD days	TPN (n=15) Mean±SD	
Time to resumption of normal oral diet	7.07±0.70	8.27±2.12	0.047[s]
Duration of enteral nutrition	5.27±0.59	NA	
Duration of total parenteral nutrition	NA	9.73±4.28	
Time to start solid food	8.20±1.01	12.87±4.50	0.001[s]
Length of hospital stay	10.47±2.10	15.27±6.41	0.010[s]

Table III : *Comparison of albumin requirement and nutrition related cost (In BDT) between two groups (n=30)*

	Group		p value
	EEN(n=15)Mean±SD	TPN (n=15)Mean±SD	
Nutrition cost	5982.67±684.49 (70.55±8.07 USD)	29055.67±13035.95 (342.64±153.73 USD)	<0.001[s]
Albumin requirement*(unit)	1.47±0.99	3.40±1.68	0.001[s]

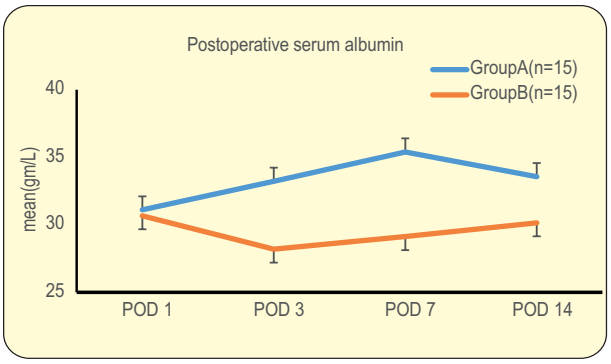

Figure 2: *Changes in serum in albumin between two groups*

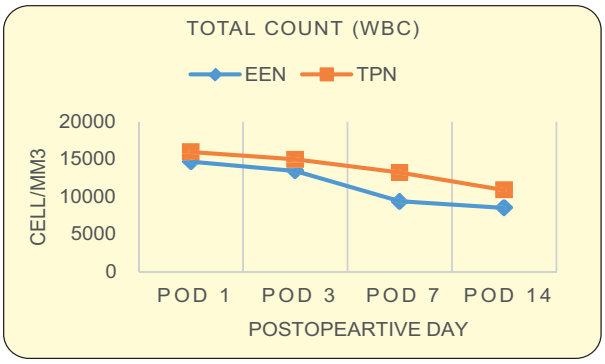

Figure 3: *Difference in inflammatory parameters on postoperative days 1, 3, 7 and 14 between two groups.*

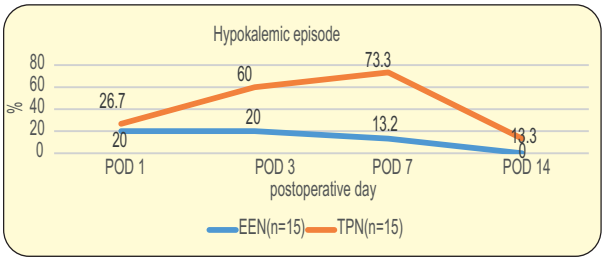

Figure 4 : *hypokalamic episodes in both groups.*

Discussion

Conventionally, post operative oral feeding for patients after gastrointestinal surgery started when flatus or defecation passed which indicated the return of normal bowel function. However, in recent years, early enteral nutrition in gastrointestinal surgery should be recommended whenever possible regardless of bowel sound appearance. EEN seems to be more physiological, better preventive in morphologic and functional alteration of the gut system, and less expensive than TPN[16-17]. As far as the efficacy of postoperative nutritional support is concerned, no study to date clearly shows that this procedure reduces postoperative complications. As far as the route of feeding is concerned, many arguments are still open for debate[18].

EEN has less incidence of wound infection than in the TPN group (NJT/TPN : 16%and 30%, P<00.02^{s})[11]. Our study also supports that data (13.3% vs 46.67%, p=0.04). Hwang et al., 2014 demonstrated rate of mortality, morbidity and LOS (25.9±8.5 days vs. 32.3±16.3 days; p=0.01), and re-operation (3.7% vs. 20%, p=0.01) were significantly lower in the early enteral group in comparison to TPN group[19]. In our study, morbidity is less (20% Vs 66.7%), no mortality (0 Vs 2) and average 5 days less hospital stay in EEN in compare to TPN (10.47 Vs 15.27, p=0.01). Incidence of bile leakage and pancreatic fistula are almost similar in both EENs its more technical than nutritionaly related. One case of readmission and 2 cases of relaparotomy needed in TPN in compare to none in EEN.

Mean duration of enteral nutrition in EEN group is shorter than in TPN group Slightly earlier resumption of oral diet in EEN group than TPN TPN ut significantly earlier start of solid food without complications in EEN group than TPN group. Postoperative first day of flatus passage is almost similar but first bowel movement are significantly earlier in EEN group than TPN group .This data are comparable to other study[20].

Albumin transfusion requirement was significantly less in EEN than TPN to maintain optimum serum albumin level at postoperative period (1.47 vs 3.40 unit, p<0.001^{s}). Theophile et al., 2017[21] reported mean nutritional cost in EEN group using commercially feeding formula was 773 euros ± 177. In our study, we found cost is significantly less in EEN in comparison to TPN (70.55±8.07 vs 342.64±153.73 USD, p<0.001^{s}). Nutritional cost included both oral and intravenous nutrition related cost except albumin.

Our observation was that nutritional, immunological parameter and inflammatory marker remain almost similar in 1st POD. Thereafter significantly improved on POD3 onwards until discharge of the patients who had initiated early enteral feeding (EEN) than who had delayed feeding (TPN). Hypokalaemia occured more frequently in TPN group than EEN group. Post-operative intrahepatic cholestasis (bilirubin and ALP) was reduced faster in the early enteral nutrition group than delayed starting oral feeding EENfter 1st POD

until discharge. All these findings can be explained by many authors[22]. Zhu et al., 2009[23] reported in absence of food in the gut has negative consequences on metabolic, endocrine, intestinal and liver function. Whereas, early enteral feeding enhances hepatic circulation, improving liver function and bile flow by several enteric hormones such as cholecystokinin, peptide and gastrin which are stimulatory to gut functions.

The present study has some limitations. The first, outcome observed up to hospital discharge only. Secondly CD4:CD8 could not be measured to see more accurate immunological effect.

Conclusion:

Postoperative EEN is safe and well tolerated. blended diet prepared from locally available food may be considered as an alternate to commercially available enteral feeding formula after PD. It significantly reduces morbidity, electrolyte imbalance, albumin requirement and nutritional cost. Thus ensure smooth patient recovery than TPN .

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the corresponding authors on reasonable request (drquiyum2051@gmail.com)

Ethics Statement

The studies involving human participants were reviewed and approved by IRB board, BSMMU, Dhaka, Bangladesh. The patients/participants provided their written informed consent to participate in this study.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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