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A Comparison of Postoperative Early Enteral Nutrition with Delayed Enteral Nutrition in Patients with upper gastrointestinal malignancies: A study at tertiary cancer center in south India.

Oncology

KEYWORDS: Upper GI malignancy, early enteral feeding, Feeding jejunostomy.

Ravi Arjunan	Associate professor, Department of Surgical oncology, Kidwai Memorial Institute of oncology, Bangalore, Karnataka, India- 560029.
Syed Althaf	Associate professor ,Department of Surgical oncology, Kidwai Memorial Institute of oncology, Bangalore, Karnataka, India- 560029.
Vikas sharma	Mch Resident, Department of Surgical oncology, Kidwai Memorial Institute of oncology, Bangalore, Karnataka, India- 560029.
K.V.Veerendra Kumar	Professor, Department of Surgical oncology, Kidwai Memorial Institute of oncology, Bangalore, Karnataka, India- 560029.
Dr Yeshwant Rajagopal	Mch Resident, Department of Surgical oncology, Kidwai Memorial Institute of oncology, Bangalore, Karnataka, India- 560029.
Dr Harish Kumar	Mch Resident, Department of Surgical oncology, Kidwai Memorial Institute of oncology, Bangalore, Karnataka, India- 560029.
Dr Vjay CR	Department of Epidemiology and Biostatistics, Kidwai Memorial Institute of oncology, Bangalore, Karnataka, India- 560029.

ABSTRACT

Introduction: Surgical resection is one of the treatment of choice of upper gastrointestinal (GI) malignancies. Malnutrition is one the most common complication of upper GI malignancies and constitutes major cause of morbidity especially in first week after operation. We present role of early enteral feeding in minimizing postoperative morbidity and improving outcome. The aim of our study is to investigate he role of early enteral feeding (EEF- in form of feeding jejunostomy) on postoperative outcomes after resection and reconstruction of upper GI tract malignancies.

Methods: Between January 2015 to December 2016, 48 consecutive patients with upper GI tract malignancies who had undergone complete resection and reconstruction were enrolled in this study. The patients were divided equally in two groups of control and EEF. Control group was treated with traditional management of nil by mouth and intravenous fluids for the first five to seven postoperative days and then with liquids and enteral regular diet when tolerated. In EEF group the patients were fed by tube jejunostomy from 1st postoperative day and assessed for nutritional status before surgery and 5 days after surgery. Both groups were monitored on the basis of clinical and para-clinical parameters and postoperative complications.

Results: Forty eight patients were equally divided to two equal groups. Both groups were operated by same surgical procedures. Basic nutritional status and demographic characters were found to be similar in both the groups.

On 5th postoperative day serum albumin was 4.29 g/dl in EEF and 3.57g/dl in control group (p= 0.000), total protein was 6.92in EEF and 6.58in control group(p=0.043). Moreover, hospital stay was shorter in EEF group (6 vs 11 days, p=0.000).There were five (20.8%) anastomotic leakages in control group and two (8.3%) in EEF group. Also there was six (25%) wound infection in control group and three (12.5%) in EEF group.

Conclusion: Postoperative morbidity and complications can be reduced by providing EEF in patients with upper GI malignancies. Tube jejunostomy may be considered as an effective method for postoperative EEF. It restores nutritional status and reduces postoperative complications like anastomotic leak and wound infection.

Introduction

Malnutrition is most common postoperative concern in patients with upper GI malignancies. As malnutrition itself is cause of various postoperative complications like anastomotic leak, poor wound healing, delayed recovery etc. Traditionally bowel rest by avoiding enteral feeding, nil by mouth and the use of total parenteral nutrition (TPN) was considered as ideal post-operative care to prevent anastomotic leak and other postoperative complications.[1]

Esophageal cancer is associated with highest incidence of malnutrition (78.9%) among other digestive and extra-digestive cancers.[2]

Patients usually present with malnutrition at the time of diagnosis itself which further increases as a side effect of multimodality treatment. Main causes of malnutrition in these patients are dysphagia, anorexia, food intolerance etc. About 70 % patients suffer from a weight loss of >10 % over a period of four months. Weight loss is associated with poor prognosis and outcomes, hence adequate intervention is necessary to provide and restore nutritional requirements.[3]

Traditionally total parenteral nutrition (TPN) is considered as an effective measure for postoperative nutritional support to reduce the consequences of malnutrition. Because of associated metabolic and systemic complications of TPN, administration of TPN requires great care and efficient monitoring. Certain studies have shown an increase in post-operative infectious complications with the use of TPN.[4]

Newer concepts include enteral feeding for the nutritional support in postoperative patients with added advantages of prevention of gut mucosal atrophy, better substrate utilization, preservation gut integrity and gut flora, and maintenance of immune competence. Prevention of endotoxic shock, improvement in protein kinetics are other advantages of enteral nutrition.[5,6]

Several studies have shown the effect of early enteral nutrition and its importance. They found EEF as better option for maintenance of postoperative nutrition.[7]

Aim

The aim of our study is to compare early enteral feeding protocol with traditional nil per oral parenteral nutrition protocol in postoperative

cases of upper GI malignancy and to assess its impact on postoperative complications and morbidities.

Methodology

This study is a prospective case control study conducted in department of surgical oncology at Kidwai memorial institute of oncology between January2015 to December 2016. All patients filled informed written consent to participate in the study.

Forty eight patients of upper gastrointestinal malignancy treated by surgery were enrolled in the study. The preoperative oncological assessment was done according to hospital protocols using chest X ray, CT scan of chest and abdomen, upper GI endoscopy and biopsy for all patient.

Patients receiving neoadjuvant chemotherapy , advanced disease patients requiring multi visceral resections, patients with comorbidities such as diabetics, COPD, cardiac diseases, hepatic and renal failure were excluded from the study.Patients were divided into two equal groups of 24 patients each. Group A consisted of patients receiving early enteral nutrition through either feeding jejunostomy or naso-enteral tube. Feeding was started within 24 hours of surgery in all patients (on morning of post-operative day one in all patients). Group B consisted of control group managed by nil per orally and intravenous crystalloids for 5-7 post-operative days after which feeding was started orally when tolerated. For patients having anastomotic leak, oral feeds were delayed and managed by total parenteral nutrition.

Both groups were comparable in terms of pre-operative patient characteristics and tumor characteristics. Group A consisted of 18 patients of gastric cancers and 6 patients of cancer esophagus. Group B consisted of 16 gastric cancer and 8 cancer esophagus patients. Patients were assessed for nutritional status before surgery and 5 days after surgery. Both groups were monitored on the basis of clinical and para-clinical parameters and postoperative complications.

Feeding protocol-

The function of the gut and the nutritional needs of the patients determined the composition of the tube-feeding formulation, the method and rate of delivery. The calorie and protein requirements of patients were estimated using time tested formulae. (Figure 1)

Daily energy requirement is estimated as A+B+C		
A. Basal metabolic rate (BMR) by Schofield's equation		
AGE	MEN(kcal/day)	WOMEN(kcal/day)
15-18	17.6W+656	13.3 W+690
18-30	15.0 W+690	14.8 W+485
30-60	11.4 W+870	8.1 W+842
>60	11.7 W+586	9.0 W+656
B. Stress factor Severe sepsis/ extensive surgery/ fracture/ trauma= 10% - 30 %		
C: Energy expenditure for physical activity +20% immobile +30% bed-bound but mobile +40% mobile in ward		
Daily estimated nitrogen requirement for adults		
Status	**Nitrogen (gm/Kg/day)**	
Normal	0.17 (0.14-0.20)	
Hypermetabolic state		
5%-25%	0.2(0.17-0.25)	
25%-50%	0.25(0.20-0.30)	
>50%	0.3(0.25-0.35)	
Depleted	0.3(0.20-0.40)	

Figure 1. formula for tube feeding

Fluid and electrolyte requirements were assessed depending upon the clinical condition of the patient. The fluid requirement was calculated as 30-35 ml/kg+500 ml per degree of pyrexia or 1ml/kcal+ 100 ml/g of nitrogen ingested. Urine output, daily weight record and serum electrolytes provided useful information for assessing changes in the fluid requirement to maintain the correct balance.

The needed calorie was estimated and then formula prepared as1 kcal/ml in boiled Water. The needed calorie consisted of 60% to 70% from carbohydrates and 30%to 40% from fat. The gavage feeding was started the 1st day after operation in EEF group. In the first 24 hours, only 5%dextrose water was fed through gavage and the formula diet started the next day. At the first day of formula feeding about 50% of calorie was provided and reached to maximum needed calorie within 3 days. The total volume of gavage was divided in small doses and fed hourly. The gavage feeding was ceased from 10pm till 6am.In control group only routine IV fluid therapy was given and at 5^{th} to 7^{th} day of operation limited amount of liquid diet started followed by semi solid and then there after solid diet.

Statistical analysis

Statistical analysis was performed using the SPSS version 22.0. Normality of distribution of quantitative data was tested by Kolmogorov-Smirnov test. Between group comparisons for the mean of variables with normal distribution was performed by independent T-test, while for data without normal distribution Mann-Whitney U-test was used. Qualitative data was analyzed with Chi-square and $p<0.05$ considered as statistically significant.

Results

Comparison of preoperative parameters between both groups-

There was no significant difference in demographic and basic nutritional status of both groups. Mean age of group A patients was 57.13 and mean age of group B patients was 55.79. Mean weight of group A patients was 60.50 kg and mean weight of group B patients was 61.21 kg with standard deviation of 5.022 and 4.60 respectively. Mean value of total protein in group A patients was 6.29 gm/dl and mean value of total protein in group B patients was 6.33. Mean value of serum albumin in group A patients was 3.75 gm/dl and mean value of total protein in group B patients was 3.71 . Mean value of preoperative hemoglobin in group A patients was 11.71 gm/dl and mean value of preoperative hemoglobin in group B patients was 11.58 .

Mean value of preoperative blood sugar in group A patients was 104.58 mg/dl and mean value of preoperative blood sugar in group B patients was 103.67 mg/dl . For all these parameters p value was not significant and groups were found to be comparable. (Table 1)

Table 1. Demographic data and basic nutritional parameters in both groups before operation.

Parameters	Group A (EEF group)		Group B(Control group)		p-value
	Mean	Standard deviation	Mean	Standard deviation	
Age(year)	57.13	3.248	55.79	2.637	0.125
Weight(kg)	60.50	5.022	61.21	4.60	0.616
Total protein (gm/dl)	6.29	0.464	6.33	0.482	0.762
Serum albumin (gm/dl)	3.75	0.442	3.71	0.464	0.752
Hemoglobin (gm/dl)	11.71	0.690	11.58	0.717	0.541
Blood sugar (mg/dl)	104.58	4.169	103.67	3.830	0.432

Comparison of preoperative parameters between both groups-

Postoperative comparison was done on 5^{th} postoperative day. Same clinical parameters along with hospital stay (days) were assessed postoperatively. Mean value of postoperative total protein in group A patients was 6.92 gm/dl and mean value of postoperative total protein in group B patients was 6.58 gm /dl and p value was found to be significant (p=0.043). Mean value of postoperative serum

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albumin in group A patients was 4.296 gm/dl and mean value of postoperative serum albumin in group B patients was 3.575 gm /dl and p value was found to be significant (p=0.000).

Mean value of postoperative hemoglobin in group A patients was 10.50 gm/dl and mean value of postoperative hemoglobin in group B patients was 10.90gm /dl and p value was found to be significant (p=0.004). Mean value of postoperative blood sugar in group A patients was 110.04 mg/dl and mean value of postoperative blood sugar in group B patients was 95.04 mg /dl and p value was found to be significant (p=0.000). Mean value of hospital stay in group A patients was 6.00 days and mean value of hospital stay in group B patients was 11 days and p value was found to be significant (p=0.000). (Table 2)

Table 2.Comparison of nutritional parameters in two groups on 5th postoperative day.

Parameters	Group A (EEF group)		Group B(Control group)		p-value
	Mean	Standard deviation	Mean	Standard deviation	
Total protein (gm/dl)	6.92	0.282	6.58	0.717	0.043
Serum albumin (gm/dl)	4.296	0.130	3.575	0.698	0.000
Hemoglobin (gm/dl)	10.50	0.271	10.90	0.568	0.004
Blood sugar(mg/dl)	110.04	3.432	95.04	5.171	0.000
Hospital stay	6.00	1.103	11.00	1.615	0.000

Comparison of postoperative complications between both groups- Abdominal distension, anastomotic leak and wound infection were assessed as parameters for complications. Although p value was not significant but postoperative complications were found to be lesser in group A (EEF group) and higher in control group. Total 4 patients had abdominal distension in group A, whereas 3 patients developed abdominal distension in group B. Anastomotic leak was lesser in group A (2 patients,8.3%) and higher in group A patients (5 patients,20.8%). Similarly wound infection was seen in fewer patients in group A (3 patients,12.5%) then in group B (6 patients,25%). (Table 3).

Table 3. Comparison of Post-operative complications between two groups

Parameters	Group A (EEF group, n=24)	Group B (Control group, n=24)	P value
Abdominal distension	4	3	0.690
Anastomotic leak	2	5	0.229
Wound infection	3	6	0.277

Discussion

Various routes of enteral feeding available are oral, NJ tube feeding, percutaneous transperitoneal jejunostomy, percutaneous transperitoneal gastrostomy etc.

The concept of EEF in postoperative patients with upper GI tract malignancies is gaining popularity. The earliest study to find out advantages of EEF in postoperative period against conventional therapy after major GI surgery was done in 1979 by Sagar et al. They concluded that patients with EEF performed well as compared to conventional group, they lost lesser weight and showed better clinical and metabolic parameters with early recovery and shorter hospitalization. [8]

Nutritional status of cancer patients is related with resectability rate and response rate to chemotherapy. [9,10]

Malnutrition imposes significant impact on wound healing and its consequences. Hence patients with malnutrition or poor nutritional status perioperatively or postoperatively have shown poor wound healing, greater morbidity, prolonged hospital stay and poor overall survival. [11]

Daly et al conducted a study to investigate the role of early enteral feeding in the patient with upper gastrointestinal (GI) cancer. They found a significant reduction in hospital stay and wound healing related complications in patients who were given enteral feeding as compared to standard formula.[7]

The study of Kenler et al. also concluded that early enteral feeding containing essential nutrients were associated with reduced postoperative infections in patients with upper GI malignancy. But there was no significant difference in length of hospital stay. [12]

Nutritional support is provided to be beneficial for malnourished patients who have potential for a positive response to treatment. Provision of adequate and early enteral nutritional support can improve their nutritional status and significantly reduce catabolic response of body to prevent cancer cachexia. [13]

Meta-analysis done by Stephen et al showed no advantages in patients who were kept nil by mouth post operatively following elective gastrointestinal resection. Whereas early enteral feeding was beneficial. [14]

Another meta-analysis done by Shrikhande et al showed that EEF was found to be superior to TPN with added advantages of better metabolic response and better sugar control. [15]

A randomized study done by Beier et al. showed reduced incidences of postoperative complications, especially infectious complications in patients who were given EEF as compared to those with TPN. Whereas another study of Hochwald et al. comparing EEF with traditional method concluded improved protein kinetics, better nitrogen balance, and reduced morbidity and mortality. [16,17]

A meta-analysis by Lewis et al compared early EF with delayed EF and concluded that early EN was beneficial in comparison to delayed EN in relation to postoperative complications, hospital stay and mortality.[18]

Kamei et al done another comparative study between EN and TPN in patients following gastrectomy procedure. Their study showed that EEF was associated with reduced hospital stay, reduced treatment cost and length of hospital stay. They concluded that EEF is an effective, easy and cheaper way of providing nutrition.[19]

A randomized study done by Braga et al showed EEF as an effective alternative to TPN after major GI surgery. They also demonstrated than an enteral formula enriched with arginine and omega-3 fatty acid was effective for malnourished patients and improvement of their nutritional status. Overall it was associated with better outcomes and reduced patient's anxiety and discomfort due to postoperative fasting.[20]

Our study shows EEF as an effective measure to facilitate nutritional requirements and to prevent postoperative complications.

Conclusion-

EEF may be considered as a safe and effective measure for nutritional support in postoperative patients of major upper GI resections and reconstruction and has advantages in reducing the incidence of postoperative wound infection, improving postoperative nutrition status, promoting early recovery of intestinal movement, shortening hospitalization time and hence reducing the cost of hospitalization.

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