Evaluation of the effect of parenteral nutrition on mortality and morbidity in hospitalized patients with non-variceal upper gastrointestinal bleeding

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ABSTRACT

Objective: Nutritional support products should preferably be administered orally whenever possible, with rare exceptions, one of which is gastrointestinal bleeding. In our study, we examined the effects of parenteral nutrition support, which we have recently introduced in the treatment of patients with gastrointestinal bleeding, on the hospitalization duration and mortality-morbidity of these patients.

Methods: We analyzed the patients admitted to the Internal Medicine Service with non-variceal upper gastrointestinal bleeding in our study. Patients were retrospectively analyzed in two groups, based on the years in which total parenteral nutrition (TPN) was initiated (2016-2017) and not initiated (2012-2013). Hospitalization durations and discharge methods were compared between the two groups.

Results: Our study included a total of 369 cases after screening and application of our exclusion criteria. 35.5% of these cases received TPN, while 64.5% did not. When evaluated based on the TPN administration status after stabilizing the Rockall score of the patients, as well as considering the need for erythrocyte suspension (ES), fresh frozen plasma (FFP) replacement, and length of hospital stay, the length of hospital stay was significantly longer in those receiving TPN compared to those who did not.

Conclusion: Although TPN may be the preferred choice in patients with upper gastrointestinal bleeding for whom oral nutrition is not suitable, our study suggests that this preference not only does not lead to a reduction in the number of blood and blood product replacements but also prolongs the hospital stay. While it is believed that complications of nutritional support with TPN may contribute to this result, our retrospective study did not provide data on this. Comprehensive prospective studies are needed on this issue.

Keywords: Parenteral nutrition, non-variceal upper gastrointestinal bleeding, mortality

INTRODUCTION

Upper gastrointestinal (GI) bleeding is defined as bleeding into the lumen from any region between the upper sphincter of the esophagus and the ligament of Treitz.[1] Gastrointestinal bleeding is a clinically significant condition characterized by high mortality, high diagnostic and treatment costs, often requiring hospitalization, and sometimes intensive care, requiring multidisciplinary management.

Approximately 80% of upper GI bleeding stops spontaneously and requires only supportive treatment.[2] The remaining 20% is severe and refractory enough to be stopped with medical and surgical treatment. Thirty percent of patients with upper GI bleeding experience recurrent bleeding within the first 48 hours after hospital admission, and the risk of recurrence increases with the severity of the initial bleeding.

Various scoring systems have been used in studies of

upper GI bleeding to assess risk and prognosis. These scoring systems are generally based on medical history and physical examination. The Rockall score is a system based on five variables designed to predict the risk of rebleeding and mortality. The Rockall Scoring System (RS) evaluates age, shock symptoms, accompanying diseases, endoscopic diagnosis, and the course of the last bleeding.[3] Blatchford and colleagues, in their study, aimed to detect early the risk of re-bleeding and mortality by evaluating factors such as blood urea level on admission, Hb level, heart rate, systolic blood pressure, the presence of syncope or melena, chronic liver disease, and heart failure. This scoring system, which is called the Glasgow Blatchford Score (GBS), is considered a system that can guide clinical practice in patients with upper GI bleeding.[4]

Studies comparing the two methods revealed that the GBS is just as good as, if not more than, the RS at predicting death from gastrointestinal bleeding.[5] The GBS has been found to be more accurate in predicting the need for endoscopic or surgical procedures as well as transfusions.[6]

In this disease, which requires close monitoring, nutritional assessment is necessary in addition to treatment. While nutritional support products should preferably be administered orally, one of the rare exceptions is gastrointestinal bleeding. Nutrition support provided intravenously is called parenteral nutrition.[7,8] However, there are insufficient data on how parenteral nutrition affects the prognosis and mortality of these patients.

In patients whose oral feeding is compromised, parenteral nutrition support is considered an indication.[7,8] In our hospital, total parenteral nutrition (TPN) has been implemented in the treatment of patients with non-variceal upper gastrointestinal bleeding in recent years, whereas intravenous glucose infusion was applied in previous years. This study will retrospectively examine the effects of parenteral nutrition support, which we have started to implement in these patients in recent years, on the hospitalization duration and mortality-morbidity of the patients.

Main Points

- A total of 369 patients with non-variceal upper gastrointestinal bleeding were included in the study, with 131 of the cases recieving total parenteral nutrition and 238 of the cases not recieving it.

- Total parenteral nutrition usage did not lead to a decrease in the number of blood and blood product replacements or in mortality.

- Total parenteral nutrition recieving group ended up having prolonged hospital stay.

MATERIAL AND METHOD

This study was conducted by retrospectively reviewing the files of patients admitted to the Internal Medicine Clinic of Health Sciences University, Umraniye Training and Research Hospital, between 2012-2013 and 2016-2017, due to non-variceal upper gastrointestinal bleeding. The study protocol was approved by the Ethics Committee of Health Sciences University with approval number 48865165-302.14.01.

A total of 369 patients were included in the study, with 131 cases receiving TPN and 238 cases not receiving TPN. Patients with gastrointestinal malignancies, variceal bleeding, or bleeding related to portal hypertension were excluded from the study. Patients who did not undergo gastroscopy were not included in the study. Patients with comorbidities such as chronic kidney disease and congestive heart failure were included in the study.

Patient records were examined for age, gender, comorbidities, hospital admission and discharge laboratory findings, endoscopic findings, examination findings, treatments, discharge methods, and the number of blood and blood product replacements. Patient records were scanned, Rockall and Glasgow-Blatchford scores were calculated based on clinical and endoscopic findings, and Forrest classification was performed. The Rockall scoring system is shown in Table 1, the Blatchford scoring system is shown in Table 2, and the Forrest classification is also presented.

Forrest Classification
1a: Active bleeding in a gushing fashion.

1b: Active bleeding in the form of leakage.

2a: Visible vein that cannot bleed.

2b: Adherent clot.

2c: Flat pigmented lesion.

3: Clean-bottomed ulcer.

Statistical Analysis
The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 21 for Mac (SPSS Inc., Chicago, IL, USA). Descriptive statistics are presented as numbers and percentages for categorical variables, and mean, standard deviation, and median for numerical variables. Homogeneity was assessed using Levene's test, and $p > 0.05$ was considered indicative of homogeneity. The distribution of continuous variables was assessed using the Kolmogorov-Smirnov normality test ($p > 0.05$)

Table 1. Rockall risk scoring system		
Variables		**Score**
A. Age	≥ 80	2
	60-79	1
	< 60	0
B.Shock	Hypotension, systolic blood pressure < 100 mmHg	2
	Tachycardia, systolic blood pressure ≥ 100 mmHg and pulse > 100 beats/min	1
	No shock, systolic blood pressure ≥ 100 mmHg and pulse < 100 beats/min	0
C. Concomitant disease	Renal failure, liver failure, metastatic cancer	3
	Heart failure, ischemic heart disease, other major comorbidity	2
	No major comorbidities	0
D. Endoscopic diagnosis	Upper gastrointestinal cancer	2
	Peptic ulcer, erosive disease, esophagitis	1
	No lesion, Mallory Weiss tear	0
E. Endoscopic finding of new bleeding	Ulcer with clear base, flat pigmented spot	0
	Blood in the upper GI tract, active bleeding, visible vein, clot	2

Table 2. Glasgow-Blatchford risk scoring		
Parameters	**Values**	**Score**
Urea	>6,5 <8,0	2
	>8,0 <10,0	4
	>10,0 <25	4
	>25,0	6
Hemoglobin	>12 <13	1
Male	>10 <12	3
	<10	6
Female	>10 <12	1
	10>	6
Systolic blood pressure	100-109	1
	90-99	2
	<90	3
Other markers		
Pulse(minutes)	>100	1
Presentation with melena		1
Presentation with syncope		2
Liver disease		2
Cardiac failure		2

in paired dependent cases. After fixing the Rockall value, recalculation was performed using the ANCOVA test. For categorical variables, Pearson's chi-square (χ2) or Fisher's chi-square test was used for multiple and pairwise group comparisons when the chi-square condition was met. The statistical significance level was set at a 95% confidence interval, with a p-value of less than 0.05.

RESULTS

In the retrospective analysis, all patients underwent esophagogastroduodenoscopy and the etiology of gastrointestinal bleeding was not identified in 20.6% of patients. Among the patients, 34.7% had no history of medication use, while 65.3% were on medication. Nonsteroidal anti-inflammatory drugs (NSAIDs) were identified as the etiological agents in 23.6% of the patients, acetylsalicylic acid (ASA) in 14.4%, smoking in 13.6%, warfarin in 10.6%, clopidogrel in 2.7%, and new oral anticoagulant drugs (NACs) in 2.2%. Furthermore, 12.2% of the patients had concomitant use of more than one drug that could contribute to the etiology.

In terms of age, the mean age was 56.8 years in the non-TPN and 60.3 years in the TPN- group, with no statistically significant difference between the groups.

Regarding gender distribution, 33.3% of the cases were female, and 66.7% were male, with no statistically significant difference between the groups.

Smoking status showed that 77.5% of the patients were non-smokers, and 22.5% were smokers, with no statistically significant difference between the TPN and non-TPN groups.

or skewness and kurtosis test, and acceptance as normal distribution was within ±1.5.

For pairwise independent group comparisons of numerical variables, the Independent T-Test was used when the assumption of normal distribution was met, and the Mann-Whitney U Test was used when the assumption was not met. The Wilcoxon Test was used for numerical variables

Among the patients, 48.8% had no chronic disease, 13% had one additional chronic disease, and 38.2% had two or more chronic diseases. The non-TPN group had a higher rate of patients with no chronic disease, which was statistically significant (p<0.05). In contrast, the TPN-receiving group had a higher rate of patients with two or more chronic diseases, which was also statistically significant (p<0.05). However, there was no statistically significant difference between TPN receipt status and the presence of one chronic disease, no chronic disease, or two or more chronic diseases (p>0.05).

According to the Rockall risk stratification system, 39.3% of the cases were classified as low risk, 60.2% as medium risk, and 0.5% as high risk. When comparing the groups according to the Rockall risk stratification system, 47.5% of those not receiving TPN were low risk, 52.1% were medium risk, and 0.4% were high risk. Among those receiving TPN, 24.4% were low risk, 74.8% were medium risk, and 0.8% were high risk. In TPN recipients, the ratio of medium risk to low risk was higher compared to non-recipients, and this ratio was statistically significant (p<0.05). There was no statistically significant difference between high-risk and low or medium-risk groups (p>0.05) (Table 3).

Evaluation of Groups According to the Forrest Classification System
According to the Forrest classification system, 0.8% had negative ulcers, 30.4% had erythematous pangastritis, 32.3% had Forrest 3, 10.3% had Forrest 2C, 10% had Forrest 2B, 6.7% had Forrest 2A, 7.8% had Forrest 1B, and 1.7% had Forrest 1A. Mallory-Weiss syndrome was present only in the non-TPN group with 10 cases. When evaluated according to the Forrest classification system,

no statistically significant difference was observed between the groups (p>0.05).

Of the cases, 95.1% were discharged, 0.5% had fatal outcomes, and 4.3% were transferred to the intensive care unit. When evaluating the groups based on discharge, fatal outcome, and intensive care unit admission status, 97.1% of those not given TPN were discharged, 0.4% had fatal outcomes, and 2.5% were admitted to the intensive care unit. Among TPN recipients, 91.6% were discharged, 0.8% had fatal outcomes, and 7.6% were admitted to the intensive care unit. There was no statistically significant difference in the mode of discharge based on TPN status (p>0.05) (Table 4).

The mean Rockall score and Glasgow-Blatchford scores were higher in TPN recipients compared to non-TPN recipients, and this difference was statistically significant (p<0.05) (Table 5).

When evaluating the length of stay, TPN recipients had a longer stay compared to non-TPN recipients, and this difference was statistically significant (p<0.05). There was no statistically significant difference between TPN recipients and non-TPN recipients in terms of ES and FFP replacement needs (p>0.05) (Table 6).

DISCUSSION

In this study, a retrospective analysis of a patient group consisting of 369 individuals with a diagnosis of non-variceal upper gastrointestinal bleeding was conducted. The files of patients admitted with this diagnosis were thoroughly examined to determine whether there is a

Table 3. Evaluation of groups according to Rockall scoring system				
		TPN		
Rockall	Total	Not received	Received	P
Low Risk	39,3% (145)	47,5% (113)	24,4% (32)	0,0001
Medium Risk	60,2% (222)	52,1% (124)	74,8% (98)	
High Risk	0,5% (2)	0,4% (1)	0,8% (1)	>0,05
Chi-square test				

Table 4. Evaluation of groups according to the mode of exit of patients				
		TPN		
Output Type	Total	Not received	Received	p
Discharge	95,1% (351)	97,1% (231)	91,6% (120)	0,063
Exitus	0,5% (2)	0,4% (1)	0,8% (1)	
Intensive Care Unit	4,3% (16)	2,5% (6)	7,6% (10)	
Total	100% (369)	64,5% (238)	35,5% (131)	
Chi-square test				

Table 5. Evaluation of groups according to Rockall and Glasgow-Blathcford scores

	TPN		
	Not received	Received	
Parameters	Mean ± SD	Mean ± SD	p
Rockall	2,62±2,02	3,77±2,04	0.000
Glasgow Blathcford	10,23±3,59	11,32±3,68	0.006
Independent T Test			

Table 6. Evaluation according to TPN receipt status after fixing rockall score, blood and blood products replacement need, and length of stay

		TPN		
		MEAN±SD		
Parameters	Number (n:463)	Not received	Received	p
ES Requirement		1,96±0,1	2,25±0,13	0,098
FFP Requirement	238/131	0,32±0,06	0,46±0,08	0,184
Length of Hospitalization Days		4,96±0,20	6,59±0,27	0,0001
ANCOVA Test				

difference in mortality and morbidity between cases treated with TPN (patients from 2012 to 2013) and those not treated (patients from 2016 to 2017).

The retrospective nature of the study is a limitation due to the potential information gaps in the records, and this should be considered when interpreting the findings. Additionally, being a high-volume tertiary research hospital may have affected the data on blood and blood product replacements, especially since most patients being treated in the emergency department before admission. This is also a point that needs to be taken into account.

As no tests were performed to assess the nutritional status of patients, our inability to provide an evaluation on this aspect in the discussion is another limitation of our study due to its retrospective nature.

Rapid assessment and management of patients with upper GI bleeding is critical. Intravenous fluids, along with red blood cell transfusion at a hemoglobin threshold of 70–80 g/L are advised for all patients with GI bleeding. Proton pump inhibitors (PPIs) should be given at the start of resuscitation. After resuscitation, endoscopy should be performed within 24 hours, albeit in high-risk patients, such as those with hemodynamic instability, although early endoscopy may be considered. Significant reductions in rebleeding rates, blood transfusion needs, length of hospital stay, surgical times, and mortality are achieved through endoscopic hemostasis.[9]

Following endoscopic treatment, patients at a high risk of rebleeding should be kept nil and admitted to the hospital for a minimum of 72 hours. Within 72 hours, the majority of high-risk lesions turn into low-risk lesions, and most rebleeding happens during this period.[10] It is also recommended to start EN early as it does not associated with higher rebleeding and mortality compared to delayed EN in patients with GI bleeding, but decreases the length of hospital stay. Early EN should be recommended as the preferred nutrition routine in patients at low risk of rebleeding.[11]

For many years, PN was prescribed only to individuals who cannot handle the severe side effects of EN, namely abrupt hyperglycemia and infectious problems. Its application has expanded due to the availability of an all-in-one PN admixture and the optimization of substrate composition, especially lipid emulsions. Comparable complications rates with EN and PN nutrition therapy have been reported in recent studies. As a result, in addition to total GI failure, other issues including inadequate EN, malabsorption, or certain needs that cannot be met with EN feeds are now included in the list of indications for PN.[8]

For patients, for whom oral nutrition is unavailable, parenteral nutrition support is considered a definite indication.[7] ESPEN guidelines on enteral nutrition (EN) state that inadequate nutrient supply will result in inadequate nutrition within 8-12 days after admission to surgical and/or intensive care units. To prevent inadequate

nutrition and associated side effects, EN should be given to all ICU patients who are not expected to complete a full oral diet within three days. For all patients whose normal nutrition is not expected within three days, PN should be given within 24-48 hours if EN is contraindicated or if they cannot tolerate it.

When PN was initially introduced, its primary ingredient was glucose.[12] As safer and less inflammatory lipid emulsions were developed, the carbohydrate content, and consequently, the frequency of hyperglycemia of the formulas decreased. By limiting glucose variability, reducing hypoglycemic events, controlling absolute blood glucose concentrations, or prolonging the duration in a normal range, total parenteral nutrition improves glucose control.[13] Observational studies in recent years have also demonstrated the benefits of high protein delivery to intensive care patients. Nicolo et al. discovered that achieving more than 80% of desired protein intake reduced mortality and length of stay.[14] Zusman et al. conducted a retrospective observational study on critically ill patients and discovered a linear relationship between protein intake and decreased mortality, with a 1% reduction in mortality for each gram of protein consumed.[15]

In line with these recommendations, our hypothesis was concluded that the application of TPN instead of intravenous glucose infusion in patients with upper GI bleeding may be a practice that reduces mortality and morbidity, and shortens the hospital stay through nutrition.

The only difference in the treatment process of patients hospitalized with non-variceal upper gastrointestinal bleeding at our hospital between 2012-2013 and 2016-2017 was that, starting in 2015, we began administering total parenteral nutrition at a daily rate of 25-30 kcal/kg instead of a daily 75-gram/day intravenous glucose infusion.

In our study, 95.1% of cases were discharged, 0.5% had fatal outcomes, and 4.3% were transferred to the intensive care unit. When the groups were evaluated based on discharge, fatal outcomes, and intensive care unit admission status, no statistically significant difference was observed in the mode of discharge between the groups.

When the TPN and non-TPN groups were compared based on the Forrest classification, no statistically significant difference was observed, although TPN recipients had a statistically significantly higher average score according to the Rockall and Glasgow-Blatchford scoring systems. It was thought that this result was reached as a result of including all patients admitted with a diagnosis of non-variceal upper gastrointestinal bleeding, excluding those

with gastrointestinal malignancy, in our retrospective study. In line with this result, covariance analysis (ANCOVA) was applied to control the pre-test Rockall scoring to compare length of hospital stay, discharge modalities, and blood product replacement needs.

When evaluated based on TPN receipt status after fixing the Rockall score, ES, TDP replacement need, and length of stay, the length of hospital stay was higher in TPN recipients compared to non-recipients, and this difference was statistically significant. There was no statistically significant difference between TPN recipients and non-recipients in terms of ES and FFP replacement needs. Contrary to our hypothesis that TPN application would have a positive effect on mortality, we found a result that did not support this, and we also observed a prolonged hospitalization, contrary to our hypothesis that it would decrease.

PN-associated complications may be categorized as metabolic, infectious, and mechanical. It can cause hyperglycemia, hypertriglyceridemia, electrolyte imbalances particularly phosphorus and potassium, hepatobiliary complications, and infectious complications.[16] It is believed that the longer length of stay in the TPN group is due to TPN complications, although our retrospective study could not obtain data to support this. Multicenter prospective studies in the future may provide more information on the subject.

CONCLUSION

In cases where oral nutrition is inappropriate in patients with upper gastrointestinal bleeding, TPN can be the first line choice instead of intravenous glucose support. In line with the studies conducted, our study, based on the hypothesis that TPN application may be a practice that reduces mortality and morbidity in patients with upper GI bleeding and shortens length of stay through nutritional support, found that this preference not only did not lead to a decrease in the number of blood and blood product replacements or in mortality, but also resulted in prolonged hospital stay in our group of patients receiving TPN.

This result is thought to be due to complications of nutritional support with TPN, although our retrospective study could not obtain data to support this. Conducting multicenter prospective studies on the subject would be beneficial."

Ethical approval: The study was approved by the Ethics Committee of Health Sciences University (Number: 48865165-302.14.01).

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