Original Research Paper

Volume - 15 | Issue - 06 | June - 2025 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Home Science

IMPACT OF HIGH PROTEIN DIET IN CRITICALLY ILL GASTROINTESTINAL SURGERY PATIENT

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ABSTRACT **Background:** The role of protein in critically ill patients is of considerable interest to improve clinical outcomes by reducing protein losses during critical illness and supporting the patients' recovery in later phases. Critically ill patients, especially those who have gastrointestinal surgery, often experience significant protein loss due to their catabolic state and the stress of surgery. A high-protein diet can help to combat this loss by providing the necessary building blocks for tissue repair and recovery. High protein intake can potentially lead to increased blood urea nitrogen (BUN) levels, though these changes may not be negatively associated with outcomes. The protein needs of each patient will vary based on their individual condition, severity of illness, and other factors. The primary objective of this study was to investigate the impact of high protein diet on clinical outcomes in critically ill patients with gastrointestinal surgery. The secondary aim was to compare the mortality, ventilator days and length of ICU stay. **Materials And Methods:** The study was conducted on critically ill adult patients with gastrointestinal surgery. The study group (SG; n = 56) was divided in two groups on high protein group (n = 30) those receiving >1.2g/kg/day and non-high-protein group (n = 26) those receiving ≤ 1.2g/kg/day. The primary endpoint was 28 days mortality and the secondary endpoints were 90 days mortality, length of ICU stay and number of ventilator days in the first 28 days. **Results:** The high-protein group had significantly lower 28 and 90 days mortality and significantly lower ventilator days and length of ICU stay but higher level of blood urea nitrogen (BUN). **Conclusion:** Provision of >1.2 g/kg/day of protein may be associated with lower mortality of tube-fed, mechanically ventilation days but no any major changes in length of ICU stay. Furthermore, while high protein intake may be associated with higher blood urea nitrogen, these changes have not seen any adverse outcomes.

KEYWORDS : Critically ill, gastrointestinal surgery, High Protein, Mechanical ventilation, Mortality, Blood urea nitrogen (BUN).

INTRODUCTION

Nutrition plays an important role in recovery after gastroenterological surgery. Severe gastrointestinal surgical stress increases muscle breakdown and lipolysis, thereby accelerating wound healing and enhancing host defense against microbes. Malnutrition is very common in such types of surgical patients. Malnourished patients have insufficient amounts of muscle and body fat. Therefore, they are not in the position to respond appropriately to surgical stress. Malnutrition is highly prevalent among gastrointestinal surgery patients and is an important independent predictor of in-hospital mortality. These patients have most often complication of underlying conditions such as sepsis, trauma, or multiple-organ failure in critically ill patients. Nutritional requirements for these patients may differ widely between every individual patient.

The role of protein in critically ill patients is of considerable interest to improve clinical outcomes by reducing protein losses during critical illness and supporting the patients' recovery in later phases. The provision of adequate protein is very crucial for critically ill patients with gastrointestinal surgery. Early provision of a high-protein diet improves the prognoses of patients in intensive care units (ICUs). The appropriate amount of protein in diet has not yet been determined. Nutritional Guidelines for the provision and assessment of nutritional support therapy in critically ill adult patients recommend providing ≥1.2–1.3 g/kg/day of protein. All the evidence that supports this recommendation has come from observational studies and this recommendation was developed by considering the amount of protein lost due to various reasons. Furthermore, some studies recommend even greater amounts of protein also.

A high protein intake increases the blood urea nitrogen (BUN). The increase in blood urea nitrogen attributable to high protein intake alone is thought to be negligible. This has not been proven definitely that high protein intake is the reason to increase blood urea nitrogen in critically ill patients. Moreover, the blood urea nitrogen on admission reportedly predicts the long-term prognoses of patients in ICUs. However, whether high protein intake can be continued in critically ill patients with an elevated blood urea nitrogen concentration remains unknown.

In the present study, we investigated the association of high-protein diet with outcomes and blood urea nitrogen in patients receiving enteral nutrition in the intensive care unit and investigated the changes in blood urea nitrogen.

Consequently, different clinical nutrition societies generally recommend higher protein delivery, whereas these recommendations are based on a low level of evidence, leading to varying dosage recommendations (ranging from 1.2 to 2.5 g/kg body weight/day) and uncertainties in the clinical practice due to the unclear benefits and risks.

A previous systematic review and meta-analysis (SRMA) included 19 randomized controlled trials (RCTs) and 1731 patients comparing higher (~ 1.3 g/kg BW/day) vs. lower (~ 0.9 g/kg BW/day) protein delivery (with similar energy delivery between groups) found that higher protein delivery was not directly associated with overall mortality but significantly attenuated muscle loss in five small RCTs. A trend towards shorter durations of mechanical ventilation (MV) and intensive care unit (ICU) length of stay (LOS) with higher protein delivery was also demonstrated but unclear about the impact on mortality . Following this SRMA, several RCTs were published, and one of them represents the large multinational, multicentre protein trial. This trial compared higher protein (1.6 g/ kg BW/day) vs. lower protein (0.9 g/kg BW/day) delivery and could not confirm any benefits or improved outcomes with higher protein delivery. Rather, these results indicate that higher protein delivery may increase mortality censored at 60 days in patients with sepsis, acute kidney injury (AKI) and high organ failure scores. Although the protein trial may it already impact clinical practice, it is crucial to aggregate all available data to provide the best evidence to inform and guide clinical practice.

Currently, evaluation of biochemical parameters and patient-centered outcomes is lacking in published SRMAs. The lack of these outcomes includes a comprehensive understanding of the associated biochemical squeal of higher protein delivery. Similarly, the pooled estimate of combining early physical rehabilitation and higher protein delivery on patient-centered outcomes is lacking. Since early physical rehabilitation may improve protein utilization, it is essential to quantify their appropriate effects.

In light of these considerations, there is an urgent need to update the previous SRMA to address the following objectives: (1) compare the effect of higher vs. lower protein delivery (with similar energy between groups) on clinical outcomes in critically ill patients with and without acute kidney injury (AKI) and early physical rehabilitation and (2) summarize the biochemical parameters and physical function outcomes of higher protein delivery.

Nutrition intake and management play a crucial role in the treatment and recovery of diseases, with particular significance in the Intensive Care Unit (ICU) with gastrointestinal surgery. Nutritional therapy for critically ill patients has emerged as a research hotspot in last few years. This therapeutic approaches aims to provide adequate energy and substrate for cellular metabolism, maintain tissue and organ structure and function, correct metabolic disorders, regulate immunity, and improve existing or potential nutritional deficiencies. These strategies collectively aim to influence disease progression and improve patient outcomes. While most studies assessing the impact of proper nutrition support on ICU clinical outcomes have focused on energy supply, an increasing amount of evidence suggests that protein intake may be more critical than calorie intake. Critically ill patients experience significantly more protein breakdown metabolism than synthesis, especially in the early stages. This imbalance is closely associated not only with ICU-acquired muscle weakness but also with immune-suppression, impaired wound healing, and other adverse consequences. Therefore, appropriate protein provision can meet metabolic demands without increasing metabolic burden, offering benefits to patients in intensive care unit.

However, controversy persists regarding the optimal doses and timing of protein supplementation in the early stages of disease. Both the American Society for Parenteral and Enteral Nutrition (ASPEN) and the European Society for Clinical Nutrition and Metabolism (ESPEN) recommend that critically ill patients should receive more protein than healthy individuals. For critically ill patients with a BMI < 30, protein requirements should be in the range of 1.2–2.0 g/kg/d, with potentially higher amounts needed for burn and trauma patients. Additionally, for critically ill patients requiring more nutritional support, enteral nutrition (EN) is preferred over parenteral nutrition (PN). However, in the early stages of critical illness, significant stress and alterations in neuro-endocrine factors result in the body relying on glycogen, endogenous protein breakdown, and fat mobilization for energy, with reduced external energy requirements. Excessive protein intake during this period may not be absorbed and lead to adverse reactions such as azotemia and hyperglycemia, thereby increasing the burden on the liver and kidneys and adversely affecting clinical outcomes. Koekkoek et al. found a time-dependent relationship between protein intake and mortality in mechanically ventilated ICU patients. Higher protein intake in the first 3 days of ICU admission was associated with increased mortality, whereas higher protein intake beyond 3 days was associated with lower mortality.

In a previous observation of 20 ICU patients, early high protein supplementation did not improve nutritional status but increased the incidence of gastrointestinal intolerance, with no impact on 28-day mortality and ventilator days. In light of these findings and in accordance with clinical guidelines, we conducted a prospective randomized controlled study building upon preliminary research. The aim of this study was to investigate the impact of early high protein intake on critically ill patients and to determine the effective and safe dose.

MATERIALS AND METHODS:

The study was conducted on critically ill adult patients with gastrointestinal surgery. The study group (SG; n = 56) was divided in two groups on high protein group (n = 30) those receiving >1.2g/kg/day and non-high-protein group (n = 26) those receiving ≤ 1.2g/kg/day. The primary endpoint was 28 days mortality and the secondary endpoints were 90 days mortality, length of ICU stay and number of ventilator days in the first 28 days.

Design:

The present study was conducted at the intensive care unit at some hospitals in Patna, Bihar. The study patients had received enteral nutrition for at least 3 days while undergoing gastrointestinal surgery in between April 2020 to December 2022.

The study comprised 56 patients who had received enteral nutrition for at least 3 days while undergoing gastrointestinal surgery in the ICU. We had a basic policy of starting early enteral feeding within 24–48 h after ICU admission or shifting after surgery. In some patients started tube feeding while other patients did not start tube feeding and were prioritized for removal from the ventilator and initiation of oral intake. In such cases, tube feeding was not always necessary. Therefore, patients who underwent tube feeding for <2 days were not included in the study. Enteral nutrition was preferred when the intestine was available, implying that patients who were started on exclusively on parental nutrition, poorly tolerated enteral feeding. Because the outcome may be poor in such patients, we targeted enteral feeding patients in this study. The exclusion criteria were an age of <18 years, and death within 3 days of commencing enteral nutrition.

Data Collection:

The following data were collected e.g. age, sex, height, body weight, body mass index, primary disease, surgical procedure, diabetes mellitus (yes/no), physical findings on arrival body temperature, blood pressure, heart rate, respiratory rate, blood chemistry data on arrival [C-reactive protein, sodium, potassium, chloride, albumin, total bilirubin, blood urea nitrogen, creatinine, glycated haemoglobin (HBA1C), white cell count, hemoglobin, hematocrit, platelet count, etc.], blood gas analysis (pH, pCO_2, pO_2, HCO_3^-, base excess), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and data after 1 week of enteral nutrition (BUN, amount of protein, carbohydrate, fat, and calories provided daily). For patients who had been taken off their ventilators and completed enteral feeding within 7 days, nutritional variables were extracted based on the contents of the last day of tube feeding. The relationship between nutritional parameters and outcomes may change when the oral intake does not proceed because of problems with appetite and swallowing dysfunction; therefore, data for the last day of tube feeding was extracted for convenience. The patient's body weight was used for nutrition calculations.

The standard protocol to follow nutrition was step-wise. We started tube feeding within 24–48 h after ICU admission or shifting and gradually increased the nutrition over 1 week, and energy, protein, carbohydrates and fat intake were recorded on daily basis. Supplemental parenteral nutrition was also used if the attending physician/consultant determined that it was necessary. Because we aimed to achieve the nutrition goal within a week after the start of enteral nutrition, we extracted the data after 1 week of enteral nutrition. The enteral and parenteral nutrition totals were calculated for all nutrients including calories. Based on the results of these calculations, the patients were divided into two groups, those who had been provided with >1.2 g/kg/day of protein (high-protein group) and those who had been provided with ≤1.2 g/kg/day of protein (non-high-protein group); the outcomes of these groups were compared. Current nutritional guidelines recommend provision of ≥1.2–1.3 g/kg/day of protein.

Outcomes:

The primary outcome was 30 days mortality. The secondary outcomes were 90 days mortality, length of ICU stay, number of ventilator-free days in the first 30 days after admission in intensive care unit, and blood urea nitrogen (BUN after 1 week of enteral nutrition − BUN on admission).

RESULTS:

Total 56 patients were included in the study. 26 of these 56 patients were in the non-high-protein group and 30 were in the high-protein group. The patients' characteristics are shown in Table 1, primary diseases in Table 2, and blood report in Table 3. In non-high protein group, 26.92% diabetes, 46.15% hypertension, 11.53% trauma, 11.53% cardiovascular disease and 19.23% patients have sepsis. In high protein group, 36.67% diabetes, 20.00% hypertension, 23.33% trauma, 14.33% cardiovascular disease and 23.33% patients have sepsis.

1 week after initiation of enteral nutrition in the high-protein and non-high-protein groups, there were significant differences in the amounts of protein, fat, and calories provided between the high-protein and non-high-protein groups. The high-protein group had significantly lower 28 and 90 days mortality and significantly lower ventilator days but there were no significant differences in length of ICU stay and higher level of blood urea nitrogen (BUN).

The present results indicate that ≥1.2 g/kg/day of protein may be beneficial for critically ill gastrointestinal surgery patients. Considering the large amount of protein that is lost during the early acute phase, provision of sufficient protein intake seems crucial. Many recent studies have also revealed the importance of avoiding overfeeding in the early acute phase, and formulas now typically have a high protein and low carbohydrate content.

Table 1.Patient Characteristics

Variable	Non-high protein group	High protein group
Age (In years)	64.3 ± 7.6	65.7 ± 8.4
Male n (%)	16	18
Female n (%)	10	12
Height (cm)	160 ± 8.5	160 ± 8.5
Weight (kg)	65.3 ± 4.8	65.3 ± 4.8
Body mass index (kg/m2)	25.50 ± 2.34	25.50 ± 2.34

Table 2. Primary Diseases:

Variable	Non-high protein group	High protein group
Diabetes mellitus n (%)	7 (26.92 %)	11 (36.67 %)
Hypertension n (%)	12 (46.15 %)	6 (20 %)
Trauma n (%)	3 (11.53 %)	7 (23.33 %)
Cardiovascular disease n (%)	3 (11.53 %)	4 (13.33 %)
Sepsis n (%)	5 (19.23 %)	7 (23.33 %)

Table 3. Blood Chemistry:

Variable	Non-high protein group		High protein group	
	Day 1^{st} in ICU	After 1 week	Day 1^{st} in ICU	After 1 week
CRP (mg/dl)	2.6 ± 5.2	2.1 ± 2.3	2.54 ± 5.3	2.3 ± 2.1
Albumin	3.5 ± 0.6	3.3 ± 0.4	3.2 ± 0.6	3.4 ± 0.6
BUN (mg/dl)	26.3 ± 19.8	18.7 ± 13.7	29.7 ± 21.8	28.3 ± 17.3
Creatinine (mg/dl)	1.1 ± 0.5	0.9 ± 0.4	0.9 ± 0.6	1.1±0.5
SGOT	86 ± 48	83 ± 21	76 ± 58	56 ± 48
SGPT	77 ± 57	65 ± 42	82 ± 54	37 ± 24
Hb%	10.2 ± 3.3	10.7 ± 2.1	9.8 ± 3.6	10.4 ± 3.1
WBC, x $10^3/mm^3$	12.6 ± 4.8	9.7 ± 2.3	13.6 ± 4.8	10.6 ± 2.7
pH	7.3 ± 0.3	7.2 ± 0.3	7.3 ± 0.3	7.3 ± 0.3
APACHE II Score	21.73 ± 6.7	17.57 ± 5.4	21.63 ± 6.3	18.6 ± 4.8

CONCLUSION:

Provision of >1.2 g/kg/day of protein may be associated with lower mortality of tube-fed, mechanically ventilation days but no any major changes in length of ICU stay. Furthermore, while high protein intake may be associated with higher blood urea nitrogen, these changes have not seen any adverse outcomes.

In critically ill gastrointestinal surgery patients, high protein intake, especially in the later phase of their illness, may improve outcomes. Studies suggest that a standard protein intake (around 1 g/kg/day) from day 5 to 11 after ICU admission may be associated with lower in-hospital mortality and potentially shorter length of hospital stays. However, early or high protein intake (up to 1.4 g/kg/day) may not offer further benefits and could even be associated with a longer time to hospital stay. Some research indicates that early high protein supplementation may not improve nutritional status and could even increase gastrointestinal intolerance, according to the National Institutes of Health (NIH).

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