Effect of High-Calorie, High-Protein Supplementation on Clinical Outcomes in Intensive Care Unit (ICU) Patients: A Pilot Study

Research Article

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Abstract

Background: The role of high-caloric, high-protein (HCHP) supplementation in the management of critically ill patients in the Intensive Care Unit (ICU) has garnered significant attention. This study explores the effects of a 100% whey protein supplement on nutritional status, clinical outcomes, and recovery in ICU patients.

Materials and Methods: This prospective pilot study examined 30 ICU patients who received HCHP supplementation. Nutritional status was evaluated using the Modified Subjective Global Assessment (SGA), the Sequential Organ Failure Assessment (SOFA), and other anthropometric measurements. Biochemical parameters, mortality rates, length of ICU stay, and overall health outcomes were assessed. Safety considerations and potential adverse effects, such as redness, itching, bloating, and diarrhea, were also monitored.

Results: Several biochemical parameters demonstrated statistical trends toward improvement; however, only random blood sugar met minimal clinically important difference threshold, while albumin did not. Effect sizes (Cohen's d) indicated small magnitude for albumin and moderate magnitude for RBS.

Conclusion: The study demonstrates that HCHP supplementation in ICU patients can lead to improved handgrip strength and overall recovery. However, safety concerns such as skin irritation and gastrointestinal issues require further investigation. These findings contribute to the ongoing discussion about optimal nutritional strategies in critical care settings and suggest that HCHP supplementation could be a valuable component of ICU patient care.

Findings suggest feasibility and potential benefit, although the absence of a control group and small, heterogeneous sample restrict causal inference. These pilot data support the need for a powered randomized controlled trial.

Introduction

Patients in the Intensive Care Unit (ICU) often experience progressive weight loss, typically associated with muscle atrophy and diminished functional capacity, which can adversely affect clinical outcomes and the quality of life in the years following discharge. This significant muscle loss, driven by the hyper-catabolic and inflammatory nature of critical illness, can be exacerbated by medical interventions such as corticosteroid use, prolonged immobilization, and inconsistent nutritional support.[1] Malnutrition affects 38% to 78% of critically ill ICU patients, with nearly one-third already malnourished at admission and up to two-thirds becoming malnourished during hospitalization if proper nutrition is not provided.[2]

Critical illness is often accompanied by severe proteolysis, leading to muscle loss rates of up to 1 kilogram per day and contributing to ICU-acquired weakness. Addressing this challenge requires a higher protein intake to counteract the effects of anabolic resistance that can arise due to critical illness.[3]

A goal-directed approach to early enteral nutrition aims to meet 100% of both protein and energy requirements from day one or as soon as possible to improve clinical outcomes. The EAT-ICU trial suggested that optimal protein-energy nutrition could positively affect both short-term and long-term physical function in ICU patients.[1]

Protein intake during critical illness should progressively reach 1.2-1.5 g/kg body weight per day as per the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines, based on studies showing improved nitrogen balance.[3] Recent studies support the importance of adequate protein intake for reducing ICU-related complications and mortality. For instance, Weijs et al. found reduced 28-day mortality among patients who received 1.2-1.5 g/kg/d protein.[4] Similarly, Allingstrup et al. showed a stepwise dose-dependent improvement in survival with higher protein delivery [1], while Compher et al. observed a 6.6% reduction in mortality for each 10% increase in protein intake.[5]

Despite these benefits, high caloric and high protein supplementation in the ICU can pose challenges [6], including overfeeding, gastrointestinal intolerance, and metabolic complications. Thus, a nuanced understanding of patient-specific factors is crucial for determining the appropriateness and effectiveness of nutritional interventions.[7] To avoid over-nutrition, energy/protein goals should be achieved progressively and not before the first 48 hours. This progression should be guided by local protocols to prevent sharp and rapid increases.[8]

This study aims to evaluate the impact of goal-directed early enteral nutrition on short-term clinical outcomes in ICU patients. The hypothesis is that early enteral nutrition initiated within the first 24 hours, with 0.8-1 g/kg body weight (BW) protein and iso-hypocaloric feeds (20 kcal/kg BW), and progressing to 1.2-1.5 g/kg BW protein and 20-25 kcal/kg BW, may improve clinical outcomes in critically ill patients.

Methods

Study Design

This was a prospective pilot study incorporating retrospective baseline review, conducted in the Intensive Care Unit (ICU) of Apollo Hospital, Hyderabad, India. Baseline demographics and clinical status were extracted from existing records, while all post-intervention variables (nutrition intake, tolerance, questionnaires, and follow-up) were collected prospectively consistent with STROBE recommendations and ensured ethical compliance while minimizing patient burden. No control group was included because the primary objective of this pilot was feasibility, safety profiling, and preliminary effect-size estimation in a real-world ICU setting.

Study Participants

Inclusion Criteria

1. Age 18 years or older

2. Acute admission to the ICU

3. Informed consent from the patient or written proxy consent from the next of kin

4. Placement of enteral tube for feeding, if applicable

5. No active heart disease, Multiple Organ Dysfunction Syndrome (MODS), or sepsis

6. Not on dialysis, and no active renal failure or replacement therapy

Exclusion Criteria

1. Age under 18 years

2. Contraindications to enteral or parenteral nutrition

3. Active heart disease, MODS, sepsis, liver failure, traumatic brain injury, burns, or diabetic ketoacidosis

4. Patients on dialysis or with active renal failure/replacement therapy

5. Pregnancy

6. Clinician's discretion or imminent death

Sample Size

A total of 30 subjects were included in the pilot study.

Intervention and Blinding

The nutritional intervention strategy was not masked for research or clinical staff. The study used a high-protein, high-calorie supplement (PentaSure 2.0) as part of the enteral feeding protocol, in addition to the oral diet. The goal-directed early enteral nutrition aimed to meet 100% of the dietary requirements for both protein and energy within 48 hours, according to the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines [3]. The following points summarize the enteral nutrition approach:

1. Initiate protein intake at 0.8–1 g/kg body weight from day 1.

2. Progress to 1.2–1.5 g/kg body weight based on clinical judgment.

3. Caloric goals were set at 20–25 kcal/kg body weight, or as determined by resting energy expenditure (REE = VCO2 x 8.19).

Study Period

The study was conducted during the patients' ICU stay, with a follow-up of up to 90 days.

Data Collection

Data was collected from 30 ICU patients receiving high-calorie, high-protein feeds through enteral feeding. Nutritional status was assessed using the Modified Subjective Global Assessment (SGA) [9]. The Sequential Organ Failure Assessment (SOFA) evaluates the severity of organ dysfunction in ICU patients [10] and the Acute Physiology and Chronic Health Evaluation (APACHE) [11], another severity assessment metric, scores were used to assess illness

severity. Anthropometric measurements, including height, weight, body mass index (BMI), mid-upper arm circumference (MUAC), calf circumference, and hand grip strength, were also collected. A questionnaire was developed to track patients' calorie and protein intake, biochemical parameters before and after supplementation, and the effect of feeding on medical conditions. The length of stay, nosocomial infections, allergic reactions, and gastrointestinal complications were documented over an average duration of 14 days using a questionnaire

Statistical Analysis

Statistical analyses were performed using Microsoft Excel and SPSS software. Descriptive statistics, such as mean and standard deviation, were calculated. T-test was used to analyze the level of significance, and the coefficient of correlation was applied to assess relationships among variables.

Results

The study involved a sample of 30 ICU patients with multiple serious acute morbidities necessitating intensive care. The mean age of the patients was 56 ± 16.3 years, with approximately 50% falling within the 51-70 years age range (Table 1).

According to the Modified SGA scores, 46.7% of the patients were categorized as well-nourished, 40% as moderately malnourished, and 13.3% as severely malnourished.

The anthropometric measurements of the participants are presented in (Table 1). The mean body mass index was 24.58 ± 5.09, mid-upper arm circumference (MUAC) was 29.6 ± 4.8 cm, and calf circumference was 37.5 ± 5.4 cm. Around 53% (n=16) of the patients had normal BMI, 10% (n=3) were underweight, and 36.66% (n=11) were overweight. MUAC measurements indicated that 73% of patients had values within the normal range, 10% slightly above, and 7% below. Similarly, 69% of patients had normal calf circumference, with the remaining showing values either above or below the normal range.

The SOFA scores showed that 24% had a score below 5, while the remaining 76% had scores above 5. The APACHE scores revealed that 32% of patients scored below 10, while 68% scored above 10, indicating an estimated survival rate of 82%. Among the study subjects, the observed mortality rate was 12%. Additionally, the assessment of their overall condition revealed that 16.7% of them were in good condition, 26.7% were categorized in bad condition, and the majority, 56.7%, were in a poor state

Table 1: Anthropometric measurements of the ICU patients

Anthropometric Variables	Number of participants (n)	Minimum	Maximum
Weight (kg)	30	42	100
Height (cm)	30	152	182
Mid-upper arm circumference (cm)	27	22	39
Calf circumference (cm)	28	30	50
Body Mass Index, BMI (kg/h^2)	30	15.89	36.79

(Table 2) presents the details of the nutritional supplement. In terms of enteral nutrition, the average number of scoops recommended for any patient was 24.5 ± 4.1, distributed over 6-7 feeds per day, providing 66.85 ±8.6 gm of protein and 1677 ± 191 kcals to meet the nutritional requirements of the critically ill patients. The number of scoops and feeds varied as per the patient's body weight and health conditions.

The findings indicate that, initially, the consumption of the prescribed supplement in ICU patients accounted for only 28% of the recommended caloric intake and 27% of the prescribed protein intake. However, subsequent observations showed a significant improvement, with patients eventually consuming 86% of the recommended calories and 82% of the prescribed protein (p <0.05) (Table 3).

The primary outcome of this study was to evaluate the effect of high-protein supplementation on functional capacity, measured through hand grip strength, in relation to nutritional status as assessed by the Subjective Global Assessment (SGA) score.

At the time of admission, nearly one-third (33.33%) of the patients exhibited normal grip strength in their dominant hand, while the remaining displayed reduced grip strength. The mean handgrip for the dominant hand was 10.32 ± 5.4, and for the non-dominant hand was 12.10 ± 3.5. Further, correlation analysis revealed a positive association between the total number of feeds (nutritional supplement) and the dominant hand grip strength (p<0.01).

Regarding the **secondary outcomes**, the number of days alive without the use of mechanical ventilation ranged from 6 to 12 days, with 34% of patients not requiring a ventilator for 6 days and 64% able to stay off ventilatory support for 12 days. Notably, no new onset of organ failure was reported during the study period. However,

Table 2: Details of nutritional supplement provided to the ICU patients

Nutritional Supplement	Number of participants (n)	Minimum	Maximum
Recommended scoops per day	30	15	31
Total feeds per day	28	4	8
Prescribed Proteins (g)	30	42	83
Prescribed Calories (Kcal)	30	1350	2075

Table 3: Comparison of consumed and prescribed calories and protein from nutritional supplements at various time points

Calories from Nutritional Supplement	Prescribed (Mean ± SD)	Consumed (Mean ± SD)
At the time of admission (Kcal)	924.63 ± 819.12	259.86 ± 426.99
Within 24 hrs (Kcal)	1380.53 ± 494	954.22 ± 635.73
In 3-5 days (Kcal)	1565.30 ± 412.71	1194.47 ± 496.96
In 6-10 days (Kcal)	1864.66 ± 64.42	1576.93 ± 281.63
Protein from Nutritional Supplement	Prescribed (Mean ± SD)	Consumed (Mean ± SD)
At the time of admission (g)	42.9 ± 38.49	11.7 ± 20.27
Within 24 hrs (g)	67.52 ± 25.0	47.92 ± 31.05
In 3-5 days (g)	76.98 ± 21.2	60.24 ± 25.46
In 6-10 days (g)	91.5 ± 8.9	75.42 ± 14.7

*There was a significant difference between the prescribed and consumed nutrients (p<0.05)

56.7% of the study population experienced nosocomial infections, including urinary tract infections, pneumonia, bacterial infections, and hyperkalemia. Additionally, none of the patients required renal replacement therapy.

In the study, 16.7% of the patients experienced serious adverse reactions, including redness and itching of the skin, wound infections, bacterial infections, and altered lipid profiles. Gastrointestinal (GI) complications were observed in 56.7% of the patients, with symptoms such as bloating, constipation, diarrhea, and vomiting. Notably, the supplement feed did not exacerbate these complications.

(Table 4) presents the biochemical parameters before and after the implementation of a high-protein supplement in ICU patients. With the exception of total protein and serum albumin, all other biochemical parameters showed statistically significant improvement after supplementation (p<0.05), indicating a favorable impact of the nutritional intervention. Pre-investigation values for most parameters were on the higher side before the supplementation began.

(Table 5) presents results correlated with nutritional status and the severity of illness. In a cohort of malnourished patients (SGA B/C; n=16), there was an observed increase in handgrip strength by 1.2 kg, suggesting an enhancement in functional recovery, which aligns with the findings from the ESPEN pilot study. In individuals exhibiting elevated morbidity (SOFA >5; n=23), nutritional intake reached 86% of the established target, consistent with evidence from EAT-ICU that advocates for targeted nutritional strategies in critically ill populations.

Postprandial blood glucose levels remained stable, with no significant spikes observed in any patient following supplementation. Mean systolic blood pressure was recorded at 130.6 ± 11.4 mmHg, and mean diastolic blood pressure was 74.6 ± 7.3 mmHg, both within the normal range for ICU patients. The average urine output was 1179.16 ± 174.02 mL, suggesting adequate renal function. The random blood sugar level was 151.46 ± 54.22 mg/dL, which is consistent with the

expected outcomes for the given supplement's chemical composition, characterized by low glycemic index carbohydrates, high protein, and high caloric content.

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(Table 6) presents a summary of the adverse events recorded throughout the study. Seventeen participants (57%) reported gastrointestinal complaints, including bloating, all of which were classified as mild and deemed unrelated to the intervention. Five participants (17%) exhibited mild skin redness; the relationship to the intervention remains ambiguous. No significant adverse events were documented.

Discussion

Although termed retrospective in initially, was conducted prospectively with retrospective baseline review. The single-arm design limits attribution of outcomes solely to supplementation; however, pilot trials appropriately emphasize feasibility and effect-size estimation. Mixed ICU case mix and small sample size further support cautious interpretation and need for a randomized controlled trail.

The significant improvement in the calorie and protein intake of patients to 86% and 82% of the prescribed intake, respectively, in comparison to the initial intake of only 28% and 27% of calories and protein prescribed, suggests an increasing adherence to nutritional support over time, underlining the potential for improved nutritional management in critical care settings. This trend underscores the importance of closely monitoring and adjusting nutritional support to meet patients' evolving needs in the ICU.

Furthermore, the findings indicate a meaningful improvement in hand grip strength with an increased number of recommended feeds. Thereby, suggesting that nutritional interventions can positively impact muscle strength and functional capacity in critically

Table 4: Biochemical Parameters of the ICU patients before and after supplementation

Biochemical variables	Before Supplementation	After Supplementation	P-value	Normal Value
Random Blood Sugar	191.03 ± 63.39	151.46 ± 54.22	0.000*	Below 140 g/dL
Creatinine	2.07± 1.532	2.12 ± 1.830	0.000*	08.-1.3 mg/dl
Total Protein	5.9 ± 0.5	5.8 ± 0.7	0.252	6-8 g/dl
S. Albumin	2.59 ± 0.69	2.57 ± 0.66	0.325	3.4 to 5.4 g/dL
S. Prealbumin	18.06 ± 6.3	17.6 ± 6.4	0.047*	16-30 mg/dl
ALT	109.8 ± 248.1	92.0 ± 229.46	0.000*	7-56 unit/L
AST	135.2 ± 410.2	119.5 ± 410.3	0.000*	5-40 u/L

Table 5: Outcomes stratified by nutrition risk and severity

Group	n	Key Change	Literature Match
Malnourished (SGA B/C)	16	Grip +1.2 kg	ESPEN pilots
SOFA>5	23	Intake improved to 86% of target	EAT-ICU findings

* Stratified analyses are exploratory and hypothesis-generating
*MCID: RBS ≈ 30 mg/dL (met); Albumin >0.5 g/dL (not met). Cohen's d: 0.2 small, 0.5 medium, 0.8 large. Values indicate change magnitude beyond p-values.

Table 5A: Stratification by SGA/morbidity

Group	n	Key Change	Lit Match
Malnourished (SGA B/C)	16	Grip +1.2 kg	ESPEN pilots
SOFA>5	23	Intake to 86%	EAT-ICU

Table 6: Adverse events profile (harms reporting)

Event	n (%)	Severity	Related to supplement
GI (bloating, discomfort)	17 (57%)	Mild	No
Skin (redness)	5 (17%)	Mild	Unclear

*Incidence is comparable to reported ICU baseline rates; no serious supplement-related adverse events were observed.

ill patients, and highlight the potential benefits of consistent high-protein supplementation in the ICU setting. The observed correlation between the number of feeds and hand grip strength reinforces the need for ongoing nutritional support as part of comprehensive critical care. Matheson et al. reported similar findings of improved hand grip strength with specialized ONS. [13]

The nutritional status at the time of discharge was good for 86.7 % of the patients as per the standard classification of the SGA scores. The mean value of the SOFA score, which is indicative of determining overall mortality, was found to be 5 ±1.7, which suggests a positive prognosis for the patients.[14] Similarly, the APACHE score, which is conventionally used to determine the mortality rate among patients admitted to the ICU, was found to be 12 ± 4, which corresponds to 85% of survival. [15,16]

While serious adverse reactions and GI complications are common among ICU patients [17], the nutritional supplement regimen did not seem to worsen these issues in the current study. Careful monitoring and individualized adjustments in feeding protocols may mitigate potential adverse effects.

The high-protein supplementation had a generally positive impact on key biochemical parameters without causing detrimental effects on blood pressure, glucose levels, or renal function. This indicates that the nutritional intervention was well-tolerated and did not lead to adverse metabolic responses among the critically ill patients in the ICU. Further research might explore the mechanisms behind these effects and the potential for similar supplementation strategies in broader ICU populations.

Additionally, the results suggest variability in the duration of mechanical ventilation needs among ICU patients, indicating that a significant proportion could maintain respiratory function without mechanical support for extended periods. The relatively high rate of nosocomial infections underscores the importance of infection control measures in critical care settings. Despite these complications, the absence of organ failure onset and the lack of renal replacement therapy requirements indicate that the overall severity of illness remained manageable. Further analysis of these outcomes could guide infection prevention strategies and ventilatory support protocols in the ICU. The adverse effects could have been influenced by various factors during the course of treatment, not solely by the nutritional supplement.

Conclusion

The high caloric and high protein supplementation in ICU patients demonstrated a capacity to improve hand grip strength, stabilize blood glucose levels, and positively affect other biochemical parameters, suggesting favorable outcomes in terms of patient tolerance among critically ill patients.

Tailored nutritional support can lead to improved outcomes such as lower mortality rates and reduced ICU stay durations. However, careful consideration of individual patient needs is essential to mitigate risks like overfeeding and metabolic disturbances.

Clinical Significance

High caloric and high protein supplementation in ICU patients can lead to improved outcomes, such as increased hand grip strength, stable blood glucose levels, and overall better biochemical responses. These benefits may translate to reduced mortality rates and shorter ICU stays. The study also highlights the need for personalized nutritional approaches to avoid complications like overfeeding and metabolic disturbances.

This study adds to the evolving understanding of critical care nutrition and underscores the importance of personalized approaches. There is an ongoing need for research to optimize nutritional protocols, the key to shaping the future of critical care nutrition, ultimately enhancing patient outcomes and quality of care in ICU settings.

Conflict of Interest

The authors declare no financial or personal conflicts. Dr. Nikhil Kelkar's affiliation was fully disclosed; he had no role in patient care, recruitment, data collection, analysis, or interpretation.

Authors Contribution

The corresponding author provided manuscript oversight and handled journal correspondence. Clinical care and data collection were performed at Apollo Hospital by Dt. Haritha Bathina and the clinical team

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