Indian Journal of
Nutrition

Open Science Publications

Volume 9, Issue 3 - 2022

www.opensciencepublications.com

Efficacy and Safety of Parenteral Amino Acids in Hospitalized Malnourished Patients: A Multicentric Case-Series

Research Article

Sheth H[1]*, Mishra PK[2], Sharma R[3], Kumar M[4] and Shukla H[5]

[1]*Consultant Surgeon, Saifee Hospital, Apollo Spectra Hospital, Bhatia Hospital, Conwest Hospital & Manjula Badani Jain Hospital, Mumbai, India*

[2]*Consultant Critical Care, Shree Aggarsain International Hospital, New Delhi, India*

[3]*Consultant Surgeon, New Delhi, India*

[4]*Medical Superintendent, Pushpanjali Medical Center, Delhi, India*

[5]*Consultant Oncosurgeon, BLK-Max Super specialty Hospital, New Delhi, India*

***Corresponding author:** Sheth H, Consultant Surgeon, Saifee Hospital, Apollo Spectra Hospital, Bhatia Hospital, Conwest Hospital & Manjula Badani Jain Hospital, Mumbai, India; E-mail: harsh86sheth@gmail.com

Article Information: **Submission:** 06/08/2022; **Accepted:** 03/09/2022; **Published:** 05/09/2022

Abstract

Background & Objective: Globally, malnutrition in hospitalized patients is increasing, with prevalence up to 30-50%. It is associated with a higher risk of adverse outcomes, including morbidity, mortality, length of hospital stay, and compromised quality of life. In India, almost two-fifths of the patients admitted to tertiary care hospitals are reported to be malnourished. Studies have suggested using nutritional markers like serum pre-albumin (SPA) and visceral protein markers like serum retinol-binding protein (S-RBP) to evaluate the nutrition status of malnourished patients. Guidelines recommend supplementing parenteral amino acids to manage the protein status in hospitalized patients with malnutrition.

This case series study aims to demonstrate the efficacy and safety of parenteral amino acids in malnourished patients admitted to the hospital ward and their impact on improving nutritional markers e.g., S-PA and S-RBP.

Methods: This multicentric case series study enrolled 80 patients admitted to the hospital ward across 49 Indian sites. Parenteral amino acid supplementation was administered intravenously once daily for five days. The primary outcomes were changes in the nutritional laboratory markers S-PA and S-RBP for improvement in nutritional status in enrolled malnourished patients.

Results: The pre-and post-assessment data for nutritional laboratory markers were available for 35 patients. A statistically significant increase was observed in the levels of S-PA and S-RBP. Additionally, similar improvements were observed in a subgroup analysis of patients treated by intensivists.

Conclusion: The results from this case series demonstrated that administering parenteral amino acid significantly improves the nutritional laboratory markers S-PA and S-RBP in hospitalized patients with malnutrition. A similar benefit was also observed in the subgroup of patients treated by the intensivists, suggesting a positive role of parenteral amino acid supplementation in critically ill patients.

Keywords: Critically ill patients, Hospitalized patients, Parenteral amino acids, Serum pre-albumin, Serum retinol-binding protein

Introduction

Malnutrition, in simple words, is any nutritional imbalance [1]. Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN) define malnutrition as the presence of any two or more of the entities, including insufficient energy intake [1-4], weight loss [1,5-8], loss of muscle mass [8-9], loss of subcutaneous fat [8-9], localized or generalized fluid accumulation [8-9], or decreased functional class [8,10-12]. Globally, malnutrition

ISSN: 2395-2326

in the hospital setting affects approximately 30-50% of patients accounting for a significant public health problem today [1,13-16]. Many patients enter the hospital with malnourished status or at risk of malnutrition. Further, the nutrition status of these critically ill patients declines during their stay, putting them at a higher risk for adverse outcomes, including increased morbidity, mortality, and length of hospital stay, with reduced quality of life following a hospital discharge [13,17-18].

European Society for Clinical Nutrition and Metabolism (ESPEN) - 2019 guidelines on clinical nutrition in the intensive care unit recommend that every critically ill patient staying for more than 48 h in the ICU be considered at risk for malnutrition. However, as per ESPEN, no specific ICU nutritional score has been validated so far and nutritional risk screening [NRS 2002] and the malnutrition universal screening tool (MUST) have the strongest predictive value for mortality, and they are the easiest and quickest to calculate [19]. On the contrary, the Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (ASPEN) expert consensus suggests a determination of nutrition risk (e.g., nutritional risk screening [NRS 2002], NUTRIC score) to be performed on all patients admitted to the ICU for whom volitional intake is anticipated to be insufficient [20-21].

Traditionally termed as a nutritional marker, serum albumin and pre-albumin quantify the amount of plasma circulating proteins and, thereby, thought to reflect nutrition status. Nutrition risk is primarily described as developing malnutrition and/or poor clinical outcomes if nutrition support is not provided. The decline in serum albumin and pre-albumin must be recognized as inflammatory markers associated with "nutrition risk" in nutrition assessment rather than with malnutrition per se [22-23].

As per the guideline recommendations, a protein intake of 1.2 to 2 g/kg weight per day should be allowed for most patients admitted to ICU, and ongoing evaluation of the adequacy of protein provision [20]. Allingstrup, MJ., et al., in their prospective observational cohort study ranked 113 ICU patients into three groups according to the amount of protein& amino acid (AA) provided; (Low; n=37, Medium; n=38, High; n=38). It was observed that patients in the high-protein group had a significantly lower risk of hospital mortality. Although overall, I.C.U. mortality did not differ, and the Kaplan-Meier survival probability at day 10 differed among protein groups (low, 49%, medium, 79%, and high, 88%; p = 0.021). Several recent observational studies support a higher protein goal demonstrating an association between adequate protein intake (i.e., at least 1.2 to 1.5 g/kg/day) and improved clinical outcomes in critically ill patients. [24-25] Visceral protein markers, such as transthyretin (TTR) and retinol-binding protein (RBP), have been associated as an indicator of protein malnutrition. Liu, K. et al., in their cross-sectional study including 682 elderly patients observed that low levels of retinol-binding protein were associated with an increased risk of sarcopenia in elderly general hospitalized patients [26].

However, from the view of the Indian setting, the available data is still inconclusive on parenteral amino acid supplementation in hospitalized patients with malnourishment and their impact on improving the nutritional markers like serum pre-albumin and retinol-bindingprotein. This case series aims to demonstrate the effectiveness of parenteral amino acids in malnourished patients admitted to the hospital ward.

Methods

Design & Setting

A multicentric case series study was conducted across 34 cities of India from August 2021 to November 2021 on malnourished patients admitted to the hospital ward. After consent from the patients, the following basic information was collected: height, weight, changes in food intake, and changes in body weight.

Sample

A total of 80 patients were enrolled with malnourishment and admitted to the hospital ward. Inclusion criteria were as follows: patients between 18 years to 90 years admitted to the hospital ward. The enrollment was done across India and distributed across 49 sites.

Intervention and Outcomes

In each admitted patient (N=80), the parenteral amino acid (Celemin 10 Plus from Otsuka Pharmaceutical India Private Limited; Composition - 10% Amino acid with electrolytes in 500 ml infusion) was administered as an intravenous infusion once daily (OD) for 5 days as per the hospital protocol. Two nutritional laboratory markers were evaluated for improvement in nutritional status in enrolled malnourished patients - a. Serum Pre-albumin (S-PA), b. Serum Retinol Binding Protein (S-RBP). Both these markers have short half-lives and changes in serum levels can be detected within 4-5 days. Changes in both parameters are known to correlate with nutrition status and prognosis in hospitalized patients.

All the patients had undergone a laboratory test for these two markers pre- and post-administration of the parenteral amino acid (Celemin10 Plus) for 5 days. The tests were conducted by SRL Diagnostics.

The primary objective of the case series was to study the

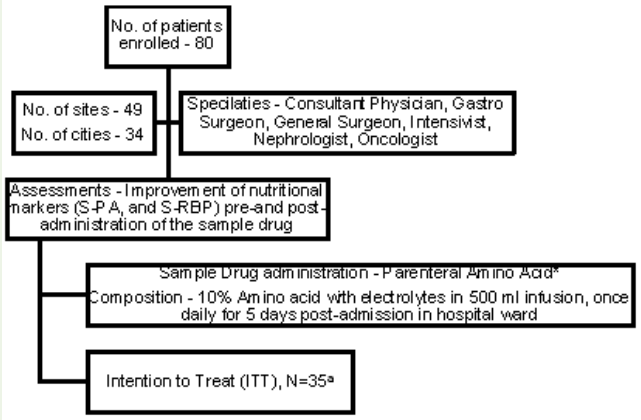

Figure 1: Study Flow Diagram.
*Celemin 10 plus (Composition - 10% Amino acid with electrolytes in 500 ml infusion, from Otsuka Pharmaceuticals Pvt. Limited)
[a]Both the pre-and post-test results were available for n=35 patients.

Citation: Sheth H, Mishra PK, Sharma R, Kumar M, Shukla H. Efficacy and Safety of Parenteral Amino Acids in Hospitalized Malnourished Patients: A Multicentric Case-Series. Indian J Nutri. 2022;9(3): 264.

effectiveness of parenteral amino acids in malnourished patients admitted tothe hospital ward by the evaluation of changes in nutritional markers (S-PA and S-RBP) levels. The study flow is presented in Figure 1.

Statistical Analysis

The major outcomes analyzed statistically were as following: a. Prevalence/incidence of malnourishment age-wise, b. Prevalence/incidence of malnourishment sex-wise, c. Nutritional laboratory markers (S-PA and S-RBP) for improvement in nutritional status in enrolled malnourished patients.

The data set was analyzed using Statistical Package for the Social Sciences (S.P.S.S.) Ver. 25. The quantitative variables were expressed as mean and standard deviation (Age, S-PA, S-RBP). The categorical variables were defined in number (n) and percentage (%) (Age groups, sex). Paired t-test was considered for comparing all the means. For comparison of categorical variables Chi-Square test or Fisher exact test (in case of sample size <6) was used. A p-value of <0.05 was considered statistically significant, and a p-value of<0.001 was highly significant.

Results

Baseline Characteristics

Out of Eighty malnourished patients admitted to the hospital ward, 42 (52.5%) were male, and 38 (47.5%) were female. Age ranges from 18-90 years, with a mean age of 51.22 years (Standard Deviation; SD - 17.66 years).

The baseline characteristics of the sample and distribution of specialties are presented in Table 1. Amongst all the specialties, the subgroup of Intensivists represented the major category, n=16 (32.65%). The age-wise prevalence demonstrates that the incidence of malnourishment was highest amongst the age group of 41-50 years.

Outcome Analysis

The data of both pre-and post-assessment for nutritional laboratory markers (S-PA,S-RBP) was available for n=35 patients, whereas the rest of the patients (n=45) were not included in the analysis due to various reasons, e.g., patients lost to follow-up, withdrawal of consent by the patient, lack of availability of test results, etc. The parenteral amino acid supplementation (10% Amino acid with electrolytes in 500 ml infusion) was administered once daily (OD) for 5 days to all these 35 patients, and the outcomes in the change in the nutritional laboratory markers are presented in Table 2 and Figure 2, and Figure 3.

In the patient population, where both pre-and post-intervention data were available, a statistically significant improvement was observed in the levels of both S-PA (pre-intervention; 0.102±0.058, post-intervention; 0.168 ± 0.086, p<0.001) and S-RBP (pre-intervention; 0.0291±0.030, post-intervention; 0.460 ± 0.036, p<0.001).

In a subgroup, analysis was conducted for the group of patients (n=15) treated by Intensivists. A significant increase in SPA [pre-intervention; 0.0993±0. 04431, post-intervention; 0.1353±0.05921, p=0.036] and S-RBP [pre-intervention; 0.022±0.0132, post-intervention; 0.034± 0.0192, p=0.004). The details are shown in Table 3.

Table 1: Baseline characteristics of patients.

Variable		N	(%)
Distribution across Specialties (n=49)	Consultant Physician	12	24.49
	Gastro Surgeon	5	10.20
	General Surgeon	10	20.41
	Intensivist	16	32.65
	Nephrologist	2	4.08
	Oncologist	4	8.16
Patient Gender (n=80)	Female	38	47.5
	Male	42	52.5
Age-wise (years) patient (n=80) distribution	≤20	4	5
	21-30	7	8.75
	31-40	14	17.5
	41-50	16	20
	51-60	14	17.5
	61-70	14	17.5
	71-80	6	7.5
	>80	5	6.25

Table 2: Change in Nutritional Markers (S-PA and S-RBP) pre-and-post supplementation of parenteral amino acid.

Variables		Mean	Std. Deviation	p-value
Serum Pre-Albumin (g/L) (n=35)	Base line (Pre-Intervention)	0.1020	0.058	<0.001
	Post Intervention	0.1683	0.086	
Serum Retinol Binding Protein (g/L) (n=35)	Base line (Pre-Intervention)	0.0291	0.0301	<0.001
	Post Intervention	0.0460	0.0362	

S-PA; Serum Pre-Albumin, S-RBP; Serum Retinol Binding Protein

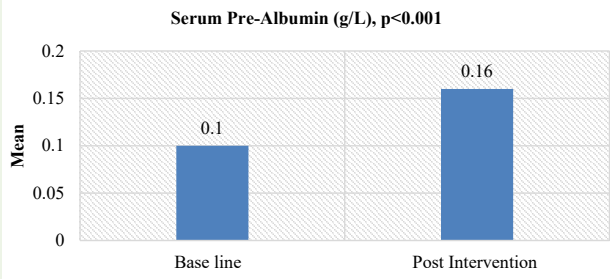

Figure 2: Change in Serum Pre-Albumin Levels (Pre-and Post-intervention).

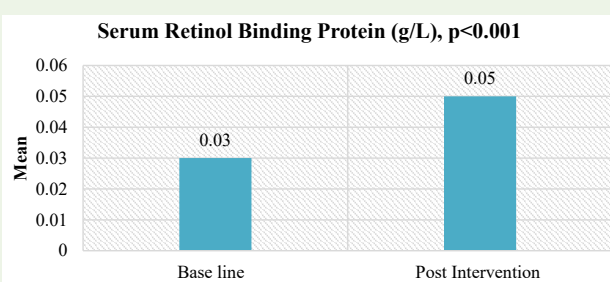

Figure 3: Change in Serum Retinol Binding Protein (Pre-and Post-Intervention).

Citation: Sheth H, Mishra PK, Sharma R, Kumar M, Shukla H. Efficacy and Safety of Parenteral Amino Acids in Hospitalized Malnourished Patients: A Multicentric Case-Series. Indian J Nutri. 2022;9(3): 264.

Table 3: Subgroup analysis for change in Nutritional Markers (S-PA and S-RBP) pre-and-post supplementation of parenteral amino acid in the patients treated with Intensivists (n=15).

Variables		Mean	Std. Deviation	p-value
Pre-Albumin (g/L) (n=15)	Base line (Pre-intervention)	0.0993	0.04431	0.036
	Post Intervention	0.1353	0.05592	
Retinol Binding Protein (g/L) (n=15)	Base line (Pre-intervention)	0.0220	0.01320	0.004
	Post Intervention	0.0340	0.01920	

Discussion

This multicentric case series was carried out to evaluate the role of parenteral amino acid supplementation in malnourished patients admitted to the hospital ward based on changes in nutritional laboratory markers (S-PA and S-RBP).

The results (as discussed above) demonstrate the benefits of parenteral amino acid supplementation on the nutritional status of this patient population. Furthermore, the subgroup analysis of patients treated by intensivists indicates a similar benefit, ascertaining the importance of parenteral amino acids in critically ill patients.

There is growing evidence of the role of parenteral amino acids supplementation in hospitalized and critically ill malnourished patients, with its ability to deliver anoptimal amount of amino acids and where the enteral nutrition (EN) is refused, inappropriate, or demonstrated to be incapable of meeting the patient's nutritional requirements [27].

A 2014 study by Aimova PP, et al. on the importance and dosage of amino acids in nutritional support of various pathological conditions in I.C.U. patients showed that amino acid requirements in parenteral nutrition (P.N.) are higher when the patient is stressed/traumatized/ infected than in the unstressed state. The study results demonstrated that 2.0-2.5 g protein/kg/day is safe and can be an optimal dose for the most critically ill adults to decrease the risk of morbidity and mortality [28].

In a systematic review by Wischmeyer PE, et al. 26 studies involving 2,484 patients demonstrated a strong trend towards reducing infectious complications, I.C.U. length of stay (L.O.S.), and a significant reduction in hospital L.O.S. establishing that parenteral amino acid supplementation, as a component of nutrition support, should be considered to improve outcomes in critically ill patients [29].

As per the ESPEN guidelines recommendation on clinical nutrition in the intensive care unit, parenteral amino acid supplementation may be considered in patients who cannot be fed adequately enterally, and a balanced amino acid mixture should be infused at approximately 1.3-1.5 g/kg/day (ideal body weight) [19].

However, there are some limitations to this case series study. Firstly, the appropriate tracking of the nutritional risk and clinical outcomes after discharge were not evaluated. Secondly, more accurate data could be obtained by expanding the sample size across different centers of India.

Conclusion

The results of this multicentric case series showed that the administration of parenteral amino acids (Celemin 10 Plus, containing 10% amino acid with electrolytes in 500ml infusion) significantly improves the nutritional markers - serum pre-albumin (S-PA) and serum retinol-binding protein (S-RBP) in hospitalized patients with malnutrition. Additionally, the benefits were also observed in the subgroup analysis of the patients under critical care treated by intensivists, suggesting nutritional benefits of parenteral amino acid administration in critically ill patients.

Acknowledgment

The authors would like to express sincere gratitude to all the investigators across the sites for their support and cooperation.

References

1. White J, Guenter P, Jensen G, Malone A, Schofield M, et al. (2012) Consensus Statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enteral Nutr 36: 275-283.
2. Kondrup J (2001) Can food intake in hospitals be improved?. Clin Nutr 20:153-160.
3. Bankhead R, Boullata J, Brantley S, Corkins M, Guenter P, et al. (2009) ASPEN enteral nutrition practice recommendations. J Parenter Enteral Nutr 33:122-167.
4. Rate DR, Site FT, Enteral FS, Hypocaloric HP (2012) Critical Illness.
5. Blackburn GL, Bistrian BR, Maini BS, Schlamm HT, Smith MF (1977) Nutritional and metabolic assessment of the hospitalized patient. JPEN J Parenter Enteral Nutr 1: 11-22.
6. Klein S, Kinney J, Jeejeebhoy K, Alpers D, Hellerstein M, Murray M, et al. (1997) Nutrition support in clinical practice: review of published data and recommendations for future research directions. Summary of a conference sponsored by the National Institutes of Health, American Society for Parenteral and Enteral Nutrition, and American Society for Clinical Nutrition. Am J Clin Nutr 66: 683-706.
7. Rosenbaum K, Wang J, Pierson Jr RN, Kotler DP (2000) Time□dependent variation in weight and body composition in healthy adults. JPEN J Parenter Enteral Nutr 24: 52-55.
8. Keys A (1948) Caloric undernutrition and starvation, with notes on protein deficiency. J Am Med Assoc 138: 500-511.
9. Sacks GS, Dearman K, Replogle WH, Cora VL, Meeks M, et al. (2000) Use of subjective global assessment to identify nutrition-associated complications and death in geriatric long-term care facility residents. J Am Coll Nutr 19: 570-577.
10. Soeters PB, Reijven PL, Schols JM, Halfens RJ, Meijers JM, et al. (2008) A rational approach to nutritional assessment. Clin Nutr 27: 706-716.
11. Matos LC, Tavares MM, Amaral TF (2007) Handgrip strength as a hospital admission nutritional risk screening method. Eur J Clin Nutr 61: 1128-1135.
12. Windsor JA, Hill GL (1988) Grip strength: a measure of the proportion of protein loss in surgical patients. Br J Surg 75: 880-882.
13. Sauer AC, Goates S, Malone A, Mogensen KM, Gewirtz G, et al. (2019) Prevalence of malnutrition risk and the impact of nutrition risk on hospital outcomes: results from nutritionDay in the US. JPEN J Parenter Enteral Nutr 43: 918-926.
14. Steiber A, Hegazi R, Herrera M, Zamor ML, Chimanya K, et al. (2015) Spotlight on global malnutrition: a continuing challenge in the 21st century. J Acad Nutr Diet 115: 1335-1341.

Citation: Sheth H, Mishra PK, Sharma R, Kumar M, Shukla H. Efficacy and Safety of Parenteral Amino Acids in Hospitalized Malnourished Patients: A Multicentric Case-Series. Indian J Nutri. 2022;9(3): 264.

15. Tappenden KA, Quatrara B, Parkhurst ML, Malone AM, Fanjiang G, et al. (2013) Critical role of nutrition in improving quality of care: an interdisciplinary call to action to address adult hospital malnutrition. J Acad Nutr Dietetics 113: 1219-1237.

16. Cederholm T, Barazzoni RO, Austin P, Ballmer P, Biolo GI, et al. (2017) ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 36: 49-64.

17. Braunschweig C, Gomez S, Sheean PM (2000) Impact of declines in nutritional status on outcomes in adult patients hospitalized for more than 7 days. J Am Diet Assoc 100:1316-1322.

18. Chakravarty C, Hazarika B, Goswami L, Ramasubban S (2013) Prevalence of malnutrition in a tertiary care hospital in India. Indian J Crit Care Med 17: 170-173.

19. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, et al. (2019) ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 38: 48-79.

20. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, et al. (2016) Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). JPEN. JPEN J Parenter Enteral Nutr 40: 159-211.

21. Compher C, Bingham AL, McCall M, Patel J, Rice TW, et al. (2022) Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. JPEN J Parenteral Enter Nutr 46: 12-41.

22. Evans DC, Corkins MR, Malone A, Miller S, Mogensen KM, et al. (2021) The use of visceral proteins as nutrition markers: an ASPEN position paper. Nutr Clin Pract 36: 22-28.

23. Lee ZY, Heyland DK (2019) Determination of nutrition risk and status in critically ill patients: what are our considerations?. Nutr Clin Pract 39: 96-111.

24. Mulherin DW, Cogle SV (2017) Updates in nutrition support for critically III adult patients. Hosp Pharm 52: 17-26.

25. Allingstrup MJ, Esmailzadeh N, Knudsen AW, Espersen K, Jensen TH, et al. (2012) Provision of protein and energy in relation to measured requirements in intensive care patients. Clin Nutr 31: 462-468.

26. Liu K, Chen Y, Liu T, Zhang K, Li Y, et al. (2021) Association Between Retinol-binding Protein and Sarcopenia in General Inpatient Older Adults: a Cross Sectional Study. Res square.

27. Hoffer LJ (2017) Parenteral nutrition: Amino acids. Nutrients 9: 257.

28. Aimova PP, Hronek M, Zadak Z (2014) The importance and dosage of amino acids in nutritional support of various pathological conditions in ICU patients. Biomed Pap Med Fac Palacky Olomouc Czech Repub 158: 346-355.

29. Wischmeyer PE, Dhaliwal R, McCall M, Ziegler TR, Heyland DK (2014) Parenteral glutamine supplementation in critical illness: a systematic review. Crit Care 18: 1-7.

Citation: Sheth H, Mishra PK, Sharma R, Kumar M, Shukla H. Efficacy and Safety of Parenteral Amino Acids in Hospitalized Malnourished Patients: A Multicentric Case-Series. Indian J Nutri. 2022;9(3): 264.