World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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Hospitalized patients receiving parenteral nutrition and supplemental enteral nutrition formulas: clinical outcomes of interest

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World Journal of Biology Pharmacy and Health Sciences, 2025, 21(02), 183-193

Publication history: Received on 02 February 2025; revised on 08 February 2025; accepted on 10 February 2025

Article DOI: https://doi.org/10.30574/wjbphs.2025.21.2.0156

Abstract

Aims; This study assessed the clinical and economic effects of incorporating supplementary enteral nutrition formulas (ENFs) alongside parenteral nutrition in malnourished patients who are hospitalised. The study aimed to ascertain the clinical ramifications of these interventions.

Methods: A study at King Hussein Medical Centre analyzed malnourished patients who received one of six tested enteral nutritional formulas and parenteral nutritional supplementation. The study included adult and elderly hospitalized patients, with exclusion criteria for missing more than 5% of data. Four nutritional cohorts were evaluated: those without supplemental enteral nutrition formulas, regular ENFs, specialized modular ENFs, and modular protein formulae. The study examined variations in albumin levels during hospitalization and modifications in the composite predictive ratio of C-reactive protein to albumin. The study also examined clinical outcomes like total hospital length of stay, mortality, gastrointestinal symptoms, and enteric gram-negative bacteria translocation.

Results: The study analyzed the distribution rates of enteral nutritional adjunctive formulas in patients with hypoalbuminemic conditions. It found no significant differences in distribution rates or average estimations across the six tested formulas. The highest average albumin level changes were observed in patients receiving ArgiMent as the standard enteral nutritional provision. The study also showed significant variations in hospital stay and overall fatality rate over 28 days. The cost expenditure for increasing albumin levels was lowest in patients using arginine/glutamine-based formulas. The study also found significant differences in gastrointestinal tolerances, with the highest incidence of intolerance symptoms in Group IV. The incidence of enterobacteriaceae positive cultures was minimal in glutamine and arginine-based formulas.

Conclusion: In conclusion, administering trophic doses of enteral feeding formulas to hospitalised patients dependent on total parenteral nutrition and exhibiting hypoalbuminemia may yield substantial clinical and economic advantages, especially if the enteral nutrition formulas are characterised by enhanced nutritional properties, including high protein density, glutamate, zinc, and prebiotic enrichments.

Keywords: Supplemental enteral feeding; Malnourished hospitalized patients; Parenteral nutrition; Kwashiorkor hypolabumenic patients

1. Introduction

Parenteral and enteral nutrition are two distinct approaches to providing nutrients to patients during illness, trauma, and operative interventions. Parenteral nutrition is provided intravenously, while enteral nutrition is provided via the

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gut [1-2]. In the setting of illness, trauma, and operative interventions, patients may be unable to maintain nutritional requirements, which can lead to malnutrition and increased hospital costs [3]. Interventions through parental or enteral nutrition can prevent nutritional deficit, improve patient well-being, and avoid inflammatory complications [4].

Patients are considered for an appropriate nutrition plan when they are unable to maintain or regain nutritional requirements and are likely to be so for five to seven days or longer [5]. Malnutrition is estimated to cost the UK healthcare service as much as £13 billion annually, but the true figure is likely greater due to increased and longer hospital costs and increased susceptibility to complications [6].

Numerous therapeutic situations necessitate nutritional care, including individuals unable to consume food or liquids, those experiencing intestinal failure or obstruction, and cancer patients [7]. Numerous published studies, including randomised controlled trials, were conducted in literature reviews to investigate the clinical impact of enteral nutritional supplementation, whether through trophic dosing, partial rates, or full enteral provision, in conjunction with partial parenteral supplemental nutritional fluids to compensate for deficits not met by enteral nutrition [8-9]. Most of the examined outcomes pertain to the duration of hospital admission, successful extubation from mechanical ventilation, complications associated with enteral and parenteral nutrition, infection rates and severities related to hyperinflammatory and immune statuses, as well as overall mortality, encompassing both early and late mortality [10-11].

However, of the hospitalised patients, the majority experienced hypercatabolic states linked with wasting syndromes. The predominant wasting symptoms observed in the stressed, hospitalised malnourished patients were associated with kwashiorkor and cachexia [12-13]. Nonetheless, the significant reliance on blood glucose as the primary cellular fuel, due to its lower VO2 rates compared to other energy-yielding macronutrients such as fatty acids and amino acids, results in the rapid depletion of glycogen stores [14-15]. This, in turn, leads to a sustained and pronounced hypercatabolic state of the endogenously lean body mass, which converts amino acid pools and reserves into the carbon backbone essential for the biosynthetic rate of gluconeogenesis [16-17].

The most significant endogenous amino acid precursors, together with the protein reserves in the lean body mass, particularly in the muscles, are circulating visceral albumin. Albumin is regarded as the biggest circulating protein in the body, and its catabolic rate is strongly connected with the hypercatabolic state in hyperinflammatory, stressed hospitalised patients [18-19]. As previously and succinctly stated, nearly all hospitalised patients are unable to satisfy their nutritional requirements through enteral nutrition alone; therefore, supplementation of at least partial nutrition is likely necessary to address deficiencies in energy, protein, and micronutrients [20-21]. There exist various categories of enteral formulas, including trophic dosing rates of approximately 10-20 ml per hour, partially provided formulas that can fulfil up to two-thirds of nutritional needs, and fully enteral provisions that may surpass 90% of total caloric and micronutrient requirements for patients [22-23]. The enteral provision of protein requirements is never fulfilled due to the elevated protein density demands in critically stressed hospitalised patients; hence, most parenteral amino acid supplementation is utilised to address these deficiencies in protein intake [24-25]. Although the enteral trophic rate offers minimal nutritional value, it presents numerous clinical advantages that contribute to the preservation of enterocyte and colonocyte integrity. There is substantial evidence indicating that it reduces enteral bacterial translocation, thereby decreasing the risk of disseminated infections caused by gram-negative bacteria, particularly those associated with extended-spectrum beta-lactamases (ESBL) and carbapenem-resistant Enterobacteriaceae (CRE) [26-27].

The present study primarily investigates and compares clinical outcomes in patients with hypoalbuminemia by evaluating the effects of various enteral nutritional formulas available at our institution, specifically Ensure®, Resource Optimum, RenaMent®, ArgiMent®, PROSource®, and Whey Protein (WP), in conjunction with parenteral nutritional supplementation.

2. Methods and materials

A retrospective, single-center, non-funded observational study was conducted across various departments of the King Hussein Medical Centre within the Royal Medical Services, focussing on malnourished patients who were administered one of six tested enteral nutritional formulas, alongside parenteral nutritional supplementation, during the study period from November 2018 to June 2023. This project received ethical approval from our Institutional Review Board (IRB) on August 27, 2024, under registration number 6_13/2024. The ultimate endorsement of this study was conducted by the Directorate of Professional Training and Planning at 2 Feb 2025. The permission form was waived in this study due to its retrospective nature, and the study adhered to the protocols and guidelines entirely compliant with the Helsinki standards.

The patients included in this trial were largely malnourished, as determined by biochemical parameters, including hypoalbuminemia with levels below 2.8 g per decilitre and an increased ratio of C-reactive protein to albumin. This study emphasised the anthropometric standard for assessing wasting and the subjective instruments for rating malnourished patients. This study comprised adult and elderly hospitalised patients, with the exclusion criterion being any patient data missing for more than 5%. The data were obtained from our institutional computer system, referred to as Hakeem, as well as from patients' written records and recorded assessment data in Excel sheets. However, the key test patient data examined in this research encompassed fundamental demographic information, diagnostic data, physical measurements, severity of wasting, and several nutritional biochemical indicators. Notably, patients in this study were eliminated if they were discharged or deceased before to completing a minimum of one week of stay.

The overall number of malnourished hypoalbuminemic patients was found to be 9,270. A total of 8,944 patients were excluded due to discharge or death before completing at least one week on dual nutritional regimens post-admission. Additionally, exclusion criteria were applied to 5821 patients who were entirely reliant on TPN or EN. Exclusion was predicated on the difficulty to gather patient data or the incompleteness identified in 3,123 cases. The final tally of patients involved in this study was 326 malnourished individuals. This study evaluated four unique nutritional cohorts: individuals without supplemental enteral nutrition formulas (ENFs), individuals receiving regular ENFs, individuals receiving specialised modular ENFs, and individuals receiving modular protein formulae.

This investigation examines percentage variations in albumin levels during hospitalisation and modifications in the composite predictive ratio of C-reactive protein to albumin in individuals hospitalised for at least one week. This study emphasised the changes in human albumin usage and the anticipated cost-effectiveness of increasing the albumin content by at least 1 g per decilitre. This study investigated the principal clinical outcomes, encompassing total hospital length of stay, overall 28-day mortality, incidence of gastrointestinal symptoms (GI Sxs), and the risk of translocation of enteric gram-negative bacteria (GNB) among the assessed enteral formulae.

The continuous variables of all patients will be represented as mean ± SD for comparisons within tested groups or as mean ± SEM for comparisons between tested groups using the ANOVA test. The categorical data were transformed into numerical values expressed as percentages via the $\chi 2$ test. The analytical values of the four examined groups (Group I-IV) were compared utilising IBM SPSS version 25 (IBM Corp., Armonk, NY, USA), whereas Microsoft Excel version 20 was employed for data collecting, filtering, and organisation. A significance level of 5% was employed in this study.

3. Results

The study found an average age of 58.4±9.9 years, with roughly 68.7% (224 cases) being male. This study did not demonstrate statistically significant differences in the distribution rates between critically ill and non-critically ill patients, nor in the distribution rates among medically and surgically admitted patients across the six tested enteral nutritional adjunctive formulas compared to supplemental parenteral nutrition. This study did not demonstrate statistically significant variance in the distribution rates or differences in average estimations across the six comparable enteral feeding cohorts concerning most of the examined baseline biochemical and nutritional variables. For example, we did not disclose statistically insignificant changes in baseline albumin levels, C-reactive proteins, and their composite ratio, the C-reactive protein to albumin ratio, across the six study groups. Furthermore, we did not observe statistically significant variations in total caloric requirements, the percentage of caloric goal attainment, or in the dual enteral nutrition combined with supplemental nutritional provision.

Upon examining the mean differences, adjusted for standard deviations, in the percentage changes of albumin levels across Groups I-VI, the highest estimated average was observed in the cohort receiving the ArgiMent formula as the standard enteral nutritional provision, with a result of 114%±19%. This was followed by the cohort utilising PROSource as the standard enteral nutrition, which showed 91%±12%. Next, the cohort that consumed reconstituted whey protein powder (25 grammes in 200 ml of distilled cold water) exhibited 46%±7%. Subsequently, the patients receiving RenaMent enteral supplementation demonstrated 33%±4%. Lastly, the cohorts using the standard enteral formulas of Resource Optimum and Ensure revealed means of 16.3%±1.8% and 14%±1.7%, respectively. Importantly, the statistically significant differences in albumin level changes during the six tested enteral nutrition regimens, administered for a minimum of one week, were concurrently associated with statistically significant variations in the daily consumption of human albumin infusion, measured in grammes, as well as in the percentage changes of the composite prognostic ratio between C-reactive protein and albumin. The Mean±SD values were -24.81±7.95 g/day, -24.07±5.67 g/day, -15.6±5.02 g/day, -11.85±3.92 g/day, -5.93±4.96 g/day, and -5.36±5.03 g/day, alongside -45%±22%, -23%±33%, -3%±42%, 16%±39%, 16.3%±50.6%, and 5.6%±55%, respectively.

Furthermore, this study demonstrated statistically significant variations in the estimated average length of hospital stay and the overall fatality rate over an anticipated period of 28 days. The means, adjusted for standard deviations and expressed as distributional rates, were observed to be highest in the cohort of patients who adopted ArgiMent as the specialised enteral nutrition, even at lower daily rates, which were close to or within the trophic dosing schedules [12.56±1.49 days and 7 (12.96%), respectively]. This study demonstrated statistically significant differences among Groups I-VI concerning the cost expenditure for increasing albumin levels by 1 gramme per decilitre. The lowest cost was observed in patients utilising arginine/glutamine-based enteral nutritional formulas, with an estimated average expenditure of approximately 20.6±6.7 USD. In contrast, the costs for 1 gramme albumin level increments in standard enteral nutritional formulas were 271.9±40.9 USD for Group II and 364.7±86.3 USD for Group I.

Nonetheless, while the economic expenditure unadjusted for the increasing albumin levels was statistically insignificant in this study, significant differences emerged when considering the variations among the six enteral nutritional formulas regarding their clinically impactful effects on serum albumin levels relative to baseline measurements. This study demonstrated statistically significant variations and disparities in gastrointestinal tolerances, highlighting the incidence of intolerance symptoms such as bloating, cramping, dyspepsia, and increased gastrointestinal residual volumes. The variations in statistically significant differences in distributional rates among the six tested enteral nutrition groups were most pronounced for the incidence rates of gastrointestinal symptoms, with Group IV exhibiting the highest rate at 38 (70.4%) and Group I the lowest at 30 (53.6%). Upon assessing the magnitude of the residual volumes in their adjusted averages relative to their standard deviations, we identified a statistically significant lower average in Group II (18.6±14.2 ml/day) compared to the higher average recorded in Group I (194.8±156.4 ml/day).

Finally, upon examining the notable differences in the prevalence of enterobacteriaceae positive cultures in the blood samples among the six comparative cohorts, we determined that the incidence was minimal in the glutamine and arginine-based enteral nutritional formulas (4 (7.4%)) and maximal in the cohorts receiving standard enteral nutritional formulas in Group II and Group I (12 (22.2%) and 15 (26.8%), respectively). The comparative results analyses are expressed below in Table 1-2.

Table 1 Comparison data among the six tested groups

Variables		**Total (N=326)**	**Standard ENFs (N=110)**		**Specialized ENFs (N=108)**		**MPF (N=108)**		**P-Value**
			Group I Ensure® (N=56)	**Group II Resource® Opt (N=54)**	**Group III RenaMent® (N=54)**	**Group IV ArgiMent® (N=54)**	**Group V PROSource® (N=54)**	**Group VI WP100% (N=54)**	
Age (Yrs)		58.4±9.9	61.3±8.7	58.8±10.4	53.9±9.1	58.9±8.9	59.6±10.2	57.7±11.1	0.004(S)
Sex	Male	224 (68.7%)	42 (75.0%)	36 (66.7%)	42 (77.8%)	28 (51.9%)	42 (77.8%)	34 (63.0%)	0.021(S)
	Female	102 (31.3%)	14 (25.0%)	18 (33.3%)	12 (22.2%)	26 (48.1%)	12 (22.2%)	20 (37.0%)	
Ward	Non Critical	160 (49.08%)	29 (51.79%)	27 (50%)	28 (51.85%)	31 (57.41%)	22 (40.74%)	23 (42.59%)	0.081 (NS)
	Critical	166 (50.92%)	27 (48.21%)	27 (50%)	26 (48.15%)	23 (42.59%)	32 (59.26%)	31 (57.41%)	
Medical Dx	Medical	153 (46.93%)	28 (50%)	25 (46.29%)	23 (42.59%)	24 (44.44%)	26 (48.15%)	27 (50%)	0.106 (NS)
	Surgical	173 (53.07%)	28 (50%)	29 (53.70%)	31 (57.41%)	30 (55.56%)	28 (51.85%)	27 (50%)	
BW_1 (Kg)		74.9±10.3	73.49±8.51	74.07±11.87	77.73±8.49	73.44±11.24	73.67±11.58	77.22±9.34	0.074 (NS)
CRP_1 (mg/dl)		6.83±3.58	7.86±4.11	2.11%±0.76%	5.92±3.02	7.75±3.72	6.00±3.02	6.85±4.15	0.05 (NS)

ALB_1 (g/dl)	2.25±0.32	2.25±0.28	2.28±0.30	2.26±0.27	2.20±0.23	2.26±0.44	2.25±0.37	0.9 (NS)
$H.ALB_1$ (g/day)	24.11±6.44	24.64±6.31	22.96±5.37	23.33±6.14	24.81±7.95	24.07±5.67	24.8±6.93	0.5 (NS)
CRP_1: ALB_1	3.18±1.94	3.63±2.14	2.98±1.49	2.81±1.75	3.66±2.11	2.72±1.56	3.26±2.32	0.064 (NS)
CRP_2 (mg/dl)	7.94±3.11	7.78±2.91	7.62±2.42	8.13±2.94	8.40±3.83	7.60±3.06	8.13±3.37	0.7 (NS)
ALB_2 (g/dl)	3.40±0.90	2.56±0.28	2.62±0.27	2.93±0.23	4.76±0.44	4.32±0.31	3.25±0.37	0.000 (S)
$H.ALB_2$ (g/day)	9.57±8.47	19.29±4.62	17.04±5.36	11.48±4.52	0.00±0.00	0.00±0.00	9.26±4.69	0.000 (S)
CRP_2: ALB_2	2.57±1.33	3.19±1.55	3.02±1.22	2.87±1.32	1.84±0.94	1.82±0.85	2.63±1.29	0.00 (S)
ΔALB (g/dl)	1.15±0.83	0.31±0.00	0.36±0.00	0.72±0.00	2.50±0.00	2.04±0.00	1.00±0.00	0.000 (S)
ΔH.ALB (g/day)	-14.54±9.56	-5.36±5.03	-5.93±4.96	-11.85±3.92	-24.81±7.95	-24.07±5.67	-15.6±5.02	0.000 (S)
%Δ ALB	52%±39%	14%±1.7%	16.3%±1.8%	33%±4%	114%±19%	91%±12%	46%±7%	0.00 (S)
%Δ CRP	36%±60%	20%±63%	36%±59%	54%±53%	19%±48%	48%±65%	42%±63%	0.007 (S)
%Δ CRP:ALB ratio	-5.5%±47%	5.6%±55%	16.3%±50.6%	16%±39%	-45%±22%	-23%±33%	-3%±42%	0.00 (S)

Data are presented as Mean±Standard deviation and are analyzed by using ANOVA test (at p-value< 0.05).

Yrs: Years.
BW: Actual body weight.
N: Number of study's hospitalized patients.
Group I: Hospitalized patients on TPN supplemented partially by Ensure®.
Group II: Hospitalized patients on TPN supplemented partially by Resource®Optimum.
Group III: Hospitalized patients on TPN supplemented partially by RenaMent®.
Group IV: Hospitalized patients on TPN supplemented partially by ArgiMent®.
Group V: Hospitalized patients on TPN supplemented partially by PROSource®.
Group VI: Hospitalized patients on TPN supplemented partially by reconstituted WP 100%.

1: baseline at admission.
2: 2 weeks after admission.
Δ: Changes.
S: Significant (P-Value <0.05).
NS: Non-significant (P-Value >0.05).
Dx: Diagnosis.
ALB: Albumin level.
CRP: C-reactive protein.
CRP: ALB: C-reactive protein to albumin ratio.
H.ALB: Human albumin.

Table 2 Comparison data among the six tested groups

Variables		**Total (N=326)**	**Standard ENFs (N=110)**		**Specialized ENFs (N=108)**		**MPF (N=108)**		**P-Value**
			Group I Ensure® (N=56)	**Group II Resource® Opt (N=54)**	**Group III RenaMent® (N=54)**	**Group IV ArgiMent® (N=54)**	**Group V PROSource® (N=54)**	**Group VI WP100% (N=54)**	
Enteric BSI	Negative	271 (83.1%)	41 (73.2%)	42 (77.8%)	44 (81.1%)	50 (92.6%)	48 (88.9%)	46 85.2%)	0.03 (NS)
	Positive	55 (16.9%)	15 (26.8%)	12 (22.2%)	10 (18.9%)	4 (7.4%)	6 (11.1%)	8(14.8%)	
TOLR	GI Sx (0,1)	200 (61.3%)	30 (53.6%)	30 (55.6%)	32 (59.3%)	38 (70.4%)	36 (66.7%)	34 (63.0%)	0.031 (S)
	GI Sx (≥2)	126 (38.7%)	26 (46.4%)	24 (44.4%)	22 (40.7%)	16 (29.6%)	18 (33.3%)	20 (37.0%)	

ENF Cost (USD/day)		1.13±0.96	1.18±0.94	0.77±0.42	1.59±0.85	1.26±0.96	1.75±1.14	0.25±0.15	0.000(S)
TPN Cost (USD/ day)		51.8±16.2	57.0±22.9	50.2±12.4	50.9±11.1	50.3±15.9	50.9±16.3	51.0±15.3	0.2 (NS)
H.ALB Cost (USD/day)		26.8±23.7	53.9±12.9	47.7±15.0	32.1±12.6	0.0±0.0	0.0±0.0	25.9±13.1	0.000 (S)
CER (USD/ +1 g ALB/dl)		147.5±136.4	364.7±86.3	271.9±40.9	116.8±29.2	20.6±6.7	25.8±8.5	77.2±23.7	0.000 (S)
TCR (Cal/kg/day)		21.10±5.32	22.34±7.04	21.06±5.49	20.33±3.33	21.55±4.89	20.93±5.22	20.40±5.17	0.36 (NS)
TCR (Cal/day)		1449±388	1548±538	1423±325	1433±265	1446±371	1441±399	1398±369	0.43 (NS)
%Goal Cal		79.4%±7.9%	81.8%±8.9%	78.8%±7.5%	81.5%±6%	77.9%±8.4%	77.1%±8.2%	79.3%±6.9%	0.15 (NS)
ENFs	Vol (ml/day)	78.2±96.0	194.8±156.4	124.8±68.8	54.2±28.9	18.6±14.2	23.4±15.2	48.8±29.7	0.000 (S)
	%Cal_TCR	5.5%±4.5%	11.2%±4.4%	8.8%±2.5%	7.3%±2.5%	2.4%±1.0%	1.3%±0.5%	1.6%±0.6%	0.000 (S)
	PRO (g/day)	5.75±3.99	7.19±5.72	5.43±2.94	4.71±2.5	5.58±4.26	5.71±3.72	5.86±3.57	0.34 (NS)
AA 10% vol (ml/day)		517.9±358.7	646.8±514.7	488.7±269.4	424.2±225.8	501.8±383.8	513.6±335.2	527.5±321.3	0.042 (S)
IFE 20% vol (ml/day)		168.16±52.06	170.00±52.28	161.96±42.18	192.8±46.6	156.3±49.9	163.7±54.0	164.0±59.8	0.005 (S)
DX 20% vol (ml/day)		751.0±277.8	846.4±365.1	738.7±260.1	751.5±169.3	761.4±289.8	713.6±310.9	690.9±207.9	0.066(NS)
Dual TPN and EN days		9.03±1.78	8.93±1.57	9.40±2.31	8.87±1.44	9.20±1.81	8.71±1.73	9.22±2.13	0.057(NS)
% PC_ TC		14.7%±5.5%	16.6%±6.5%	14.6%±4.1%	12.6%±4%	14.07%±6.1%	14.8%±5.3%	15.6%±5.5%	0.004 (S)
% Carb Cal_ TC		35.2%±5.4%	36.9%±5.7%	35.2%±4.9%	36.2%±4%	35.8%±5.2%	33.3%±6.6%	34.0%±5.3%	0.005 (S)
% Lipid Cal_ TC		29.5%±5.7%	28.3%±5.4%	29.1%±5.6%	32.8%±3.7%	28.0%±6.7%	28.9%±5.5%	29.6%±5.7%	0.000 (S)
g Carb: g Lipid ratio		3.43±1.29	3.67±1.05	3.45±1.20	3.01±0.50	3.83±2.01	3.30±1.30	3.27±1.12	0.013 (S)
Hospital Stay day(s)		15.02±2.39	17.82±1.27	16.59±1.46	14.89±2.57	12.56±1.49	13.44±1.51	14.74±0.65	0.000 (S)
Overall 28-day Survival		246 (75.46%)	35 (62.5%)	38 (70.37%)	40 (74.07%)	47 (87.04%)	44 (81.48%)	42 (77.77%)	0.031 (S)
Overall 28-day Mortality		80 (24.54%)	21 (37.5%)	16 (29.63%)	14 (25.93%)	7 (12.96%)	10 (18.52%)	12 (22.22%)	
Data are presented as Mean±Standard deviation and are analyzed by using ANOVA test (at p-value< 0.05).									

4. Discussion

This retrospective study focused on malnourished patients with wasting admitted to the King Hussein Medical Centre from 2018 to 2023. We specifically examined the patients' albumin levels due to the high prevalence of hypoalbuminemia associated with the kwashiorkor condition in these patients, which primarily relies on amino acid-derived gluconeogenesis for optimal glucose utilisation in stressed individuals. This study involved three kwashiorkor patients who received nutritional support through dual enteral nutritional supplementation, utilising a comparative analysis of six enteral formulas, including standard, specialised, and modular protein formulas, alongside parenteral nutrition to address the macronutrient deficiencies not fulfilled by enteral nutrition. The study found that the average volume of parenteral nutritional supplementation was approximately 517.9±358.7 ml/day for amino acids at 10%, 168.16±52.06 ml/day for intravenous fat emulsions at 20%, and 751.0±277.8 ml/day for dextrose glucose water 205 solution. The average total volume of enteral nutritional supplements assessed in this study was 78.2±96.0 ml/day, representing approximately 5.5%±4.5% of the estimated average total energy requirements.

This study, however, provided a thorough assessment and comparison of the most frequently utilised enteral nutritional formulas in clinical practice, encompassing standard formulas like Ensure and Resource Optimum, specialised high-caloric formulas such as RenaMent, specialised formulas with elevated arginine and glutamine content like ArgiMent, and specific protein modular formulas, including the ready-to-use PROSource package and the reconstituted whey protein powder. Nevertheless, all the examined enteral nutritional formulas were administered through tube feeding, predominantly via nasogastric tubes, at varying rates largely determined by the patient's gastrointestinal tolerance, including the extent of residual amounts. Nonetheless, the gastrointestinal symptoms that predominantly impact the tolerance to enteral nutrition are bloating, cramps, diarrhoea, and dyspepsia. In instances of gastrointestinal intolerance, various global guidelines and expert opinions advocate for a gradual tapering strategy, aimed at facilitating gastrointestinal rehabilitation for timely weaning from parenteral nutrition and minimising associated complications. This approach primarily relies on the supplementation of parenteral nutritional fluids until the protein density provisional rate reaches at least two-thirds of the total patient requirements, a target rarely met in severely stressed hospitalised patients, particularly those in critical care. Consequently, a dual nutritional strategy is often necessary, incorporating primarily enteral nutrition supplemented by parenteral nutrition, predominantly in the form of amino acids and micronutrient fluids [28-30].

This research study implemented trophic dosing of an average of 10 ml per hour from an enteral specialised nutritional formula for 16 hours daily, with overnight interruption, in accordance with our institutional feeding protocols. This resulted in a total trophic feeding volume of approximately 150±10 ml per day, which would optimally equate to 160 ml per day in the absence of any feeding interruptions. The recommended target is 160 ml per day of enteral trophic feeding, supplying patients with a minimum of 160 Cal/day for normal enteral nutritional formulas, perhaps exceeding 200 Cal per day for specialised enteral nutritional formulas. It is crucial to consider the adoption of specialised enteral nutritional formulas within the trophic feeding strategy, whether as an initial feeding rate or as a continuous feeding protocol for patients with severe gastrointestinal intolerance. Approximately 5 grammes of protein, particularly in the form of specialised nutritive amino acids such as glutamine, with or without arginine, should be utilised, as demonstrated in the cohort of patients in group IV who received specialised enteral nutritional formulas rich in glutamine, arginine, and other micronutrients like ascorbic acid and zinc [31-33]

Our overarching hypothesis in clinical nutrition posits that augmenting the protein density of any enteral nutritional formula, particularly specialised formulations, enhances the probability of meeting the targeted protein requirements without incurring the risks associated with hypercaloric overfeeding and fluid overload. This adjustment is also associated with improved gastrointestinal tolerance and a reduced likelihood of elevated gastrointestinal residual volume [34-35]. In this study, we present a proposed theory demonstrating that the specialised enteral nutritional formula, characterised by higher caloric and protein density and enriched with enterocyte nutritive agents, resulted in the Group IV cohort exhibiting a statistically significant reduction in the incidence of gastrointestinal bloating, cramping, and other indicators of gastrointestinal intolerance, alongside a statistically significant decrease in gastric residual volume.

Patients who are naïve to enteral nutrition feeding, even with trophic dosing schedules, may exhibit compromised integrity of the enterocyte and colonocyte systems, resulting in an increased susceptibility to bacterial translocation of gram-negative Enterobacteriaceae pathogens, primarily including but not limited to extended-spectrum beta-lactamases (ESBL) and carbapenem-resistant Enterobacteriaceae, as well as carbapenemase-producing Enterobacteriaceae from genera such as E. coli, K. pneumoniae, Enterobacter, Morganella spp., Serratia spp., Providencia spp., and other enteric gram-negative bacteria. These enteric gram-negative bacteria are widely prevalent among hospitalised patients and are a significant contributor to the excessive use of broad-spectrum antibiotics, particularly

carbapenems. Trophic feeding utilising a specialised enteral nutritional formula predominantly comprising glutamine, as observed in the Group IV cohort, is significantly evidenced by numerous emerging studies in the literature to mitigate the risk of translocation of enteric gram-negative bacteria and, consequently, gastrointestinal-related Enterobacteriaceae sepsis [36-38].

Patients without adequate dietary Fiber (EF) may compromise the integrity of enterocytes and colonocytes, increasing the risk of bacterial translocation and gastrointestinal-related enterobacteriaceae sepsis. Enterocyte-specific nutrients, such as short-chain fatty acids (SCFAs), are crucial for maintaining enterocyte integrity. However, their efficacy depends on prebiotic bacteria for fermentation, which may be influenced by antibiotics. GLT, another enterocyte nutrient, operates independently of prebiotics and is unaffected by broad-spectrum antibiotics. The GLT theory may explain the enhanced ENF GIT tolerance and positive clinical outcomes in patients with ALB, GIT-related systemic inflammatory response syndrome (SIRS), and GIT-related enterobacteriaceae sepsis. ArgiMent®, a unique formulation, showed the most significant positive clinical and economic outcomes across all variables due to its high protein density, superior protein quality, elevated caloric density, immune-enhancing nutrients, and prebiotic galacto-oligosaccharides (GOS or Bimuno) and zinc. These factors may explain the enhanced liver albumin synthesis observed in patients with short bowel syndrome or other total parenteral nutrition indications, particularly those with a strong suspicion of zinc deficiency [39-40]. This research is constrained by its retrospective approach and reliance on single-centre data. Nevertheless, our facility is a proficient and high-capacity unit, therefore our data may be beneficial for other centres. A comprehensive, multisite, prospective investigation is required to account for many confounding variables.

5. Conclusion

In conclusion, administering trophic doses of enteral feeding formulas to hospitalised patients dependent on total parenteral nutrition and exhibiting hypoalbuminemia may yield substantial clinical and economic advantages, especially if the enteral nutrition formulas are characterised by enhanced nutritional properties, including high protein density, glutamate, zinc, and prebiotic enrichments.

Compliance with ethical standards

Acknowledgments

Our appreciation goes to staff of the departments of Royal Medical Services for their enormous assistance and advice.

Disclosure of conflict of interest

There is no conflict of interest in this manuscript

Statement of ethical approval

This project received ethical approval from our Institutional Review Board (IRB) on August 27, 2024, under registration number 6_13/2024. The ultimate endorsement of this study was conducted by the Directorate of Professional Training and Planning at 2 Feb 2025. The permission form was waived in this study due to its retrospective nature, and the study adhered to the protocols and guidelines entirely compliant with the Helsinki standards.

Statement of informed consent

Owing to the retrospective design of this study, the informed consent form was waived.

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