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REVIEW ARTICLE

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Major approaches to parenteral nutrology therapy in the intensive care unit: a systematic review

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Abstract

Introduction: In the context of parenteral nutrition, critically ill patients are associated with a state of catabolic stress and a systemic inflammatory response. Patients admitted to intensive care units (ICU) have a prevalence of malnutrition greater than 35%. **Objective:** It was to carry out a systematic review to list the main approaches to macro and micronutrients in parenteral therapy in intensive care units. **Methods:** The PRISMA Platform systematic review rules were followed. The research was carried out from June to July 2025 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** 115 articles were found. A total of 45 articles were evaluated and 25 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 20 studies with a high risk of bias and 32 studies that did not meet GRADE. It was concluded that several clinical studies critically analyzed the evolution and changes that marked the development of parenteral nutrition in intensive care units. Standard solutions of crystalline amino acids, although devoid of side effects, remain incomplete about their composition (e.g., glutamine). Lipid emulsions have evolved a lot and are now included in bi- and tri-compartmented feeding bags, allowing true total parenteral nutrition, as long as daily micronutrients are prescribed. The question of exact individual energy, macro and micronutrient needs has not yet been resolved. Many complications attributed to total parenteral nutrition are the consequence of under- or overfeeding. The historical concept of hyperalimentation is the main cause, along with the use of fixed weight-based predictive equations (incorrect in 70% of critically ill patients).

Keywords: Parenteral therapy. Macronutrients. Micronutrients. Parenteral nutrition. Intensive care unit.

Introduction

In the context of Nutritional Therapy (NT), critically ill patients are associated with a state of catabolic stress and a systemic inflammatory response **[1]**. Patients admitted to intensive care units (ICUs) have a prevalence of malnutrition greater than 35% **[2,3]**. When analyzing only trauma patients, it is observed that, even if they are well-nourished, after hospital admission, they tend to develop protein-calorie malnutrition rapidly. Studies conducted with critically ill patients found that 40% of patients experience weight loss of more than 10 kg in the period immediately following ICU admission **[4-6]**.

While the prevalence of malnutrition in childhood has been decreasing in recent decades, it remains higher than in developed countries. Similarly, the percentage of deaths from severe malnutrition at the hospital level is well above the World Health Organization recommendation **[7]**.

In the case of patients over 80 years of age, a Dutch study published at the 39th edition of the European Congress of Clinical Nutrition (ESPEN) in 2017 **[4]** and updated in 2023 **[2]** found an association between the percentage of muscle mass and complications and hospital death. In the group with low muscle mass, 45% had complications and 23% died in the hospital, compared to 15% and 4%, respectively, in the group with normal muscle mass.

Studies have shown that disease severity, body temperature, and certain drugs, such as muscle relaxants and sedatives, can increase or decrease energy metabolism. Variations occur according to the population evaluated; in general, an increase in total energy expenditure (TEE) of 110-120% is observed in patients undergoing elective surgery, and in clinicians, 135-150% in post-trauma situations, and 150-170% in sepsis **[6]**.

Therefore, the present study aimed to conduct a systematic review to list the main approaches to macronutrients and micronutrients in parenteral therapy in intensive care units.

Methods

Study Design

The systematic review guidelines of the PRISMA Platform (Transparent reporting of systematic review and meta-analysis) were followed. Available at: www.prismastatement.org/. Accessed on: 06/25/2025.

Data Sources and Search Strategy

The search strategies for this systematic review were based on the keywords (DeCS/MeSH Terms): *"Parenteral therapy. Macronutrients. Micronutrients. Parenteral nutrition. Intensive care unit".* The search was conducted from June to August 2025 in the Web of Science, Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. Furthermore, a combination of keywords with the Boolean operators "OR", "AND", and "NOT" was used to target scientific articles of interest.

Study Quality and Risk of Bias

Studies were selected that rigorously presented the results of the search process, demonstrated scientific quality according to the GRADE classification, and did not present a significant risk of bias, that is, that could compromise the reliability of the results. According to GRADE recommendations, the quality of scientific evidence in the studies addressed was classified as high, moderate, low, or very low, according to the risk of evidence bias, sample size, clarity of comparisons, precision, and consistency in the effects of the analyses. High-quality evidence was assigned using four criteria: 1) Randomized or prospective controlled clinical trials; 2) Retrospective clinical trials or case series; 3) Sample size greater than 15 participants; 4) Studies with statistically well-constructed results; 5) Studies published in indexed journals with a significant impact factor; 6) Descriptive, interpretive, theoretical (credibility of methods), and pragmatic validity.

The Cochrane Instrument was adopted to assess the risk of bias in the selected studies using Cohen's test to calculate the effect size - the magnitude of the difference in results between the studies addressed in this study (effect size) versus the inverse of the standard error (precision or sample size) to determine the risk of bias of the studies using the Funnel Plot.

Results and Discussion

Summary of Literature Findings

115 articles were found. Initially, duplicate articles were excluded. After this process, the abstracts were evaluated, and a further exclusion was carried out, removing articles that did not include the theme of this article, resulting in 45 articles. A total of 25 articles were evaluated in full and included and developed in this systematic review study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 20 studies with a high risk of bias and 32 studies that did not meet the GRADE criteria.

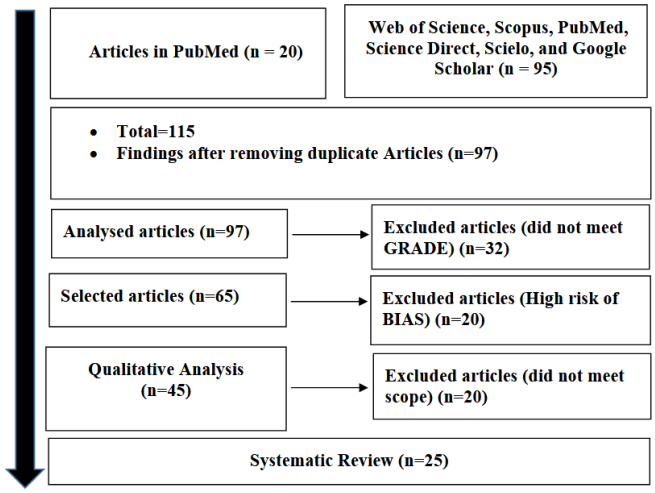

Figure 1. Flowchart showing the article selection process. Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's d test. Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph showed a symmetrical behavior, not suggesting a significant risk of bias, both between studies with small sample sizes (lower precision) shown at the bottom of the graph and in studies with large sample sizes shown at the top.

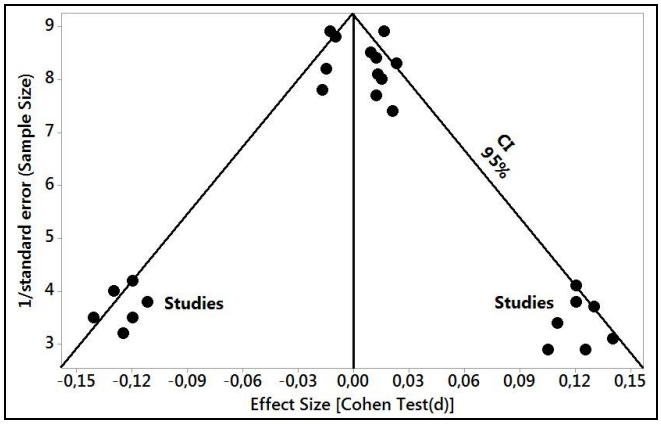

Figure 2. The symmetrical funnel plot does not suggest a risk of bias among the small sample size studies shown at the bottom of the graph. Studies with high confidence and high recommendation are shown above the graph (n=25 clinical studies). Source: Own authorship.

Main Approaches to Parenteral Therapy in ICUs

In this sense, the American Society for Parenteral and Enteral Nutrition (ASPEN) and ESPEN have described the use of Parenteral Nutrition (PN). PN can be considered a third route for human nutrition after oral intake and enteral nutrition. The main objective of PN is to provide a mixture of nutrients closely related to requirements safely and avoid complications **[1-3]**. However, PN presents a considerable risk of overfeeding, which can be as harmful as underfeeding. Long-term survival data (expressed as 6-month survival) will also be considered a relevant outcome measure **[4]**.

The critically ill patient is a heterogeneous individual in relation to the stages of the underlying disease, such as the number and severity of organ dysfunction. Pathophysiological changes or therapeutic measures may vary considerably among individual critically ill patients. To be effective, therapy for a specific disease requires a correct indication, and it is necessary to precisely define the disease. Furthermore, TN in a critically ill patient is an adjuvant therapy, but never replaces the causal therapy of the underlying disease, for example, sepsis resulting from peritonitis or pneumonia, hemorrhagic shock, severe trauma **[2,4]**.

In this way, macronutrients and micronutrients stand out. Macronutrients, represented by carbohydrates, proteins, and fats or lipids, are distributed in foods and must be ingested daily to ensure a healthy diet. Although, as a general rule, a daily percentage of each macronutrient is established, it should be remembered that people perform different activities in different routines and, also due to pathologies, may require different dietary and supplement demands **[3]**.

Micronutrients, on the other hand, are represented by vitamins and minerals and are present in a wide variety of foods. Each of these nutrients performs specific functions, essential for the health of our cells and for harmonious functioning. Unlike macronutrients, vitamins and minerals are needed in small quantities. However, to meet the recommended intake of these nutrients, their supply through food or supplements must be daily and from different sources, also depending on the clinical conditions of each individual **[1-3]**.

After several assessments, considering various aspects of the patient, nutritional therapy (NT) is initiated in critically ill patients. In this context, guidelines and practical clinical reviews published by nutrition societies for the nutritional management of the patient are consulted, such as the American Society for Parenteral and Enteral Nutrition (ASPEN), the European Society for Clinical and Metabolic Nutrition (ESPEN), and the Brazilian Guidelines on Nutritional Therapy (DITEN). These guidelines contain recommendations for energy and macronutrients, such as proteins, carbohydrates, and lipids, for various types of patients, including critically ill and severely ill patients **[8]**.

Nutritional Screening and Diagnosis

Nutritional screening is a process that aims to identify individuals who are malnourished or at risk of malnutrition, with the objective of performing a specific nutritional assessment and subsequently implementing appropriate NT. Patients at nutritional risk, or already malnourished, have increased length and cost of hospitalization, a greater number of complications, and an increased risk of mortality **[1,2]**.

Thus, the Brazilian Society of Enteral and Parenteral Nutrition (BRASPEN), aligned with several other TN societies, recommends nutritional screening within 48 hours of hospital admission. Considering the rapid deterioration of nutritional status that occurs in critically ill patients, efforts should be made to screen within the first 24 hours of admission, with subsequent, more detailed nutritional assessment in patients who present nutritional risk **[4]**.

There are several tools for nutritional screening of hospitalized patients, they generally use the parameters that determine the deterioration of nutritional status (recent weight loss, low body mass index, altered food intake), such as Nutritional Risk in the Critically Ill Patient (NUTRIC), Nutritional Risk Screening-2002 (NRS-2002), Subjective Global Nutritional Assessment (SGA), Mini Nutritional Assessment (MNA), Malnutrition Screening Tool (MST), Universal Malnutrition Screening Instrument (MUST) **[4]**.

However, considering that the inflammatory and hypercatabolic state of critically ill patients accelerates the malnutrition process, the severity of the disease should be interpreted with emphasis, since the nutritional risk of the critically ill patient depends not only on the nutritional status, but also on factors that alter the length of stay, days of mechanical ventilation, and mortality **[3]**.

In this way, NUTRIC and NRS-2002 are tools that contemplate the assessment of disease severity. NUTRIC allows for a more accurate analysis of severity, as it uses a set of prognostic indices in the ICU, the Acute Physiology and Chronic Health Evaluation II (APACHE II), and the Sepsis-Related Organ Failure Assessment (SOFA). NRS-2002 uses only the APACHE II > 10 cutoff point to determine maximum severity, which has proven to be a limited interpretation because around 80% of patients would fit these characteristics **[4]**.

According to DITEN, there is strong evidence that malnutrition is both a cause and an effect of serious diseases, and not a consequence, as was commonly believed a few years ago. Underestimating it would therefore bring serious problems to the patient. Furthermore, the Project states that nutritional therapy should be initiated within the first 24-48 hours, especially in patients diagnosed with malnutrition and/or intense catabolism resulting from the pathological condition **[4]**.

The most recent guideline, organized by the Society of Critical Care Medicine (SCCM) and the ASPEN in 2016, recommends that, for estimating the energy needs of critically ill patients, a pocket formula based on a ratio of 25–30 kcal/kg/day should be used (when the use of indirect calorimetry is unavailable). In addition, the entities warn of the importance of regular reassessments according to changes in the clinical picture. DITEN, on the other hand, recommends offering 20 to 25 kcal/kg/day to critically ill patients, respecting the patient's tolerance **[4,8]**.

In pediatrics, screening to assess nutritional risk is fundamental and should be incorporated as part of the hospital admission procedure. The pediatric nutritional screening tool should be quick and easy to use. It can be performed by a qualified healthcare professional using specific tools available, but, in general, the nutritionist is responsible for applying nutritional screening in most hospitals **[7,9]**. The screening instrument should be applied at the time of hospitalization or as early as possible after hospital admission, preferably within the first 24 hours, and reapplied every 7 days for patients without nutritional risk and with moderate risk. The screening scores should be recorded in the medical records **[9]**.

The STRONG Kids tool, although not validated, is the one that best adapts to the Brazilian reality. For hospitalized children under 2 years of age, nutritional assessment upon admission and monitoring by measuring daily weight, height, and weekly head circumference is recommended, with data recorded in a sequential graph. In children over 2 years of age, nutritional assessment upon admission and monitoring by measuring weekly weight and monthly height is recommended. This monitoring can be carried out at shorter intervals, depending on the impairment of nutritional status upon admission or the severity of the underlying disease **[7]**.

For nutritional classification, the body mass index for age (BMI/A) expressed as a percentile or Z-score is used. The reference standard employed is that of the World Health Organization. In this context, to estimate the energy needs of adult patients, indirect calorimetry is considered a safe, practical, non-invasive method with the ease of use of portable equipment. The method can be used at the bedside to estimate the energy needs of critically ill patients, obese patients, those with liver disease, and in other conditions that require accurate and individualized assessment. If indirect calorimetry cannot be applied, it is

recommended to estimate energy expenditure by calculating kilocalories per kilogram of body weight. In the case of eutrophic patients or when the goal of nutritional therapy is to maintain the current condition, it is recommended to start caloric intake with 25 kcal/kg/day, with adjustments according to clinical evolution. The energy recommendation for critically ill patients is 20–25 kcal/kg/day, regardless of the TN route used **[1-4]**.

In addition to calculating kilocalories per kilogram of body weight, the Mifflin-St10 equation is recommended to estimate the TEE of non-obese and obese individuals, showing an accuracy of 82% in non-obese individuals and 70% in obese individuals. For critically ill patients, several predictive equations for TEE have been validated, such as the Ireton-Jones equation. Bioimpedance is also a method used to measure resting energy expenditure, although its greatest application is for determining body composition **[3,4]**.

Nutritional Recommendations for Macro and Micronutrients

In the context of patients at high nutritional risk and unable to use the digestive tract, parenteral nutrition (PN) should be initiated as early as possible. Supplemental PN should be considered in cases of unsatisfactory enteral therapy <60% of protein-calorie intake after five to seven days. Thus, the use of early PN significantly reduces the incidence of complications only in the group of malnourished patients **[1,2]**. Furthermore, there is lower mortality and a lower risk of infections in malnourished patients with PN compared to standard therapy. In a controlled clinical study, the use of PN preoperatively demonstrated a higher incidence of sepsis, which did not occur in the subgroup of malnourished patients, who, when using PN, showed a significant reduction in non-infectious complications **[10-14]**.

Thus, it is suggested to consider the use of supplemental PN after 5 to 7 days in patients who have not been able to achieve protein-calorie intake >60% via the digestive tract. Based on the available evidence, the use of supplemental PN should be considered on a case-by-case basis, after a period of 5 to 7 days, during which enteral nutrition should be initiated whenever possible. This period appears to be sufficient for patients to be better classified into risk categories and for the intervention to be initiated with greater precision and effectiveness **[3,6]**.

Lipid emulsions should be included as an integral part of PN, as a caloric source, and also to ensure the provision of essential fatty acids for patients with prolonged ICU stays. More balanced lipid emulsions containing medium-chain triglycerides (MCTs), olive oil (OO), and fish oil (FO) should be considered in critically ill patients who are indicated for PN **[6]**.

Soybean oil-based lipid emulsions should be avoided in critically ill patients. Lipid formulations used in PN are composed of triglycerides, with phospholipids as emulsifiers. There are several types of lipid formulations available on the market for use in NP **[4]**. The addition of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) to lipid emulsions has demonstrable effects on cell membranes and inflammatory processes. Lipid emulsions with fish oil likely reduce the length of stay of critically ill patients in the ICU. There is no evidence of clinical superiority between the use of ready-to-use PN and compounded PN **[4]**.

It is recommended that the target blood glucose level be set between 140 and 180 mg/dL for clinical patients under intensive care. Although specialist societies may disagree regarding the lower limit of the tolerance range (SCCM 150–180 mg/dL vs. ASPEN 140–180 mg/dL), there is consensus that strict glycemic control targets should not be used, at the risk of increased mortality. Blood glucose levels above 180 mg/dL are increasingly associated with greater comorbidity. Randomized studies have also shown that measurements of glucose dispersion and minimum glucose levels are necessary **[4]**.

Parenteral use of glutamine is contraindicated in patients with multiple organ dysfunction, renal dysfunction, hepatic dysfunction, or hemodynamic instability. In other situations, in association with well-indicated and designed PN, it can bring clinical benefits to critically ill patients, and may be considered on a case-by-case basis **[1,2]**. In this sense, glutamine participates in many physiological, metabolic, immunological, antioxidant, synthetic, and structural processes. Due to its physicochemical characteristics, L-glutamine has been completely omitted from PN solutions. These solutions contain exclusively crystalline amino acids (AAs), with their own specific solubility and thermal stability. Glutamine dipeptides (alanyl-glutamine, or glycyl-glutamine) are more soluble and stable in aqueous solution, have come to fill an important gap in the AA concentrations of PN solutions, restoring, or even increasing, the AA content in these solutions **[1,2]**.

Serum phosphate should be monitored in critically ill patients undergoing enteral/parenteral nutrition, as frequent monitoring of serum phosphorus in critically ill patients and appropriate replacement when necessary is crucial. Hypophosphatemia is a frequent laboratory finding in critically ill patients and has been associated with sepsis, refeeding syndrome, diuretic use,

continuous dialysis methods, and alkalosis. Thus, by reducing the production of 2,3-diphosphoglycerate and ATP, negative effects on diaphragmatic contractility have been documented, which may result in delayed ventilator weaning in critically ill patients **[4]**.

As evidence of this, in a cohort study with 66 patients in which 123 weaning attempts were made, it was observed that weaning success was correlated with serum phosphorus levels (1.18±0.27 mmol/L vs. 1.06±0.31 mmol/L, p=0.008). Those with serum levels < 0.8 mmol/L had a higher risk of failure than those with phosphorus within the laboratory reference value (RR=1.18; 95% CI, 1.06-1.32; p=0.01). In another retrospective study, including 67 COPD patients on mechanical ventilation with a high incidence of hypophosphatemia (56.72%), a correlation was also observed (34.21 vs. 10.34%, p<0.05) between weaning failure and low phosphorus (< 0.87 mmol/L) **[6]**. In addition, PN should be used in the early postoperative period in malnourished patients or those at high nutritional risk who are unable to be fed orally or enterally. In well-nourished patients with contraindications to the use of the digestive route, 5-7 days should be allowed before starting PN. In this context, regarding the distribution of macronutrients, the emphasis is on protein intake, which should correspond to values between 1.2–2.0 g/Kg/day (ASPEN), considering the current weight and the degree of stress on the body, with the proportions of carbohydrates and lipids following the traditional recommendations for the general public **[1]**.

According to ASPEN, it is important to emphasize that in the TN of the critically ill patient, protein intake should be prioritized over energy intake because of its role in reducing mortality. For DITEN, it is important to observe whether there is a need to adjust the energy supply when deciding on protein intake, because if the energy supply is below the needs, protein will be used as the main energy source **[4]**.

In relation to the pediatric context, hospitalized children are vulnerable to malnutrition during serious illnesses or recovery from injuries and are at subsequent risk of increased morbidity and growth retardation. In cases where enteral nutrition is not possible, PN can be used to ensure that patients at nutritional risk receive appropriate amounts of macro and micronutrients. Nutritional needs cannot be met by a single standard PN formulation in pediatric patients (up to 18 years of age) due to the wide variety of needs according to age, weight, maturity level, and disease status. Individualized PN preparation is associated with several limitations, including prescription errors, stability issues, and risk of infection. These risks can be avoided by the availability of a variety of pediatric PN formulations supplied as premixed 3-chamber bags. A prospective study previously demonstrated the practical handling and ease of use of two such bag formulations, one designed for term infants up to 2 years of age and one for children and adolescents aged 2 to 18 years. Most pharmacists and nurses described the bag as easy to use and favored it over individual bottles. Therefore, these formulations offer a means to improve the quality of care in hospital pediatric units, particularly in the absence of a nutritional support team **[15]**.

Another pediatric study reviewed the current literature evaluating the clinical outcomes of early and late initiation of PN among critically ill children. The timing of PN initiation varies among critically ill children and derives from an assessment of nutritional status, energy needs, and physiological differences between adults and children, including higher nutritional requirements and lower body reserves. A recent randomized controlled trial among critically ill children suggests better clinical outcomes by avoiding PN initiation on the first day of admission to the pediatric ICU. Although there is no consensus on the ideal timing for PN initiation among critically ill children, recent literature does not support immediate PN initiation upon admission to the pediatric ICU **[16]**.

Energy requirements are altered in critically ill patients and are influenced by clinical status, treatment, and stage of the process. Therefore, the most appropriate method for calculating caloric intake is indirect calorimetry. In the absence of this technique, fixed calorie intake (between 25 and 35 kcal/kg/day) or predictive equations, such as the Penn State formula, can be used to obtain a more accurate assessment of metabolic rate. Carbohydrate administration should be limited to a maximum of 4 g/kg/day and a minimum of 2 g/kg/day. Plasma glucose should be monitored to avoid hyperglycemia. Fat intake should be between 1 and 1.5 g/kg/day. The recommended protein intake is 1-1.5 g/kg/day, but may vary according to the patient's clinical condition. Special attention should be paid to micronutrient intake. There is a lack of consensus on micronutrient requirements. Some vitamins (A, B, C, E) are of great importance in critically ill patients, especially those undergoing continuous renal replacement therapy, patients with severe burns, and alcoholics, although the specific requirements for each of these patient types have not yet been met **[17]**.

In this context, a retrospective study evaluated whether the removal of a soybean oil-based lipid emulsion from the PN regimen in humans is associated with improved triglyceride and liver enzyme concentrations. Thus, the medical records of 40

patients with hypertriglyceridemia (> 4.50 mmol/L) while receiving PN were analyzed. Patients received 20% Intralipid as part of an all-in-one system containing all necessary macronutrients and micronutrients, electrolytes, trace elements, and vitamins. The lipid emulsions were removed from the all-in-one mixture for a median of 5 (range, 1-23) days, after which triglyceride concentrations decreased significantly (mean difference -2.5 ± 0.30 mmol/L, p<0.001). Aspartate aminotransferase and leukocyte counts decreased significantly (mean difference 35 ± 17 U/L, p=0.049 and 3.8±1.7*10E9 /L, p=0.028, respectively), while albumin levels increased significantly (mean difference 2.1 ± 0.9 g/L, p = 0.027). Alanine aminotransferase showed a non-significant reduction (mean difference 30 ± 22 U/L, p=0.194). In 11 patients, lipid emulsion was reintroduced, after which triglyceride levels showed a significant increase (mean difference 1.5 ± 0.30 mmol/L, p=0.001). Short-term withdrawal of the lipid fraction in the PN mixture is associated with a significant reduction in plasma triglyceride concentration. Reintroduction was associated with an increase in triglyceride concentration. Furthermore, liver enzyme abnormalities and leukocyte count decreased, while albumin levels increased, suggesting that even with the withdrawal of the lipid emulsion, hepatocellular damage and systemic inflammation decreased **[18]**.

Patients suffering from chronic liver failure (CLF) are frequently malnourished and do not achieve adequate nutrient intake, particularly protein. The main goal of nutritional intervention is to provide sufficient protein (1.2-1.5 g/kg/day) and ensure adequate energy intake (total energy 30 kcal/kg/day). The livers of patients with CLF are depleted of glycogen, and therefore, prolonged periods of fasting (>12 h) should be avoided in order to prevent further breakdown of muscle protein in gluconeogenesis. Therefore, late-night snacks or even nighttime oral nutritional supplements improve total body protein status and are therefore recommended. Nutritional intervention should be intensified from nutritional counseling to oral nutritional supplements, enteral tube feeding, or parenteral nutrition, as appropriate. As with other malnourished patients, care should be taken to prevent refeeding syndrome or vitamin/trace element deficiency **[19]**.

Inflammatory bowel disease (IBD) is a chronic disease mediated by the immune system and characterized by inflammation of the gastrointestinal tract. This study aims to understand how the use of PN can affect the adult population diagnosed with IBD. Thus, a systematic review, meta-analysis, and meta-regression study was conducted. After a full-text review, only 15 studies were selected for qualitative synthesis and 10 for metaanalysis and meta-regression. The variables used were Crohn's Disease Activity Index (CDAI), albumin, body weight (BW), and postoperative complications (COM). PN demonstrated efficacy in the treatment of IBD and is compatible with other medications. CDAI and albumin improve, although the effect of PN is greater after some time. However, the effect on albumin may be less than the value observed in the meta-analysis due to possible publication bias. BW does not change after the intervention. COM using PN was observed, although the proportion is low **[20]**.

Long-chain n-3 polyunsaturated fatty acids modulate immune cell functions. In this sense, a study evaluated the impact of different lipid emulsions (LE) with supplemented doses of fish oil (FO) on serum cytokine concentration and in vitro cytokine production in patients with intestinal failure on home parenteral nutrition (PN). It was hypothesized that FO supplementation would decrease lipopolysaccharide (LPS)-stimulated cytokine production. Twelve patients receiving Smoflipid for at least 3 months received FO (Omegaven) for an additional 4 weeks. After this cycle, patients were randomized to subsequently receive 1 cycle with Lipoplus and 1 cycle with ClinOleic for 6 weeks or vice versa, plus 4 weeks of Omegaven added after each cycle, in a crossover study model. Comparison of baseline EL regimens showed lower LPS-stimulated IL-1β production in patients on Lipoplus than on the Smoflipid and ClinOleic regimens, as well as lower IL-8 compared to the Smoflipid regimen. Omegaven reduced serum IL-8 concentration under the Lipoplus regimen and decreased LPS-stimulated IL-1β production under the Smoflipid and ClinOleic regimens. IL-6 and TNF-α production was reduced only in those on the Smoflipid regimen. Regardless of the EL regimen used, patients compared to healthy controls showed higher concentrations of IL-6, IL-8, and TNF-α in serum and LPS-stimulated IL-6 production, as well as lower n-6/n-3 long-chain polyunsaturated fatty acids in erythrocyte phospholipids. LPS-stimulated IL-6 production correlated negatively with the parenteral dose of eicosapentaenoic acid + docosahexaenoic acid. In conclusion, OP-supplemented PN suppresses cytokine production in vitro **[21]**.

Another work, based on a special nutrient issue, contains 13 manuscripts (two reviews and 11 original publications) reflecting the broad spectrum of research currently conducted in the field of dietary minerals. The manuscripts in this special issue collection include populations from several countries,

including the USA, Germany, Australia, Brazil, Poland, Japan, Colombia, Mexico, Saudi Arabia, Russia, Italy, South Korea, and Israel. The manuscripts presented cover a wide variety of topics in the field of minerals for NP, with emphasis on the antimicrobial properties of magnesium and its potential to develop healthier foods, the link between Nrf2 and dietary selenium, iron, zinc, and copper, the association between nicotinamide and deoxymuginic acid as enhancers of iron bioavailability, and investigation of dietary silicon and its impact on plasma silicon concentrations in humans. Minerals make up only five percent of the typical human diet, but they are essential for normal health and function. Therefore, macrominerals are defined as minerals required by adults in amounts greater than 100 mg/day or making up less than one percent of total body weight. Trace elements (or minerals) are generally defined as minerals needed in amounts of 1 to 100 mg/day by adults or less than 0.01% of total body weight. Ultra-trace minerals are generally defined as minerals that are needed in amounts less than 1 microgram/day. Selenium deficiency is uncommon but has been reported in parts of China where the local diet is devoid of selenium; this deficiency also occurs in individuals maintained on total PN without minerals. The clinical features of selenium deficiency are cardiomyopathy and skeletal muscle dysfunction **[22]**.

Finally, although mortality from critical illnesses has fallen over the decades, the number of patients with long-term functional disabilities has increased, leading to decreased quality of life and significant healthcare costs. As an essential part of the multimodal interventions available to improve critical illness outcomes, optimal nutritional therapy (NT) should be provided during critical illness, after ICU discharge, and after hospital discharge. Thus, a narrative review study summarized the most recent scientific ideas and guidelines on NT in the ICU, primarily parenteral nutrition (PN). Based on recent literature and guidelines, gradual progression to caloric and protein targets is recommended during the initial phase of ICU stay. After this phase, a full caloric dose can be provided, preferably based on indirect calorimetry. Phosphate should be monitored to detect refeeding hypophosphatemia, and caloric restriction should be instituted when it occurs. For protein, at least 1.3 g of protein/kg/day should be targeted after the initial phase. During the chronic phase of the ICU, and after ICU discharge, higher protein/calorie targets should be provided, preferably combined with exercise. Several pharmacological options are available to combine with TN to improve the anabolic response and stimulate muscle protein synthesis. During and after ICU care, optimal TN is essential to improve long-term outcomes and reduce the likelihood of the patient becoming a critical illness victim. Nutritional goals are not met at any stage of recovery. Personalized TN, respecting different targets during the phases of the patient's journey after a critical illness, should be prescribed and monitored **[23]**.

Enteral feeding, while desirable for many reasons, is difficult, causing a worldwide recurrence of malnutrition due to insufficient food supply. The indications for total parenteral nutrition (TPN) have evolved towards its use alone or in combination with enteral nutrition. Several controversial trials published in 2011-13 investigated the timing of TPN, an issue that remains unresolved. The time of initiation varies by country, ranging from admission (Australia and Israel), day 4 (Switzerland), and day 7 (Belgium, USA). The most important issue may be individualized prescription, dependent on the timing of the feeding route, energy, and substrates **[24,25]**.

Conclusion

It was concluded that several clinical studies critically analyzed the evolution and changes that marked the development of parenteral nutrition in intensive care units. Standard crystalline amino acid solutions, although devoid of side effects, remain incomplete regarding their composition (e.g., glutamine). Lipid emulsions have evolved significantly and are now included in bi- and tri-compartment feeding bags, allowing for true total parenteral nutrition, provided daily micronutrients are prescribed. The question of the exact individual needs for energy, macro and micronutrients remains unresolved. Many complications attributed to total parenteral nutrition are a consequence of under- or overfeeding. The historical concept of hyperalimentation is the main cause, along with the use of predictive equations based on fixed weight (incorrect in 70% of critically ill patients).

CRediT

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