CASE REPORT

Pediatrics Sciences Journal (*PedScij*) 2025, Volume 6, Number 2: 53-58
P-ISSN: 2722-0427, E-ISSN: 2722-1474

Pediatric Sciences Journal

Published by
Pediatrics Sciences Journal

Comparison of tolerance of peptide-based formula versus standard formula on outcome of critically ill children: an evidence-based case report

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Received: 2025-08-28
Accepted: 2025-10-11
Published: 2025-11-16

ABSTRACT

Introduction: The clinical benefit of peptide-based formulas remains controversial in critically ill children.
Objective: To conduct a critical review to compare the effects of peptide-based versus standard polymeric formulas on feeding tolerance and whether this would affect outcomes in critically ill children.
Methods: An online search was conducted using PubMed, Cochrane, and the New England Journal of Medicine (NEJM) databases using the keywords "Peptide-based Formula," "Standard Formula," "Critically ill Children," and "Enteral Feeding."
Results: Three articles were found: a case-control study and two prospective cohort studies. The results of the case-control study suggested that critically ill patients receiving peptide-based formulas showed significant reductions in feeding disturbances and abdominal distension and achieved full enteral feedings sooner compared with patients receiving standard formulas. The results of the first prospective cohort study showed that the peptide-based formula was better tolerated than the standard formula in children after bowel surgery, and the second study stated that choosing the peptide-based formula as the first prescription for enteral nutrition was associated with higher severity of clinical conditions in patients.
Conclusion: The peptide-based formula was better tolerated than the standard polymeric formula in critically ill pediatric patients.

Keywords: Peptide-based Formula, Standard Formula, Enteral Feeding, Critically-ill Children.
Cite This Article: Permadi, P.I., Melinda., Yuliarto, S., Kadafi, K.T., Koentartiwi, D., Putra, G.C. 2025. Comparison of tolerance of peptide-based formula versus standard formula on outcome of critically ill children: an evidence-based case report. *Pediatrics Sciences Journal* 6(2): 53-58. DOI: 10.51559/pedscij.v6i2.122

INTRODUCTION

Nutritional support is a fundamental component of the management of critically ill children and plays a pivotal role in promoting recovery, preserving organ function, and reducing morbidity and mortality. In the pediatric intensive care unit (PICU), inadequate nutritional intake is frequently associated with prolonged hospitalization, increased risk of infection, impaired wound healing, and poor clinical outcomes. Consequently, early and appropriate enteral nutrition has become a cornerstone of supportive therapy in critically ill pediatric patients.[1,2] Enteral feeding is generally preferred over parenteral nutrition due to its physiological benefits, including maintenance of gut integrity, modulation of immune responses, and lower risk of infectious complications.[3] However, critically ill children often present with gastrointestinal dysfunction, such as delayed gastric emptying, impaired intestinal motility, mucosal ischemia, and malabsorption, which can compromise feeding tolerance and limit the effectiveness of enteral nutrition. These challenges highlight the importance of selecting an enteral formula that is not only nutritionally adequate but also well tolerated.[4]

Standard enteral formulas typically contain intact proteins that require normal digestive and absorptive capacity.[5] In contrast, peptide-based formulas consist of partially hydrolyzed proteins that may facilitate faster digestion and improved absorption, potentially reducing gastrointestinal intolerance in patients with compromised gut function. This theoretical advantage suggests that peptide-based formulas may be beneficial in critically ill children who are vulnerable to feeding intolerance and metabolic stress.[6]

Despite growing interest in the use of peptide-based formulas, existing evidence remains inconclusive. Most studies evaluating the clinical impact of peptide-based versus standard formulas have been conducted in adult critically ill populations, with conflicting results regarding feeding tolerance, inflammation, and clinical outcomes.[7] Importantly, data in the pediatric population are limited, and current clinical guidelines do not provide clear recommendations on the routine use of peptide-based formulas in critically ill children.[8]

Given the high prevalence of feeding intolerance and its potential impact on outcomes in the PICU, there is a clear need for pediatric-focused evidence to guide nutritional decision-making. Therefore, this evidence-based case report aims

to compare feeding tolerance between peptide-based and standard enteral formulas and to explore their potential impact on clinical outcomes in critically ill children.

CASE

A 6-month-old girl was brought to the RSSA Emergency Room due to complaints of shortness of breath for 7 days. Shortness of breath worsened 1 day before admission and was accompanied by fever. History of intermittent drinking since birth and difficulty gaining weight. From physical examination, tachypnea was found with a respiratory rate of 60 times/minute, heart rate of 160 times/minute, blood pressure of 80/50 mmHg, and a temperature of 38.2 degrees Celsius. Intercostal retraction, fine basal rhonchi (+), and continuous murmur in the left ICS 2 midsternal line were found. The patient was then intubated and treated in the Pediatric Intensive Care Unit (PICU). From the echocardiography results, Patent Ductus Arteriosus (PDA), Atrial Septal Defect (ASD), and Pulmonary Hypertension were found. The patient was given a peptide-based formula as enteral nutrition while treated in the PICU.

CLINICAL QUESTIONS

Based on the case illustration above, a clinical question arises: Does using a peptide-based enteral formula, compared with an intact protein-based formula / standard formula, provide better outcomes in critically ill pediatric patients?

LITERATURE SEARCH METHOD

The literature search procedure to answer the above questions was done by searching for references online through PubMed, Cochrane, and the New England Journal of Medicine (NEJM) search engines. The keywords used included "Peptide-based Formula," "Standard Formula," "Critically-ill," and "Enteral Feeding" (see Table 2). After the articles were found, they were selected based on inclusion criteria; namely, the language of the article was English, and publications within the last ten years. Exclusion criteria included studies in the form of review articles, similar articles, and articles without full text. After selection, two relevant articles were available and analyzed, considering validity, relevance, and application to patients (see Figure 1).

Table 1. Clinical questions according to the PICO method

Population (P)	Intervention (I)	Comparison (C)	Outcome (O)
Critically ill patients treated in the PICU	Peptide-based formula administration	Standard formula	Tolerance of nutritional intake

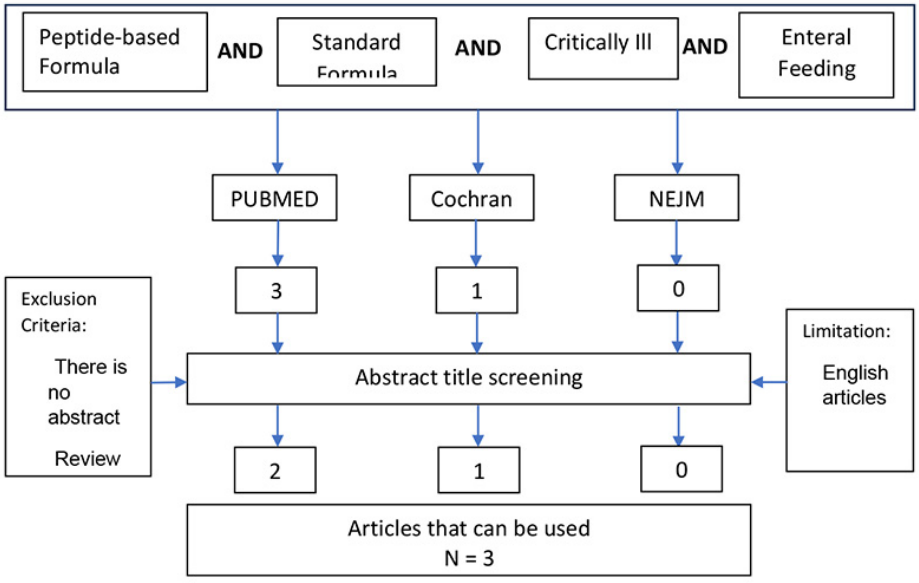

Figure 1. Literature selection flowchart

RESULTS

After a literature search, three articles were found relevant to the clinical question. A case-control study (2020)[9]: Peptide-based versus standard-based polymeric formula for critically ill children: is it superior for patients' tolerance? (level of evidence 3) by Ibrahim et al. compared the administration of peptide-based formula to 90 critically ill children admitted to the PICU and assessed the tolerance of enteral nutrition and outcomes such as duration of ventilator use, length of stay in the PICU, and mortality. The study was conducted at the PICU of Ain Shams University Hospital, Cairo, Egypt. The study subjects were 180 patients divided into two groups, each receiving a peptide-based or standard formula. The mean age of the study subjects was 3.3 years in the group receiving the peptide-based formula and 2.5 years in the group receiving the standard formula. Exclusion criteria were patients with gastrointestinal disorders during initial PICU admission. In this study, the group receiving peptide-based formula achieved whole oral caloric intake faster (2.6 ± 0.74 days vs 5.36 ± 1 day) and experienced fewer feeding disturbances compared to the standard formula group (1.73 ± 1.32 days vs 4.26 ± 1.61 days). At the end of the study, the peptide-based formula group experienced more weight gain (0.19 ± 0.44 kg) than the standard formula group, which even experienced weight loss (-0.04 ± 2.1 kg). From this study, it is concluded that the use of a peptide-based formula is more easily tolerated than a standard formula in critically ill children.

Prospective Cohort Study (2021)[10]: Peptide-based enteral formula vs a whole protein enteral formula after major intestinal surgeries in children (level of evidence 3) by Mostafa et al. compared the administration of peptide-based formula in 30 children undergoing major gastrointestinal surgeries (resection and reanastomosis after intussusception) and assessed the tolerance of enteral nutrition

and albumin and prealbumin levels after surgery. This study was conducted at Ain Shams University Hospital, Cairo, Egypt. The study subjects were 30 patients undergoing gastrointestinal surgery, divided into two groups receiving peptide-based formula or standard formula. Both groups were given enteral nutrition on the third postoperative day. The mean age in both groups was 15 ± 1.5 months. Exclusion criteria in this study were patients who showed signs of peritonitis before surgery or who experienced intestinal perforation and peritoneal contamination during the surgical procedure. In this study, there was no difference in changes in albumin levels before and after surgery in both groups (-11.8 ± 4.8% in the peptide-based formula group vs. -10.2% ± 2.7% in the standard formula group). However, there was a significant difference in changes in prealbumin levels after surgery, where the increase in prealbumin levels was higher in the peptide-based formula group (62.5%) compared to the standard formula group (7.69%). In this study, 10 of 15 patients in the standard formula group experienced intolerance to enteral nutrition, while in the peptide-based formula group, only 1 of 15 patients experienced enteral nutrition intolerance. The postoperative hospital stay in the standard formula group was longer, with an average of 6.3 days, compared to the standard-based formula group, with an average of 4.5 days.

The second prospective cohort study (2012)[11]: Factors associated with peptide-based formula prescription in a pediatric intensive care unit (level of evidence 3) by Vigidal et al., identified factors associated with the choice of peptide-based formula in the first enteral nutrition prescription for critically ill children. This study was conducted in a teaching hospital's pediatric intensive care unit (PICU) at the University of São Paulo, Brazil. The subjects were 291 patients admitted to the PICU from July 2007 to January 2009. The mean age of the sample was 11 months (3-65 months). In this study, predictive factors for the use of hydrolyzed formula were malnutrition (OR 2.94, p 0.001), a 2-day fasting period (OR 3.46, p 0.001), and the use of alpha-adrenergic blockers before starting the diet (OR 2.32, p 0.01).

Table 2. Search strategies, sources used, and search results

Search Portal	Keywords	Articles obtained	Articles used
Pubmed	(((peptide-based formula) AND (standard formula)) AND (critically ill [MeSH Terms])) AND (enteral feeding [MeSH Terms])	3	2
Cochrane	Peptide-based formula in All Text AND "standard formula" in All Text AND "critically ill" in All Text AND "enteral nutrition" in Title, Abstract, Keyword	1	1
NEJM	"Peptide based formula" AND "Standard formula" AND "Critically ill" AND "Enteral Feeding"	0	0

Table 3. Critical assessment of case-control

Article	Ibrahim et al. (2020)[9]
Study design	Single-blind case–control study
Level of Evidence	III
PICO P I C O	 Critically ill patients in the PICU Peptide-based enteral nutrition formula Standard polymeric enteral nutrition formula Enteral feeding tolerance, time to achieve full enteral feeding, frequency and duration of feeding interruption, sepsis duration, mechanical ventilation duration, length of PICU stay, and mortality
Introduction	The study clearly articulates its objective: to compare the effects of a peptide-based formula versus a standard polymeric formula on enteral feeding tolerance in critically ill children and to evaluate subsequent clinical outcomes during PICU hospitalization.
Methods	This was a single-blind case–control study involving 180 critically ill pediatric patients admitted to a single PICU. Participants were allocated into two equal groups (n = 90 each) based on the type of enteral formula received. Subject recruitment was conducted using total sampling. Statistical analysis was performed using appropriate parametric tests, with a p-value < 0.05 considered statistically significant.
Results	The results were clearly presented and aligned with the predefined analysis plan. Patients receiving the peptide-based formula demonstrated significantly improved feeding tolerance, including fewer feeding interruptions, reduced gastrointestinal intolerance symptoms, faster achievement of full enteral feeding, improved weight gain, and shorter sepsis duration. No statistically significant differences were observed between groups in mechanical ventilation duration, PICU length of stay, or mortality.
Discussion	The authors critically discussed the study findings and acknowledged its main limitation, namely the single-center design, which may limit generalizability. They noted that enteral nutrition practices and patient characteristics could differ across other PICUs, potentially influencing outcomes.

DISCUSSIONS

Enteral nutrition is the preferred route for nutritional support in the pediatric intensive care unit (PICU).[12] The advantages of enteral nutrition include metabolic, immunologic, and mucosal protection against bacterial translocation. Therefore, early initiation of enteral nutrition is recommended within 24 hours of admission to the intensive care unit. However, gastrointestinal dysfunction has been a significant barrier to early enteral nutrition in critically ill patients. Intolerance to enteral nutrition has been reported in up to 60% of patients in the intensive care unit.[13] Impaired gastrointestinal motility can cause discomfort, nausea, vomiting, bloating, distention, and diarrhea. Evaluation of nutritional intolerance can be challenging in critically ill patients because of factors such as sedation, mechanical ventilation, and altered mental status that often interfere with the patient's ability to verbalize their gastrointestinal symptoms.[14]

Gastrointestinal motility disorders that occur in intensive care patients can be divided into two main types: postoperative ileus and motility disorders due to critical illness (trauma, multiple organ dysfunction syndrome, sepsis).[15] In addition, some patients may have primary or secondary motility disorders such as gastroparesis, achalasia, or chronic intestinal pseudo-obstruction that already existed before entering the intensive care unit.[16]

Gastrointestinal motility disorders are pervasive in critically ill patients. For example, delayed gastric emptying has been found in 50% of patients receiving mechanical ventilation and 80% of patients with increased cranial pressure following head injury.[17,18] Because of the high overall rate of motility disorders in ICU patients, clinicians tend to be hesitant to initiate enteral tube feedings early.[19]

The etiology of abnormal gastrointestinal motility disorders in critically ill patients is multifactorial but remains elusive. Shock, inflammatory cytokines, electrolyte abnormalities, hyperglycemia, disease, and medications may contribute to gastrointestinal dysfunction.[20] Catecholamines, which are often given to critically ill patients, can slow the gastric emptying rate by stimulating beta-adrenergic receptors.[21] Opioids interfere with gastrointestinal motor activity and autonomic function by inhibiting neurotransmitter release and altering neuronal excitability. Opioids slow gastric emptying by increasing antral and pyloric tone and decreasing fundal tone.[22]

Significant developments in enteral formulas over the past few years have made tube feeding the most common method of nutritional support for critically ill patients.[23] However, the increasing variety of enteral formulas available may increase the risk of inappropriate use of these products, especially those designed for specific situations. Nutritional support with disease-specific formulas can increase costs up to 3-fold in intensive care units.[24] According to the observations of Vidigal et al., in pediatrics, peptide-based formulas are often used as an alternative to polymeric formulas despite the lack of scientific evidence to support their clinical benefit.[11] This substitution is based on theoretical reasons, which suggest that there is better nutrient absorption from partially digested material under conditions of pathophysiological changes common to inflammatory diseases, which are believed to modify digestive and absorptive functions, thereby impairing the utilization of intact proteins, carbohydrates, and lipids.[25]

Studies examining the clinical benefits of peptide-based formulas in critically ill patients have been conducted in adult patients, and the results have

Table 4. Critical appraisal of a prospective cohort

Article	Mostafa et al[10]
Study design	Prospective cohort study
Level of Evidence	III
PICO P I C O	Pediatric patients undergoing major intestinal surgery Peptide-based enteral nutrition formula initiated postoperatively Whole-protein enteral nutrition formula initiated postoperatively Feeding tolerance, postoperative nutritional status (serum albumin and pre-albumin levels), and length of hospital stay
Introduction	The study clearly states its objective: to compare peptide-based and whole-protein enteral formulas regarding postoperative tolerance, nutritional outcomes, and hospital stay in children following major intestinal surgery. The clinical relevance is well established, given the high risk of malnutrition and feeding intolerance in this population.
Metode	This prospective cohort study included 30 pediatric patients divided into two non-randomized groups (15 patients per group). All participants underwent similar surgical procedures and followed an identical postoperative feeding protocol, differing only in the type of enteral formula administered. Statistical analysis was performed using Student's t-test, paired t-test, and Mann–Whitney U test, with a p-value < 0.05 considered statistically significant.
Results	The results were presented clearly and in accordance with the predefined analysis plan. Patients receiving peptide-based formula demonstrated significantly higher postoperative pre-albumin levels, better feeding tolerance with fewer interruptions, and a significantly shorter hospital stay compared to those receiving whole-protein formula. No significant differences were observed in postoperative albumin levels between groups.
Discussion	The authors appropriately interpreted their findings and related them to existing literature. Study limitations were acknowledged, particularly the small sample size and non-randomized design, which may limit external validity. The discussion also addressed the economic implications of peptide-based formulas in relation to reduced hospital stay.

Table 5. Critical appraisal of a prospective cohort

Article	Vidigal et al[11]
Study design	Prospective cohort study
Level of Evidence	II
PICO P I C O	Critically ill pediatric patients admitted to the PICU and receiving enteral tube feeding for ≥48 hours. Initial prescription of peptide-based enteral nutrition formula Initial prescription of standard polymeric enteral nutrition formula Factors associated with peptide-based formula prescription, clinical severity indicators (mortality, length of ventilation, PICU length of stay), feeding tolerance (diarrhea), and direct enteral nutrition costs
Introduction	The study clearly defines its aim: to identify clinical and nutritional factors associated with the prescription of peptide-based formulas as first-line enteral nutrition in critically ill children and to compare the direct costs of peptide-based versus polymeric formulas in a PICU setting.
Metode	This prospective cohort study included 291 pediatric patients admitted to a single university PICU. Eligible patients received enteral nutrition for at least 48 hours. Multiple demographic, nutritional, and clinical variables were analyzed as potential predictors of peptide-based formula prescription using bivariate and multivariate logistic regression models. Direct cost analysis of enteral formulas was also performed. Statistical significance was set at $p < 0.05$.
Results	Peptide-based formulas were prescribed as the initial enteral nutrition in 29.2% of patients. Their use was independently associated with malnutrition at admission, fasting period longer than two days, and use of α-adrenergic drugs. Patients receiving peptide-based formulas demonstrated higher mortality rates, longer durations of mechanical ventilation, and longer PICU stays, reflecting greater baseline illness severity. Peptide-based formulas were substantially more expensive, with costs up to ten times higher than polymeric formulas.
Discussion	The authors appropriately contextualized their findings, emphasizing that peptide-based formula prescription reflects greater clinical severity rather than superior clinical outcomes. Study limitations were acknowledged, including the single-center design and the observational nature of the study, which preclude causal inference. The authors highlighted the need for randomized controlled trials and cost-effectiveness analyses to establish evidence-based criteria for peptide-based formula use in critically ill children.

been controversial. There are no recommendations for using polymeric or peptide-based formulas for critically ill pediatric patients. To our knowledge, there has been little research on this subject. The limitations of this EBCR are that it does not discuss in depth several types of peptide-based formulas for critically ill pediatric patients, and a recorded clinical trial needs to be conducted to compare how significant the influence of tolerance of peptide-based formulas is with standard formulas for critically ill pediatric patients.

CONCLUSION

Peptide-based formulas were better tolerated than standard polymeric formulas in critically ill pediatric patients. However, the selection of patients receiving peptide-based formulas needs further evaluation, as the cost of enteral nutrition with peptide-based formulas is higher than that of standard formulas. A cost-effective approach is required to make the right choice. More importantly, these findings suggest prospective randomized controlled trials (RCTs) need to test the hypothesis that peptide- or amino acid-based formulas have potential advantages over standard formula diets in critically ill children.

DISCLOSURES

FUNDING

The authors declare that the study received no funding.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest to disclose.

ETHICAL APPROVAL/CONSENT FOR PUBLICATION

Informed consent has been obtained and approved by the patient's parents

AUTHOR CONTRIBUTION

Study conception and design: PIP, M, SY, KTK, DK, GCP; data collection: PIP; literature search: PIP, M, SY, KTK, DK, GCP; analysis and interpretation of results: PIP, M, SY, KTK, DK, GCP; draft manuscript preparation: PIP, M. All authors prepare the manuscript and agree for this final version of manuscript to be submitted to this journal.

ETHICAL APPROVAL/CONSENT FOR PUBLICATION

Informed consent has been obtained and approved by the patient's parents.

ACKNOWLEDGMENTS

I want to express my sincere gratitude to all those who have contributed to the successful completion of this work. I want to acknowledge the invaluable technical support provided by the Faculty of Medicine, Brawijaya University, which facilitated this work. Lastly, I am thankful to all those who have indirectly contributed to the success of this project. Your support has been invaluable.

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