The Effects of Enteral and Parenteral Nutrition on Pediatric Hematopoietic Stem Cell Transplant Patients:

An Integrative Review

Abstract

Children receiving hematopoietic stem cell transplants (HSCT) are at risk for malnutrition which may negatively affect their quality of life. These risks include impaired oral feeding from factors such as pre-transplant conditioning causing vomiting, diarrhea, and mucositis. Enteral nutrition (EN) and parenteral nutrition (PN) are support options for this patient population when oral feeding is impaired. This integrative review will evaluate the literature to determine outcomes of EN and PN in pediatric HSCT patients and implications for practice. Outcomes impacted by EN and PN include platelet and neutrophil engraftment, mucositis, acute graft versus host disease, infection, electrolytes imbalances, weight gain, hospital length of stay, mortality, morbidity, and survival rate. Suggestions for optimizing nutritional support in pediatric HSCT are presented, as well as recommendations for further research.

Keywords: enteral nutrition, parenteral nutrition, hematopoietic stem cell transplant, pediatric

The Effects of Enteral and Parenteral Nutrition on Pediatric Bone Marrow Transplant Patients: An Integrative Review

Hematopoietic stem cell transplant (HSCT) is a treatment for a diverse range of diseases including malignant and nonmalignant conditions in children. Approximately 2,600 children undergo HSCT each year in the United States (Mangurian et al., 2018). HSCT may be indicated in patients with oncological, hematological, metabolic, and immunological disease (Eyrich & Schulze, 2019). HSCT is an infusion of hematopoietic stem cells to reestablish a functional hematopoietic system (National Cancer Institute [NCI], 2023). A stem cell transplant can be either allogeneic or autologous. Allogeneic refers to a stem cell donation from an individual other than the patient and autologous means a stem cell donation from the patient themselves (NCI, 2023). HSCT matching for allogeneic transplants is based on finding a suitable donor through human leukocyte antigen matching (Eyrich & Schulze, 2019).

The steps of HSCT include conditioning, stem cell infusion, neutropenic phase, engraftment phase, and post-engraftment period (Moore et al., 2023). Prior to the intravenous infusion of hematopoietic stem cells, the first phase is the conditioning period where the patient must follow a preparative regimen. This regimen includes creating marrow space, suppressing the patient's immune system, and eradicating malignant cells in those with cancer (NCI, 2023). Suppression of the patient's immune system is intended to prevent the complication of graft rejection (Giralt & Bishop, 2009; NCI, 2023). The process of conditioning lasts 1-2 weeks and may include chemotherapy, immunotherapy, and/or radiation (Moore et al., 2023). Following the conditioning phase is stem cell infusion, which is a relatively simple intravenous infusion process performed at the bedside (Moore et al., 2023). After the stem cell infusion is the neutropenic phase, which can last 2-4 weeks. During this phase, the patient's immune system is weakened, causing patients to be more susceptible to infection (Moore et al., 2023).

The following phase is engraftment, which is the process of infused hematopoietic stem cells producing mature cells in peripheral circulation (Khaddour et al., 2023). The engraftment phase lasts several weeks and during this phase the healing process of mucositis and other acquired lesions begins (Moore et al., 2023). Neutrophil engraftment is defined as the first day and three consecutive days with an absolute neutrophil count of >500/mm^3 (Sahdev & Abdel-Azim, 2016). Platelet engraftment is identified as the first day and three consecutive days with a plalet count of >50,000/mm^3, while remaining platelet transfusion free for at least 7 days (Sahdev & Abdel-Azim, 2016). However, patients are at greatest risk for acute graft versus host disease (GVHD) and viral infections during this time (Moore et al., 2023). Finally, is the post-engraftment phase, which is the period after engraftment (Moore et al., 2023). This phase can last months to years and is a period that includes the weaning of immunosuppressives, management of GVHD, and immune reconstitution (Moore et al., 2023).

Nutrition is an important key factor for children receiving HSCT. Nutrition is needed for cellular biochemical reactions and protection against oxidative damage (Tripodi et al., 2023). Adequate nutrition energy requirements in patients with HSCT are needed as patient's bodies are under extremely stressful conditions requiring energy consumption due to cancers, steroid therapies, antineoplastic drugs, and radiation (Tripodi et al., 2023). Underweight patients may experience higher rates of chemotherapy-related toxicities, profound myelosuppression, and febrile neutropenia and obese patients may experience altered serum protein binding, metabolism, and renal function (Tripodi et al., 2023). Therefore, encouraging adequate nutrition may mitigate drug-metabolism alterations allowing for better clearance of drugs and decreased adverse effects (Tripodi et al., 2023). Nutrition can be classified as delivery of both macronutrients and micronutrients (National Institute of Environmental Health Services [NIEHS], n.d.). Macronutrients are protein, carbohydrates, and fat, which primarily provide energy to the body (NIEHS, n.d.). Micronutrients are vitamins, minerals, and electrolytes that the body uses (NIEHS, n.d.). For children, receiving balanced nutrition from birth and throughout development is vital to ensuring their appropriate growth along with physical and neurocognitive development (Woods et al., 2019). For all children, despite a difference in caloric need by age, a diet meeting all daily requirements is imperative in the prevention of disease and support of the immune system (Koziol-Kozakowska, 2023).

According to Mehta et al. (2013), pediatric malnutrition is defined as “an imbalance between nutrient requirements and intake that results in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development, and other relevant outcomes” (p. 462). Malnutrition is related to illness or environmental factors and may be acute (fewer than 3 months) or chronic (greater than 3 months) (Mehta et al., 2013). Children with a cancer diagnosis facing HCST undergoing extreme physical stress during chemotherapy regimens may potentially have depleted nutrients leading to malnutrition. The etiology of malnutrition in cancer is multifactorial: tumor type and stage, baseline nutritional status, intensity of treatment, host factors, and socio-economic status of the family.

Given the serious sequelae from high doses of chemotherapy and radiation, children who then go on to undergo HSCT are at further risk for malnutrition and decreased quality of life due to nausea, vomiting, diarrhea, poor appetite, taste changes, mucositis, and increased catabolic demands (Murphy, Cooke et al., 2024). Children undergoing a HSCT are estimated to have a 5-50% risk of acquired malnutrition (Evans et al., 2021). Prior to transplant, oral intake is impaired due to mucositis from conditioning, which may cause vomiting, anorexia, and diarrhea. Mucositis is erythema, edema, and ulcerations of the oral mucosa (Bell & Kasi, 2023). Murphy, Cooke, and colleagues (2024) reported that the prevalence of post-infusion HSCT malnutrition was 47%, while 81% had inadequate oral intake. Complications such as acute gastrointestinal GVHD may also impact oral intake. GVHD is a complication that is immune-mediated, caused by the activation of donor T lymphocytes that results in malabsorption and diarrhea (Muratoe et al., 2023). These factors can lead to a reduction in caloric intake resulting in a well-nourished child at risk for malnutrition, or worsening malnutrition that is present (Murphy, Cooke et al., 2024). Therefore, understanding body composition, quality and type of diet, and response to nutrition are integral to the overall care process. A focus on nutritional care in children experiencing different stages of HSCT is essential to optimize outcomes (Tripodi et al., 2023).

Current evidence from the American Society for Parenteral and Enteral Nutrition (ASPEN) recommends the use of enteral nutrition (EN) over parenteral nutrition (PN) and suggests the use of PN when EN is contraindicated (Murphy, Cooke et al., 2024). EN is an effective way to provide nutrition with minimal complications and can support mucosal gut integrity reducing bacterial translocation (Evans et al., 2021). Physiological advantages of EN include an improved immune response and mitigation of the stress response of the illness or injury (Brown et al., 2015). PN has traditionally been used post-infusion of hematopoietic stem cells to bypass the alimentary canal, although it has been associated with increased infection rates, electrolyte imbalances, and liver dysfunction (Murphy, Cooke et al., 2024). Although ASPEN provides recommendation for nutritional support, the recommendations are not being uniformly instituted within the pediatric HSCT population (Murphy, Cooke et al., 2024; Oratz et al., 2022).

Significance

There is currently a paucity of research focused on evidence-based guidelines for pediatric cancer and HSCT nutrition (Evans et al., 2021; Woods et al., 2019). When there is not a clear protocol, timing of nutrition therapy is subjective. This in turn can increase risk of complications and ultimately delay nutritional support, which can affect quality of life. Malnutrition is associated with reduced therapy tolerance, delayed wound healing, increased risk for infection, longer hospital stays, and GVHD compared to those who maintain good nutritional status (Evans et al., 2021; Murphy, Cooke et al., 2024). Inadequate nutrition in these complex patients may result in complications such as delayed clearance of chemotherapy and decreased tolerance to other treatment regimens (Murphy, Cooke et al., 2024). Therefore, this may cause a delay in treatment. Malnutrition can increase risk for complications such as GVHD and increase risk of mortality and morbidity of patients (Murphy, Cooke et al., 2024). Additionally, malnutrition in pediatric HSCT patients can increase hospital length of stay (LOS) and healthcare costs (Murphy, Cooke et al., 2024). Therefore, clear, evidence-based guidelines for nutrition support this population are needed to optimize outcomes.

Framework

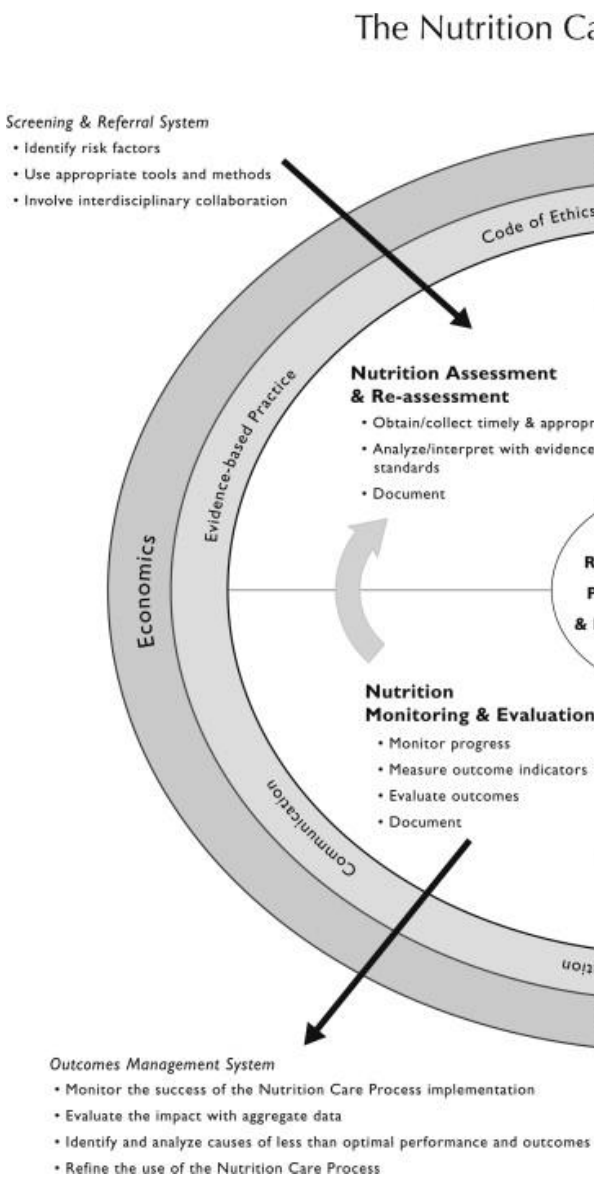
The Nutrition Care Process Model (NCPM) is a framework that utilizes a systematic problem-solving method that food and nutrition professionals use to address nutritional problems (Writing Group of the Nutrition Care Process/Standardized Language Committee [Writing Group of NCP/SLC], 2008). However, the healthcare interprofessional team may also utilize this model. Figure 1 shows the model with four steps in the inner ring, which are nutrition diagnosis, nutrition intervention, and nutrition monitoring and evaluation (Writing Group of NCP/SLC, 2008). Each step in the model informs decision making for the next step, providing an ongoing assessment of nutritional status (Writing Group of NCP/SLC, 2008).

The model also provides a representation of influences of nutrition outcomes from the practice settings, health care systems, social systems, and economical factors in the outer ring. The practice setting reflects regulations of practice; the health care systems reflect the amount of time available for services and professionals; the social system reflects the patient's and family's knowledge, values, and time toward nutrition; and the economics portion reflects nutritional resources to the patient as well as the cost to the nutritional professional (Writing Group of NCP/SLC, 2008). The middle ring of the NCPM represents professional attributes of the nutritional professionals (Writing Group of NCP/SLC, 2008). The core is the collaborative relationship with the patient (Writing Group of NCP/SLC, 2008). The model suggests that all layers and an engaged relationship with the healthcare team will contribute to optimal patient outcomes.

The model also addresses the screening and referral system, and the outcomes and management system. The screening and referral system requires interprofessional collaboration for referral to a nutritional professional to identify patients who may have nutritional problems (Writing Group of NCP/SLC, 2008). The outcomes and management system are based on data collected to determine the performance of the NCPM (Writing Group of NCP/SLC, 2008). Originally, the NCPM was created for the use of nutritional professionals; however, concepts can be utilized by the healthcare interprofessional team and applied the pediatric HSCT population.

Figure 1

The Nutrition Care Process



Note. From "Nutrition Care Process and Model Part I: The 2008 Update," by Writing Group of the Nutrition Care Process/Standardized Language Committee, 2008, *Journal of the American Dietetic Association, 108*(7), 1113–1117. Copyright 2008 by Journal of the American Dietetic Association.

The interprofessional team may utilize this model to continuously monitor patient nutrition (Writing Group of NCP/SLC, 2008). Following the concepts in the inner ring facilitates continuous monitoring of HSCT patients, including timely nutrition assessment, diagnosis, intervention, and evaluation during all steps of the transplant. Use of this model may appropriately identify the timing and type of nutritional support needed, while taking into consideration conditioning and complications of pediatric HSCT patients. Nutritional interventions will be analyzed through the use this model and adjusted according to patient needs (Writing Group of NCP/SLC, 2008). Due to the constant monitoring of nutritional status the interprofessional team may utilize this model for identifying and providing early intervention for the need of EN or PN.

Constructs within the middle ring focus on professional attributes of the nutritional professionals, which in return affect the inner ring (Writing Group of NCP/SLC, 2008). Nutritional professionals are a part of the interprofessional team, who bring critical expertise for informed decision-making of nutritional care to pediatric HSCT patients. These professionals may provide recommendations regarding timing and composition of both EN and PN. Partnering with these professionals can optimize nutritional support for pediatric HSCT patients. Additionally, this could be extended to the interprofessional team as it may also be beneficial to have knowledge of concepts such as EN and PN knowledge, skills and competencies, critical thinking, and evidence-based practice knowledge.

Practice setting, health care systems, social systems, and economics are a part of the outer ring of the NCPM (Writing Group of NCP/SLC, 2008). The outer ring contains external factors, such as social determinants of health or environmental factors that may affect pediatric HSCT patients. Parents and families may have their own knowledge, values, and time related to nutritional support of the patient which can influence nutritional decision making (Writing Group of NCP/SLC, 2008). Economic factors of families may impact their ability to purchase adequate nutritional foods. Other social factors that can also affect the nutritional status of HSCT patients are food deserts and fast-food outlets (NIEHS, n.d.). Food deserts are described as geographic areas where grocery stores are not nearby and people do not have access to affordable and healthy food options (Food Empowerment Project, n.d.). The health care system may influence the amount of time the nutritional professional spends with the patient; therefore, time spent with patients must be focused (Writing Group of NCP/SLC, 2008). This may happen inpatient when nutritional professionals are caring for complex acutely ill patients, such as pediatric HSCT patients. Additionally, rules and regulations, such as hospital protocols, may affect the practice setting in what the nutritional professional may incorporate in their care plan for patients (Writing Group of NCP/SLC, 2008). For example, if hospitals do not have uniform protocols for EN and PN for pediatric HSCT patients, nutritional support may be delayed, adversely affecting the patient. The concepts of each of these rings influence the subsequent rings and when utilizing this model in clinical practice it can ultimately affect patient outcomes.

Although the concepts of the rings discuss the effect of having a nutritional expert on the team and influence of nutritional care for patients, the model may also be utilized and applied to the interprofessional team. If the NCPM can influence a standard approach to assessment, evaluation, and management nutritional status to continuously assess and evaluate patient outcomes for adjustments in nutritional care. Therefore, the use of the NCPM may help impact quality of life in pediatric HSCT patients.

Clinical Question and Purpose

The purpose of this integrative literature review is to determine the outcomes of EN and PN in pediatric HSCT patients and to discuss evidence-based implications summarized through this review. Therefore, this integrative review poses the question of "What is the impact of EN and PN on healthcare outcomes for pediatric HSCT patients?" Furthermore, the objective of the integrative literature review is to summarize evidence that can be implemented into practice to improve patient nutrition and positively affect quality of life outcomes in patients undergoing HSCT.

Literature Review and Synthesis

For this integrative review, a robust literature review search was conducted. The search terms and recommended databases were identified via collaboration with a nursing informationist, a librarian that specializes in nursing research, through a medical library. At this time a table of evidence (Table 1A) and an annotated bibliography (Appendix B) has been completed.

Methods

Design

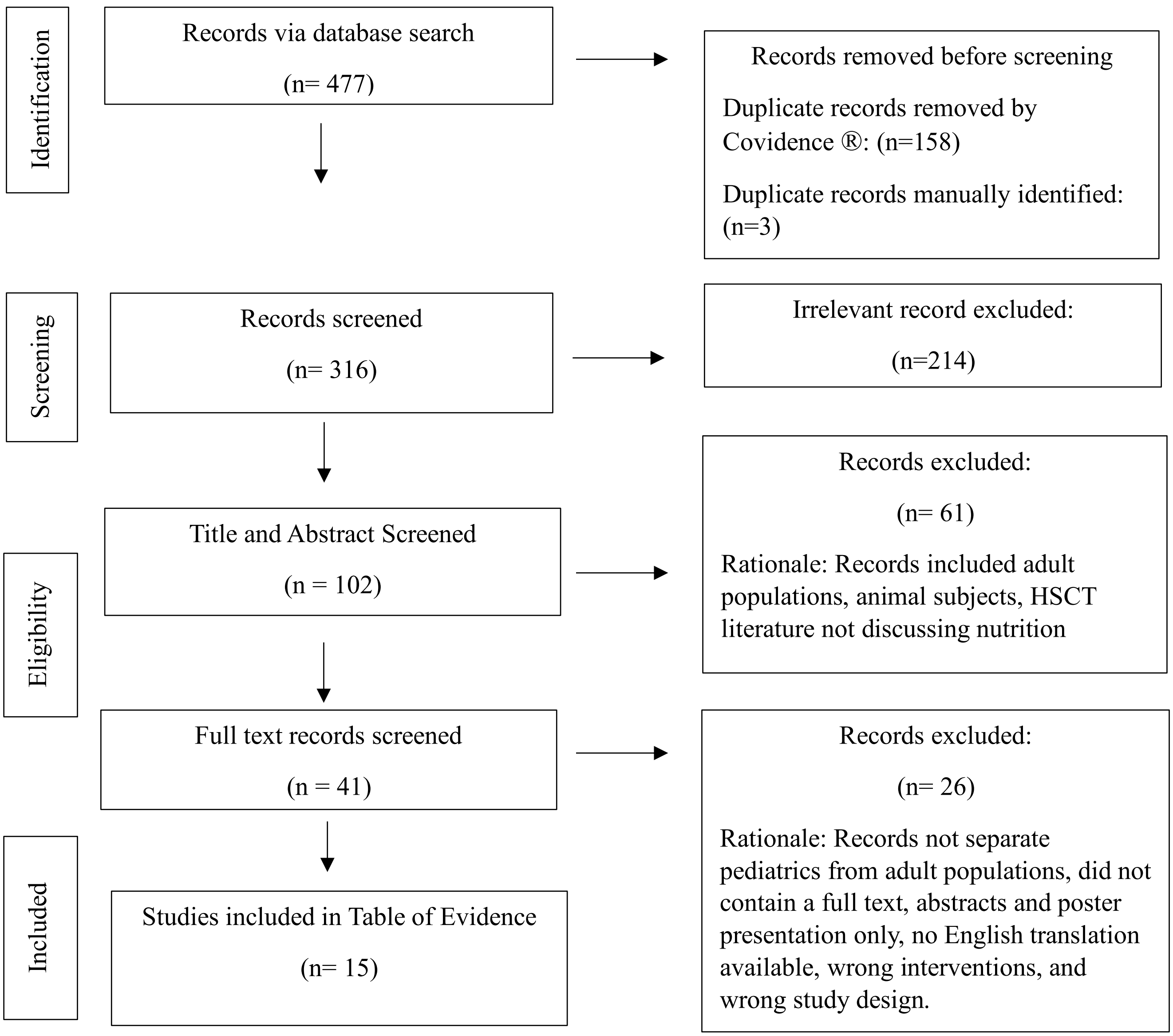
The literature search on EN and PN for pediatric HSCT patients was conducted using the following databases: PubMed, CINAHL, Cochrane, and Healthsource: Nursing/Academic Edition. Mesh terms (for PubMed) and key words were used to search for concepts regarding EN, PN, and pediatric HSCT or bone marrow transplant (BMT). Boolean connector words such as "OR" and "AND" were utilized to combine terms. Variant keywords were used in the search engines to maximize the number of results. After completing the search, 477 studies were identified and Covidence ®, a screening and data extraction tool, was utilized to identify for eligible literature. Covidence ® identified 158 duplicates, three duplicates were manually identified, and all duplicates were removed. Of the 316 eligible papers, 214 papers were irrelevant, which left 102 relevant studies for title and abstract screening, and 41 papers were identified for a full text review. After the full text review, 15 papers were selected, and a table of evidence was conducted for analysis of the literature. See Figure 2 for further details. This integrative review meets criteria of non-human subjects and does not meet requirements for research as defined by Emory Institutional Review Board.

Inclusion and Exclusion Criteria

Inclusion criteria for this integrative review were: 1.) pediatric patients from 0-21 years of age 2.) HSCT patients that include allogeneic and/or autogenic 3.) EN and/or PN. Exclusion criteria were: 1.) papers focused on research with animal subjects 2.) HSCT literature not discussing nutrition 3.) Literature that is published in a foreign language without translation available. The search strategy included randomized controlled trials (RCTs), prospective and retrospective cohort studies, case control studies, cross sectional studies, systematic reviews, and meta-analyses.

Figure 2

Literature Flow Diagram



Population, Sample, and Setting

The focus of the integrative review is pediatric HSCT population receiving EN and/or PN. Pediatric patients are identified as those ages 0-21 years old. These patients may receive EN and/or PN in the acute care setting. Papers included EN administered through various routes including nasogastric tubes (NGT) and gastronomy tubes (g-tube). The timing of administration of EN and/or PN is dependent on study and/or patient requirements. Patients' nutritional status may vary prior to EN and/or PN. As this is not a systemic review with meta-analysis, this integrative review did not limit sample size and may include studies with varying sample sizes.

Barriers

There are few studies determining best evidence-based guidelines for pediatric cancer and HSCT nutrition (Muratoe et al., 2023; Woods et al., 2019). Because of a gap in the literature there are few evidence-based practice nutritional recommendations, including a lack of protocols or guidance for use of EN and PN in this population. In addition, literature may be limited due to ethical considerations of RCTs for deciding which patients to place on EN and PN, which could explain the limited amount of RCTs. However, there are RCTs that compare approaches to feeds and may adjust feeding regimens if the child is not meeting nutritional needs.

Project Management Plan

Appendix A Table 2 provides a visual presentation of the integrative review timeline and when tasks of the integrative review will be completed. This project did not require a budget. The goal is to complete the integrative review by August 2024 with dissemination in the Fall of 2024.

Resources, Key Stakeholders, and Site Support

Search engines utilized were CINAHL, Cochrane, Health Source: Nursing/Academic Edition, and PubMed through Emory University Libraries. Emory University Libraries provided access to databases and access to full-text literature. Nursing informationists were available through Emory University Libraries to aid in database searching and Covidence ® usage. The project team members included are faculty members at Emory University and staff from Children's Healthcare of Atlanta (CHOA). The project team lead is Dr. Christina Calamaro, PhD, Director of Research and Evidenced Based Practice at CHOA and an Associate Professor at Emory University's Nell Hodgson Woodruff School of Nursing. She is my project site lead CHOA and site lead at Emory University. Additional members of the project team include: Dr. Brooke Cherven, PhD who is a part of Nursing Research and Evidence Based Practice at CHOA, who is a renowned pediatric cancer survivor researcher, and an Emory University School of Medicine Assistant Professor; and Dr. Ann-Marie Brown, PhD an Emory University Professor and Director of the Acute Care Pediatric Nurse Practitioner Specialty, who is a national expert in pediatric critical care, and a Nurse Scientist at CHOA. All members were available for assistance. Key stakeholders include clinical partnership with CHOA's research and the BMT department. Site support is provided by CHOA and Emory University.

Plan for Dissemination to Key Stakeholders

This scholarly product is an integrative review that evaluates the effects of EN and PN on pediatric hematopoietic stem cell transplant patients (HSCT). The integrative review will look at the outcomes of EN and PN diet in this population with the intent to improve practice. The primary end users are pediatric HSCT providers, clinicians, researchers, nurses, and others interested. I will provide an interactive presentation during my dissemination for the end users. I can access the following individuals, organizations, and networks to help: Dr. Christina Calamaro, PhD, Dr. Brooke Cherven, PhD, Dr. Ann-Marie Brown, PhD, and CHOA's Aflac Cancer & Blood Disorders Center.

I plan to communicate the results and provide engagement by presenting at the ASPEN Nutrition Science and Practice Conference in March 2025 and to participate in CHOA's symposium in February 2025. Additionally, the integrative review will be submitted for publication to the Journal of Pediatric Hematology/Oncology Nursing during that time. Other potential delivery methods include attendance of a conference or podium presentation with the Association of Pediatric Hematology/Oncology Nursing during 2025. Potential obstacles that I face in disseminating my research include lack of participant attendance and participation. I plan to encourage feedback from end uses and dissemination partners by providing a question-and-answer session at the end of the presentation.

Results

By determining the need for future research on standardization of EN and PN for the HSCT pediatric population, adverse outcomes identified in this review may be mitigated. The outcomes identified for this integrative review include: clinical outcomes of EN and PN, potential complications, and overall hospital and survival outcomes were identified as themes within HSCT pediatric patients. Clinical outcomes are outlined in several papers and include platelet and neutrophil engraftment, degrees of mucositis, and GVHD. Potential complications of EN and PN include infection, electrolyte imbalance, tube placement, and variable weight gain. Finally, overall hospital and survival outcomes were described throughout the literature.

Clinical Outcomes of EN and PN

Engraftment

Five papers reported that EN has favorable outcomes on the rate of platelet engraftment in patients. In the systematic review of randomized and non-randomized studies by Evans, Hirani et al. (2019), platelet engraftment was more frequent in the EN than PN group by day 100 post-transplant. However, delayed platelet engraftment could be attributed to GVHD in allogeneic HSCTs (Evans, Hirani et al., 2019; Gonzales et al., 2018). GVHD may cause thrombocytopenia, and/or long-term administration of intravenous (IV) lipid emulsion. This long-term lipid IV lipid emulsion is thought to cause hyperactivation of monocyte macrophage system leading to prolonged platelet engraftment (Evans, Hirani et al., 2019). Furthermore, this lipid hypothesis could be supported by autologous recipients that utilize long-term IV lipid emulsion and have delayed platelet engraftment (Evans, Hirani et al., 2019). Another consideration of delayed platelet engraftment is due to GVHD in the setting of the PN group, which can contribute to longer hematologic recovery as GVHD can block hematologic stem cell due to medullar insufficiency (Gonzales et al., 2018).

Platelet engraftment criteria were similar across different studies. Platelet engraftment was determined as seven consecutive days of a threshold of ≥50*10^9/L by Azarnoush et al. (2012). The median platelet engraftment was day 23 for the EN group and day 29 for the EN-PN group (Azarnoush et al., 2012). The study by Gonzales et al. (2018) also looked at platelet engraftment at a threshold of ≥50*10^9/L and found faster engraftment in the EN group with a median day of 23 days compared to 29 days in the EN-PN group as well. Although platelet engraftment is defined as ≥50*10^9/L, in one study by Zama et al. (2020), it was found that platelet engraftment was shorter in the PN than EN group with a threshold of >20*109^9/L on days 23.1 vs 35.7 respectively (*p*= 0.04). Although there was shorter platelet engraftment period found in the PN group of this study, however the correlation was not found with the threshold of >50*10^9/L (Zama et al., 2020).

Although platelet engraftment is faster when EN was selected as the nutritional system of delivery there was no difference found in neutrophil engraftment in four papers. In the study by Azarnoush et al. (2012) neutrophil engraftment was determined as three consecutive days of a threshold of ≥0.5 10^9/L and the results showed a median day of 23 in the EN group versus day 24 in the EN-PN group. In the study by Gonzales et al. (2018), to promote neutrophil engraftment, growth factor was administered to both EN and PN, but was administered more in PN (P <0.0001). In the same study, neutrophil engraftment was identified as three consecutive days of a threshold of ≥0.5 10^9/L without transfusions and the results did not differ in the EN versus PN groups despite the use of growth factor (Gonzales et al., 2018). Zama et al. (2020) had the same criteria of neutrophil engraftment and reported a mean of 17.31 days in the EN group and 16.86 days in the PN group. The similar timing of neutrophil engraftment between EN and PN groups was also identified in the systematic review by Evans, Hirani et al. (2019).

Mucositis

Mucositis is a common complication for pediatric patients receiving HSCTs. It can cause variable gastrointestinal effects causing tissue injury (Alsalamah et al., 2022). Mucositis can occur due to conditioning and is common after HSCT (Alaslamah et al., 2022). Papers did not discuss the scale in which mucositis was graded. However, Hasting et al. (2006) classifies mucositis as mild, moderate, and severe. Mild is identified as erythema of the mucosa, moderate is considered as patches of pseudomembranous <1.5 cm in diameter and noncontiguous, and severe is patches of pseudomembranous >1.5 cm in diameter and contiguous (Hastings et al., 2006). The National Cancer Institute grades mucositis by functional/symptom exam and clinical examination seen in Table 3 (Bell & Kasi et al., 2023).

PN was used commonly for severe mucositis and NGTs were used less frequently in one study (Alsalamah et al., 2022). Notably, high grade mucositis was found in 106 (72.2%) of patients receiving PN, while it was found in only 22 (26.2%) of patients who were NGT or orally fed (p= 0.001) (Alsalamah et al., 2022). The study by Gonzales et al. (2018) and the systematic review by Evans, Hirani et al. (2019) did not identify a difference in rates of mucositis between EN and PN groups. Zama et al. (2020) did not see a difference in the duration of grade III-IV of mucositis between patients receiving EN and PN. 5 patients in the EN group and 3 patients in the PN group had grade III-IV mucositis (p= 0.10) (Zama et al., 2020). Hastings et al. (2006) discussed how PN was used when EN feedings were not tolerated like in the setting of mucositis and when mucositis was severe. It was found that oral mucositis led to worse well-being when in the setting of PN (Evans, Hirani et al., 2019; Papadopoulou, 1998). Evans, Hirani et al. (2019) specifically mentioned worse well-being at the start of PN compared to the start of EN (p< 0.001). When considering the use of EN versus PN in HSCT patients, Oratz et al., (2022) discussed implementing a pathway to standardize EN initiation and tube placement on or around day of transplant for HSCT patients. This pathway discussed how mucositis can interfere with tube placement decreasing the use of EN (Oratz et al., 2022). PN can be beneficial for patients with severe forms of mucositis, or when tube placement for EN is not tolerated.

Table 3

National Cancer Institute Mucositis Grading System

	Functional/Symptoms Based Examination	**Clinical Examination**
Grade I	Asymptomatic or mild symptoms, normal diet	Mucosal erythema
Grade II	Moderate pain or ulcer, requires modified oral diet	Patchy ulceration or pseudomembranes
Grade III	Severe pain, interferes with oral intake	Minor trauma, bleeding, confluent ulcers, or pseudomembranes
Grade IV	Life-threatening consequences, requires urgent intervention	Tissue necrosis, spontaneous bleeding, life-threatening
Grade V	Death	Death

Note. Bell, A., & Kasi, A. (2024). Oral Mucositis. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK565848/

Graft Versus Host Disease

As previously mentioned, GVHD is a complication of HSCT, and malnutrition can impact the incidence and severity of GVHD. Early nutritional intervention is imperative; therefore, these patients are at risk for GVHD. Seven studies reported GVHD was more frequent and more severe in patients receiving PN. Several papers mentioned less severe grades of GVHD in EN and grades III-IV were found more in PN. In the study by Azarnoush et al. (2012), six patients had to stop EN due to severe grade III-IV of gut GVHD. EN was often stopped due to poor tolerance, including vomiting, severe diarrhea, and patient refusal (Azarnoush et al., 2012). The systematic review by Evans, Hirani et al. (2019) also identified grades III-IV of GVHD being more common in PN groups by day 100. Gonzales et al. (2018) found that GVHD was lower in all grades in the group that received EN. Woods et al. (2019) discusses the combination use of EN and PN and found that GVHD was more severe or frequent when both groups are used than EN alone. However, the author does not discuss the results of PN used alone in GVHD.

Azarnoush et al. (2012), suggests that EN started early may decrease the incidence and severity of gut GVHD, as starting EN late is associated with a high risk of grade III-IV of GVHD. Poor oral nutrition or no oral intake in patients receiving PN only after HSCT is correlated with more severe GVHD (Azarnoush et al., 2012). Additionally, damage to the gut after conditioning and gut rest causing increased mucosal atrophy and intestinal permeability during PN has led to alterations in gut microbiota further worsening GVHD (Evans, Hirani, et al., 2019).

Additionally, there have been recent findings of NGT versus g-tube feeding methods in the setting of HSCT patients. Papers by Evans, et al. (2023) and Evans, Needle et al. (2019) discuss GVHD with EN delivered by NGT versus g-tube and found no significant difference of effects on GVHD between the use of tubes. Despite the difference of delivery of EN, it is suggested that the protective effects of EN on GVHD can improve gut microbiota in HSCT patients (Evans et al., 2023). Furthermore, EN is beneficial in the maintenance of mucosal gut integrity and barrier (Muratore et al., 2023). PN is recommended for use in the setting of intractable vomiting, ileus, severe malabsorption, or symptomatic gut GVHD (Muratore et al., 2023; Ringwald-Smith et al., 2023). However, when EN versus PN is used there is it associated with a lower grade of GVHD (Muratore et al., 2023).

Potential Complications

There are various complications that can arise from the use and delivery system of EN and PN. Infection, electrolyte imbalance, tube placement, and weight gain are complications identified throughout papers discussed.

Infection

There are lower rates of infection in patients who receive EN in five papers mentioned (Muratore et al., 2023; Papadopoulou et al., 1998; Ringwald et al.,2023; Soussi et al., 2019; Zama et al., 2020). Two papers mention no difference in infections in both the EN and PN groups (Gonzales et al., 2018; Evans, Hirani et al., 2019). The study by Gonzales et al. (2018) found no difference in bacterial versus viral infection in EN or PN. The systematic review by Evans, Hirani et al. (2019) discussed no difference in septicemia, viral infections, and positive blood cultures between the two groups. Another paper mentions that the use of NGTs did not introduce any infections (Azarnoush et al., 2012). Muratore et al. (2023) discussed that EN helps maintain the mucosal gut integrity and barrier and therefore decreasing the risk of infections as compared to PN. Papadopoulou et al. (1998) described several infections within the PN group ranging from rotavirus, cytomegalovirus, and nine infections of unidentified etiologies. Soussi et al. (2019) discusses PN complications in HSCTs and mentions 24 central venous catheter associated infections and 20 episodes of septicemia, which is 43% and 37.2% of patients respectively. However, Soussi et al. (2019) also mentioned that the central venous catheters were also used for other medications as well as PN, so it cannot be confirmed that the central venous catheter associated infections were associated with PN use. Zama et al. (2020) found that central venous catheter infections and bacterial infections from endogenous intestinal flora into the blood stream. Blood stream infections were more common in the PN group (p= 0.02) and could be caused by either severe GVHD or central venous catheter infection (Zama et al., 2020). The paper does not separate the cause of the blood stream infections in data reported. Central venous catheter associated infection can be reduced by the EN group due to reduced use of PN and less central venous line accessing (Zama et al., 2020). Additionally, PN can induce gut mucosal atrophy and dysbiosis allowing for bacterial translocation, while EN can promote gut epithelium and gut microbiota reducing bacterial translocation (Zama et al., 2020).

Electrolyte Imbalance

Several papers discuss the imbalance of electrolytes occurring when PN is infused. Several different types of electrolyte imbalances are identified in literature and there are also findings of protein imbalance. Azarnoush et al. (2012), mentions findings of both hypoalbuminemia and hypophosphatemia in the EN-PN. In the study completed by Hastings et al. (2006) some EN patients experienced hypokalemia and hypomagnesemia, but one patient on PN developed severe hypokalemia and mild hypomagnesemia. Hypomagnesemia, hypophosphatemia, and zinc deficiency were common in both EN and PN, but hypoalbuminemia and biochemical selenium deficiency were worse in the PN group (Papadopoulou et al., 1998). The most observed electrolyte imbalance identified in patients receiving PN by Soussi et al. (2019) was hypokalemia followed by hyponatremia. There were also other electrolyte imbalances identified such as hyper and hypocalcemia, hyper and hypophosphatemia, hypernatremia, hyperkalemia, hyperglycinemia, and hypercholesterolemia (Soussi et al., 2019). To note, electrolyte imbalance can also be exacerbated due to loss of electrolyte absorption through the gut. Papadopoulou et al. (1998) mentions possible protein loss from the gut, further worsening hypoalbuminemia. Overall, it appears that both EN and PN can result in electrolyte imbalances, with more occurrences and severe imbalances identified in the PN group.

Tube Placement Issues

A common complication within the EN group is tube placement issues, which could impact the nutrition delivered to the patient via EN. At times it can be difficult to place an NG or naso-jejunal tubes (NJT) in patients. In a study by Oratz et al. (2022), if NJTs were dislodged many patients refused replacement of the tube. NGT refusal was also seen in the study completed by Evans et al. (2023). Other considerations for NGT placement include the risk of bleeding during tube placement in patients that have thrombocytopenia and uncontrollable vomiting (Ringwald-Smith, et al., 2023). NGT refusal and consideration may lead to PN use (Evans, Needle et al., 2019; Ringwald-Smith, 2023). Other patients that did not have tubes replaced were patients experiencing severe mucositis (Oratz et al., 2022). In this case, patients would receive PN. G-tubes can be considered if NGT feeding is deemed unrealistic (Evans et al., 2023). Complications of g-tubes can include mechanical issues, dislodgement, and infection of the g-tube site (Evans et al., 2023). Evans et al. (2023) mentions a study where PN was initiated earlier in patients with refusal of NGT than those that had a gastrostomy. NGTs, NJTs, and g-tubes are reasonable methods of EN with various complications surrounding placement.

Weight Gain

There is variation of weight gain reported between the EN and PN groups post HSCT. In the study by Azarnoush et al. (2012), body weight gain was not significantly higher in the EN-PN group compared to the EN group. There were five patients who lost 10% of their initial body weight, one in the EN-PN group and four from the EN group (Azarnoush et al., 2012). Evans, Hirani et al. (2019) found no difference in children losing ≥10% in weight in EN or PN groups. Papadopoulou et al. (1998), found no difference in weight for height between EN and PN groups. In Bickali et al. (2012), 68% of patients gained or maintained their weight in the EN group.

Weight gain was identified in a PN group, however many patients in this group had edema, which could contribute to the weight gain (Gonzales et al., 2018). In the study by Hastings et al. (2006), 87% of patients were above the 50^{th} percentile for weight for age and at discharge it dropped to 80% of children that received EN. There are findings of weight gain in EN delivered through NGT and g-tube in HSCT patients. However, there has been no significant difference in weight gain in the use of NGT versus g-tube delivery of EN past day 91 (Evans et al., 2023). Overall, there were varying results when comparing weight gain between EN and PN.

Overall Hospital and Survival Outcomes

Morbidity, mortality, and LOS were discussed in some of the papers reviewed. Several papers reported decreased LOS in the EN group. LOS was also found to be longer in the PN group in a review by Woods et al. (2019). In a study by Gonzales et al., (2018), it was found that EN had a shorter LOS than PN ($p < 0.0001$). However, in a study by Zama et al. (2020) LOS was higher in the EN group with a mean of 71.8 days versus 60.1 days in the PN group. Although mean LOS was higher in the EN versus the PN group, there was no significance found in LOS (Zama et al., 2020).

Additionally, morbidity and mortality also had variable results reported between EN and PN fed groups post HSCT. It was found that morbidity and mortality was decreased in patients who received EN (Azarnoush et al., 2012). Regarding mortality, in a systematic review of randomized and non-randomized studies by Evans, Hirani et al. (2019) found no difference in day 100 non-relapse mortality in EN and PN groups. Woods et al. (2019) also identified no deaths reported after day 100 (Woods et al., 2019). In the study completed by Alsalamah et al. (2022) and Azarnoush et al. (2012), survival rate was the same in EN and PN groups. It was also discussed in a narrative review that overweight children before HSCT have a reduced probability of survival than ideal weight children (Muratore et al., 2023). Children were identified as overweight if the patient's body weight and ideal body weight ratio was higher than 1.1 (Muratore et al., 2023).

Implementation Case Study

To further understand the impact of nutrition in the pediatric HSCT population, a simulated case study may be useful. In this integrative review, a 10-year-old, female patient diagnosed with acute lymphoblastic leukemia and was hospitalized for 22 days post-HSCT. Prior to HSCT the patient received a seven-day conditioning regimen consisting of chemotherapy. She received her allogenic HSCT on day 0. NGT placement was ultimately delayed to later during the hospitalization and placed during day 5. Due to the delayed NGT placement the patient developed grade III GVHD by day 9 and was then placed on PN administered through a central line. While on PN, the patient did not develop any infections. The patient did have electrolyte imbalances such as hypokalemia and hyponatremia that were corrected through PN adjustments and IV supplements. Once stabilized, the patient was able to tolerate NGT placement and EN by day 15. EN was started while on PN until the patient was able to be weaned from PN. The patient was able to be weaned from PN by day 19. In this scenario, EN was started later in the hospitalization during HSCT. This integrative review may help better understand the best standard of care for this patient.

Discussion

This integrative review identifies how delivery of nutritional regimen, whether EN or PN may affect outcomes in pediatric HSCT patients. Overall, EN has been associated with platelet engraftment, improved gut microbiome and therefore potentially lessening severity of GVHD and mucositis. PN is used during higher grade GVHD and severe mucositis. HSCT patients that receive PN are more likely to experience electrolyte imbalances and acquire infections. According to ASPEN and the European Society for Parenteral and Enteral Nutrition (ESPEN), it is recommended to implement EN as a first method of nutrition support for HSCT patients (Ringwald-Smith et al., 2023). In addition, the European Blood and Marrow Transplantation and ESPEN guidelines recommend the use of early EN as a first-line option and PN use should only be used when EN is contraindicated (Ringwald-Smith et al., 2023; Zama et al., 2020). Despite recommendations, centers still report use of PN over EN due to availability and convenience of central venous lines and the perceived invasiveness of EN (Zama et al., 2020). There were no differences in survival rates, neutrophil engraftment, or weight gain between EN and PN supported HSCT patients.

Weight gain and body mass index (BMI) are widely used to evaluate nutritional status (Evans, Hirani et al., 2019). However, weight and BMI do not provide details of body composition. Mid-upper arm circumference (MUAC) or bioelectrical impedance analysis (BIA) are found to be more sensitive markers for nutrition evaluation (Evans, Hirani et al., 2019). The BIA estimates body composition by measuring the opposition of body tissues to the flow of an alternating electrical current that is applied to the skin through electrodes (Orsso et al., 2022). CDC provides a MUAC chart for children and adolescents aged 2 months through 19 years old (Fryar, 2016). However, there is no standardized calculations for BIA in children (Rudney et al., 2020). There may even be electrical differences in BIA instruments that result in different measurements in standardization of body composition (Rudney et al., 2020). In order to improve accuracy of nutritional status, future research should include the use of MUAC or BIA.

Interventions to support the use of EN include placements of tube systems such as NGTs, NJTs, or g-tubes. G-tubes may be a feasible option as there are currently no differences found for post-transplantation outcomes compared to NGTs (Evan, Needle et al., 2019). However, those with g-tubes utilize EN longer than the non-gastrostomy group and often are discharged home with EN (Evans, Needle et al., 2019). Placing an NGT prior to the first signs of mucositis can reduce the need and duration of PN (Ringwald-Smith et al., 2023). There is currently no consensus regarding an appropriate timeline of placing tubes (Murphy, Symons et al., 2024). Implementing a pathway for tube placement can be useful to standardize an approach to EN support for patients undergoing HSCT (Oratz et al., 2022). More research is needed regarding pathways for EN and PN nutrition.

Implications and Recommendations for Practice

Evaluation of the evidence suggests that EN should be considered as first line therapy for HSCT patients. It may be reasonable to initiate a NGT, NJT, or g-tube prior to HSCT. As previously mentioned, conditioning for HSCT may include chemotherapy, immunotherapy, and/or radiation causing vomiting, diarrhea, and mucositis. Initiating EN prior to conditioning may enhance outcomes and potentially limit implementation of PN. Initiating EN early may increase tolerance of tube placement due to the absence of irritable factors such as vomiting and mucositis. PN may be considered if EN cannot be tolerated due to uncontrollable vomiting, severe mucositis, diarrhea, and/or if tube placements are poorly tolerated. When possible, EN should be given with PN to help fortify gut microbiota as first line of defense against infection and to promote healing. Although, more studies are needed for a standardized approach to implementation of EN.

Comprehensive nutritional assessments may ensure patients are nourished prior to the start of HSCT. Nutritional assessments are important to consider as malnutrition is an independent risk factor for non-relapse mortality (Evans, Hirani et al., 2019). A comprehensive nutritional assessment during HSCT can provide sensitive markers for nutritional status and may limit complications (Evans, Hirani et al., 2019). Providing a consistent anthropometric measure throughout HSCT can help evaluate nutritional status (Evans, Hirani et al., 2019). Anthropometric measurements to consider using are the MUAC or BIA assessments.

Limitations

This integrative review includes limitations as studies included were primarily retrospective reviews with few randomized control trials. Studies also had small samples with papers having less than 100 patients. This integrative review looked at various types of literature; therefore, studies included may also be mentioned in systematic, narrative, or other reviews of literature. Studies mentioned within systematic reviews were not looked at individually.

Conclusion

Nutrition is an important factor in pediatric patients receiving HSCT. Nutrition can modify the impact of HSCT complications including GVHD and mucositis. Early nutritional intervention can also mitigate side effects of conditioning prior to transplant. EN is the recommended first line option and helps with overall outcomes of patients undergoing HSCT. There are increased complications associated with PN such as electrolyte imbalances and higher rates of infection. However, PN may be necessary when EN is no longer tolerated due to serve mucositis, vomiting, diarrhea, or in the setting of GVHD. Additionally, to accurately measure nutritional status, more research is needed in the use of the MUAC and bioelectrical impedance.

There is currently a paucity in research regarding a nutritional timeline for standardized approach to implementation in this population. More research is needed in early EN administration. Prospective studies will aid in providing information supporting nutritional interventions in this population.

Evaluation of the Process and Experience

Moving forward, I have found that nutrition is imperative to health outcomes of pediatric patients, especially those undergoing HSCT. In my project I focused on HSCT patients, but the importance of nutrition can extend to other disciplines within healthcare. It is evident that the medical community needs to consider adequate nutrition intervention as an important first line therapy for fighting disease, treating patient illness, mitigating complications of standard therapies such as chemotherapy for cancer, and improving outcomes. Additionally, I have learned that there is still much to know about the value of EN and the effects on health outcomes in all diseases and conditions. As I begin practicing as a nurse practitioner, I will take into consideration patients' nutritional status and ensure they are receiving the proper nutrition.

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Appendix A

Table 1. *Synthesis of Evidence for "The Effects of Enteral and Parenteral Nutrition on Hematopoietic Stem Cell Transplant Patients: An Integrative Review"*

Reference, Year	Study Design	Population, Setting	Study Objectives	Study Results	Comments	Level of Evidence, quality
Alsalamah et al., 2022 "The outcome and complications of total parenteral nutrition in pediatric hematopoietic stem cell transplantation"	Quantitative: Retrospective study	Patients <14 years old who received HSCT between 2015-2019	Analyzed the impact of PN in pediatric HSCT patients and its impact on survival and possible related complications.	PN is commonly used for severe mucositis. NGT feeding were found to be the least used method in this retrospective study. Sinusoidal obstruction syndrome was a statistically significant finding. GVHD was associated more frequently with TPN patients than EN.	Limitations: -Retrospective study -Unmeasured confounders could may have caused assignment to each group to be biased.	Level III, High Quality
Azarnoush et al., 2012 "Enteral nutrition: a first option for nutritional support of children following allo-SCT?"	Quantitative: Prospective cohort study	Patients <18 years old who received MAC allo-SCT in France between 2003-2010 Acute leukemia and	Analyzed the outcome of systematic early EN in a pediatric population that underwent MAC allo-SCT.	Neutrophil recovery was not different between EN and EN-PN groups. Platelet recovery was shorter in the EN group. Length of hospital stay was shorter in the EN group. GVHD was more frequent and severe in the	EN was started the day after transplant on all patients. If PN was needed it was started 14 days after transplant. It was started for poor gut intolerance and severe grade III-IV GVHD. In 6 patients EN was stopped. It was suggested that early use of EN may lessen morbidity and mortality and cost. Also, PN	Level III, High Quality

		non-malignant hematological conditions		EN/PN group. BMI Z-score was not significantly higher in the groups. Hypoalbuminemia and hypophosphatemia were more frequent in EN-PN. EN was seen to decrease both incidence and severity of GVHD, due to seeing low frequency of GVHD and gut manifestations.	should be used only as a rescue option. It is recommended that when possible PN should be used in combination with EN. Limitation: -This is the largest cohort assessing the effectiveness of early systematic EN in children who underwent HSCT. -There is an absence of data on children under 4.	
Bicakli et al., 2012 "Enteral nutrition is feasible in pediatric stem cell transplantation patients"	Quantitative: Retrospective study	100 children transplanted between 2005-2009	Aimed to demonstrate if EN if feasible in daily practice of HSCT.	5% of patients could not tolerate EN and required PN. 68% of patients gained or maintained their weights. EN was found to be a feasible option of nutritional delivery.	Limitations: -Retrospective study -Only used weight for evaluation of nutritional status.	Level III, Good Quality

Evans, Hirani et al., 2019 "Nutritional and post-transplantation outcomes of enteral versus parenteral nutrition in pediatric hematopoietic stem cell transplantation: A systematic review of randomized and nonrandomized studies"	Systematic review	Children < or = 18 years undergoing autologous or allogenic HSCT	Determined the efficacy of EN vs PN in HSCT, through randomized and observational studies. The primary outcomes considered efficacy in relation to nutritional parameters, including nutritional intakes, nutritional status, and use of nutritional interventions. Secondary outcomes included various post-transplantation parameters, such as mortality, infections, and GVHD.	EN was well tolerated with 70% to 100% of EN groups that used only EN. There were conflicting results of EN vs PN for interventions, nutritional intakes, biochemical anthropometric changes, mortality, infections, LOS, and neutrophil engraftment. Although the evidence of EN was favorable over PN in GVHD and platelet engraftment. There was inconsistent reporting of nutritional intakes and anthropometric measurements between EN and PN. It is recommended to use the MUAC or bioelectrical impedance as more sensitive markers of nutritional status. The article found that PN	The authors recommend standardization of nutritional measurement. Limitations: -Some studies had absence of baseline confounding parameters, statical control, selection bias, randomization, and control groups -Retrospective studies	Level I, High Quality

				had more hypoalbuminemia. There were not more infections in PN. EN had lower GVHD grades, better gut microbiome, less mucosal atrophy, and reduced risk of bacterial translocation.		
Evans et al., 2023 "Complications and outcomes of gastrostomy versus nasogastric tube feeding in paediatric allogeneic bone marrow transplant: A prospective cohort study."	Quantitative comparative: Prospective study	United Kingdom. Children received allogeneic HSCT from 2021-2022. 19 patients had a NGT and 24 had a g-tube	Aimed to compare enteral tube complications and nutritional and clinical outcomes between children with gastronomies and NGT throughout HSCT.	87% of g-tube patients had complications and 97% of those were minor complications. The most common complication was mechanical at 58%. The most common complication of NGT was dislodgement. There was no significant difference in survival between NGT and g-tubes.	It is suggested that when NGT cannot be tolerated to use a g-tube. Limitations: -Not randomized -Small sample size -Single center study -Nutritional intake was measured 3 days monthly from months 2-6	Level III, High Quality
Evans, Needle et al., 2019 "Early outcomes of gastrostomy feeding in	Quantitative: Retrospective cohort study	Patients <18 years old who received allogenic HSCT or myeloablativ	Primary objective was to compare PN use between gastrostomy vs. non-gastrostomy	There was no difference of PN duration between g-tubes and non g-tube fed children. There was no difference	Limitations: -No randomization -Retrospective study - Only know early outcomes	Level III, High Quality

paediatric allogenic bone marrow transplantation: A retrospective cohort study.”		e conditioning (MAC) in the United Kingdom between 2014-2018	fed children during admission for HSCT. The secondary objective was to compare further nutritional and post-transplantation outcomes, which includes weight and albumin changes, GVHD, positive blood cultures, and survival between EN and PN.	was found in the hypoalbuminemia. G-tube fed children required less PN and if PN was require it was initiated later. PN was provided first line in 21% in non g-tube group due to NGT refusal. More children with gastrostomies required EN at discharge than those in the non g-tube group. EN only had shorter admission, less GVHD grade III and IV, and faster platelet engraftment than the EN-PN group. There was no difference in catheter associated infections.	-Long-term impact of g-tube feeding post-discharge was not reported -Some selection bias as those with g-tubes are more likely to choose EN	
Gonzales et al., 2018 “Better early outcome with enteral rather than parenteral nutrition in children	Quantitative: Retrospective study	Pediatric patients from 2003-2013 in 3 different French centers, <18 years	Compared the early administration of EN versus PN in: -rate of overall survival at day 100	EN had a greater day 100 overall survival rate at 99% vs. 86.4% for PN (p=0.013). Also the LOS was shorter. There was a lower rate of non-relapse mortality at 1.0% for EN vs. 7.2%	Limitations: -Study only included EN patients from a single center -Did not accurately determine the daily oral intake or the amount of EN or PN delivered. -Retrospective study	Level III, High Quality

undergoing MAC allo-SCT"			-rate of non relapse mortality at day 100 - incidence of GVHD within 100 days -neutrophil and platelet engraftments -number of transfusion of RBCs and platelets between day 0 and engraftment -infections within day 30 -mucositis -length of stay - overall nutritional status within day 100 -biological data	for PN (p=0.066). Lower incidences of GVHD grade III-IV were in the EN group at 10% vs. 29% in the EN-PN group (p=0.032). There was also lower gut GVHD at 6% for EN vs. 39% for EN-PN (p=0.0001). Platelet engraftment was better in EN with engraftment at day 23 vs. day 29 in EN-PN. There was no difference of neutrophil engraftment. No difference was found in bacterial and viral infections and mucositis. The length of time of nutritional support was significantly shorter for EN. There was greater weight loss in EN group at discharge and day 100.		

Hasting et al., 2006 “Enteral nutrition and bone marrow transplant”	Quantitative: Retrospective study	1999-2000 Pediatric patients undergoing allogeneic HSCT	Evaluated the efficacy of enteral feeding in meeting nutritional and energy requirements in patients undergoing HSCT. Secondary aim was to document the complications associated with the HSCT process and the ability to maintain enteral feedings.	The patients in the study were able to tolerate EN. One patient needed PN for 1 week due to excessive gastrointestinal toxicity. Complications of EN included vomiting, diarrhea, and mucositis. However, they were not severe enough to stop EN in all patients except one. The authors question the assumption that weight is an accurate indicator of nutritional status. 32% of daily energy requirements were met with NGT. On discharge 80% of patients were above the 50^{th} percentile for weight for age.	Limitations: -Small sample size -Retrospective study	Level III, Good Quality

Muratore et al., 2023 "The emerging role of nutritional support in the supportive care of pediatric patients undergoing hematopoietic stem cell transplantation"	Narrative review	Pediatric patients	Aimed to comprehensively review evidence on nutritional support for pediatric HSCT patients. To discuss the relationship between HSCT and nutritional status and type of nutrition between different phases of transplant. Address the relationship between nutritional status and clinical outcomes and evaluation of nutritional supports (from diets to artificial feeding).	There is a lack of a homogeneous way to assess malnutrition in children. Also, it is challenging to address nutritional needs in different ages. Children who are overweight before allo or auto HSCT have a reduced probability of survival than compared to ideal-weight children. There are lower incidences of GVHD grade II-IV in EN than PN. Faster platelet engraftment was found in the EN group. The possible use of g-tubes in children undergoing HSCT was also assessed and it was found that it the approach was feasible with lower rate of PN.	How to measure nutrition: -Mid-upper arm circumference (MUAC) is a sensitive parameter to detect the risk of malnutrition in children undergoing HSCT (good projection of whole-body muscle and fat mass) -SCAN (nutrition screening tool for child hood cancer) type of cancer, intensity of treatment, presence of GI symptoms, food intake over the past week, weight loss over 1 month, presence of signs of undernutrition -DEXA (Dual Energy X-ray Absorptiometry): based on the different absorption of two peaks of x-rays by the soft tissue and the bone, it is the current clinical gold standard for bone and body composition -BIA (Bioelectrical Impedance Analysis): evaluates cellular electrical properties Limitations: - Data on pediatric patients are few	Level V, High Quality

Oratz et al., 2022 "Nutritional Support: Enteral Nutrition Pathway for Children Undergoing Hematopoietic Stem Cell Transplantation."	EBP quality improvement project	24 pediatric patients	Evaluated the safety and feasibility of implementing an EN pathway for children undergoing HSCT.	22 patients were discharged without any significant difference in their weight, despite receiving chemotherapy for their conditioning regimen. All patients who survived through discharge (n = 22) were able to consume some or all their daily calories orally by discharge. 17 patients received EN via an NJT and 4 via NGT. Implementation of the a pathway for EN tube placement did not lead to statistically significant changes	Limitations: -Inconsistency of placing a NJT at bedside and maintaining the tube -Pre and post implementation pathway change groups were small	Level IV, High Quality

Papadopoulou et al., 1998 “Nutritional support in children undergoing bone marrow transplantation”	Quantitative: Prospective study	39 pediatric patients undergoing HSCT	Compare EN with PN with respect to maintaining weight, improving general 'well-being', and reversing nutrient deficiencies in children undergoing HSCT.	No significant deterioration in anthropometric measurements. Oral mucositis was associated with poorer 'well-being' at the start of PN compared with EN (P< 0.0001). Hypomagnesaemia, hypophosphataemia, and biochemical zinc deficiency were common in both groups. However, hypoalbuminaemia and biochemical selenium deficiency were worse in the PN group. EN was associated with a better nutritional response.	Mentions indications for nutritional intervention when weight loss was more than 5% of the admission weight and/or a greater than 10% decrease in mid-arm circumference. Limitations: -Lack of randomization -Small sample size	Level III, High Quality

Ringwald-Smith et al., 2023 “Nutrition management of pediatric patients undergoing hematopoietic stem cell transplantation: Guidelines, gaps, and research”	Literature Review	Pediatrics HSCT	Highlighted gaps in current guidelines and research regarding nutrition management.	Recommendation to place NGT before or at the first signs of mucositis, as this can reduce the need for PN. PN should only be used to in patients who are unable to tolerate and/or nutrition is not being met by oral or EN. EN has shorter length of stay, mortality rate, severity of GVHD grade II-IV and gut GVHD, less blood stream infection.	Limitations: -Lack of clear guidelines for managing nutrition -Not enough publications outlining how to determine macro and micro nutrition needs throughout transplant and when/what type of nutrition is needed	Level V, High Quality
Soussi et al., 2019 “Parenteral nutrition complications in children undergoing bone marrow transplantation.”	Quantitative: Retrospective and observational study	51 allografted children 2-17 years of age	Reported and described all observed PN-related complications in children undergoing allogenic bone marrow transplantation in a tertiary center and determined the possible risk factors.	92% of patients (n=47) developed a total of 136 complications attributable to PN. Infectious complications (32.3%) and electrolytic disorders (27.9%) were the most common identified. There were 24 episodes of infection associated with catheters. There were 20 episodes of	Limitations: -Difficulty in establishing an affirmative cause and effect relationship between PN and the onset of the complications -The results may have overestimated PN complications -Retrospective design	Level III, High Quality

				septicemia. The most common electrolyte imbalance was hypokalemia as 17 patients (33.3%) presented with hypokalemia. Eight patients (16%) had hyponatremia. 6 patients (11.8%) had hyperglycemia. Emphasized that EN protocols would be the best way to avoid these complications.		
Woods et al., 2019 "Enteral and parenteral nutrition: An integrative literature review on nutrition in pediatric recipients of hematopoietic stem cell transplantation."	Integrative review	experimental and non-experimental research studies 6 papers utilized	Evaluated the effectiveness of EN versus PN to meet nutritional and energy needs of pediatric HSCT patients.	EN should be recommended over PN because of its preservation of the GI tract. EN has been shown to limit complications, minimize length of hospital stays, and promotes better quality of life in this population.	Limitations: -Only two papers had a sample size greater than 100 patients, most studies were of a smaller sample size -Only one randomized blind study	Level V, High Quality
Zama et al., 2020 "Enteral nutrition protects	Quantitative: Retrospective	42 pediatric patients undergoing allo-HSCT	Evaluated the role of EN regarding clinical and	There were less blood stream infections in the EN ($p= 0.02$).	Limitations: -Small sample size -To date, no study exists in the literature evaluating how long	Level III, High Quality

children undergoing allogeneic hematopoietic stem cell transplantation from blood stream infections.”		Between 2016-July 2019	nutritional outcomes in paediatric allo-HSCT recipients and comprehend the impact of the type of nutritional support on the main complications of allo-HSCT.	Platelet engraftment was shorter in the PN group than in the EN group for a threshold of >20*109/L (p =0.04) (23.1 vs 35.7days). However, it was not shorter for the threshold of > 50*109/L. Earlier oral realimentation was observed in the EN group(p=0.08)(20.9vs .27days). There was no statistically significant difference found regarding nutritional outcomes between the two groups. EN is a feasible and nutritionally adequate method of nutritional support for children undergoing allo-HSCT. The time to neutrophil engraftment and days of G-CSF administration were not different between the groups. PN may	EN should be administered with the aim of inducing a protective effect on the microbiome	

				induce gut mucosal atrophy and greater dysbiosis. This in turn can promote bacterial translocation. Central venous catheter (CVC) infections may be reduced in the EN group due to less handling of the CVC.		

Table 2. *Timetable for "The Effects of Enteral and Parenteral Nutrition on Pediatric Hematopoietic Stem Cell Transplant Patients: An Integrative Review"*

	March 2024	April 2024	May 2024	June 2024	July 2024	Fall 2024
Data Evaluation and Date Reduction in the form of a table of evidence	X					
Data Analysis in the form of annotated bibliography		X				
Methods		X				
Integrative Review Findings and Summary				X		
Evidence-Based Practice (EBP) Implementation Case Study				X		
Discussion and Conclusions, Implications and Recommendations					X	
Present project to organization						TBD X

Appendix B

Annotated Bibliography

Alsalamah, S., Alramyan, R., Alakel, R., Altheyeb, F., Alrashed, R., Masuadi, E., Alyousif, G., Bin Sunaid, F. F., Alsultan, A., & Essa, M. F. (2022). The outcome and complications of total parenteral nutrition in pediatric hematopoietic stem cell transplantation. *Pediatric Transplantation*, *26*(3), e14198. https://doi.org/10.1111/petr.14198

Summary

The purpose of this study is to analyze the impact of total parenteral nutrition (TPN) in pediatric hematopoietic stem cell transplant (HSCT) patients and its impact on survival and possible related complications. In the retrospective study it was found that TPN was commonly used for severe mucositis and that nasogastric tube (NGT) feedings were least used method. TPN was used with 63.2% of patients. The survival rate was the same in TPN patients and non-TPN patients. However, a significant association with feedings was not found. There was a statistically significant finding of sinusoidal obstruction syndrome (SOS) in the TPN group, with most of the patients receiving myeloablative conditioning (MAC). TPN use was also associated more with acute graft versus host disease (GVHD) than enteral nutrition (EN).

Analysis

Limitations include the retrospective study and that assignment to each group may have been biased due to unmeasured confounders. There was also a small sample size with only 228 patients. Further investigation may be needed to see if TPN caused SOS, or if it was caused by myeloablative conditioning. It was beneficial to know that survival rate did not change in each group; however, the TPN group had a larger population. Patients who did use TPN were more likely to have mucositis.

Application

This paper suggests that TPN was used more in patients with GVHD and severe mucositis, which were more likely to receive MAC regimens. The paper also mentions SOS developing in TPN use especially in patients who received MAC for hemoglobinopathies, this may be a reason to avoid TPN use. This could help understand when TPN was used. This study also displayed there was no impact on survival.

Azarnoush, S., Bruno, B., Beghin, L., Guimber, D., Nelken, B., Yakoub-Agha, I., & Seguy, D. (2012). Enteral nutrition: A first option for nutritional support of children following allo-SCT? *Bone Marrow Transplantation*, *47*(9), 1191–1195. https://doi.org/10.1038/bmt.2011.248

Summary

The purpose of this prospective study was to analyze the outcomes of systemic early EN in a pediatric population undergoing MAC allogenic stem cell transplant (allo-SCT). There was a standardization in this study as all patients were started on EN the day after transplant and if PN was needed it was started 14 days after transplant for poor gut intolerance, severe GVHD, or for acute respiratory distress. The study found that neutrophil recover was not different between the EN and EN/Parenteral Nutrition (PN) groups. Platelet recovery was shorter in the EN group. Hypoalbuminemia and hypophosphatemia were more frequent in the EN/PN group. In the EN/PN group, GVHD was more frequent and severe. The study found that the low frequency of GVHD, especially gut manifestations, suggest that EN started early can help decrease incidence and severity. BMI Z-scores were not significantly higher in either group. Hospitalization was shorter in the EN group.

Analysis

The study suggest that early use of EN may help lessen morbidity and mortality. It suggested that PN should only be used when needed as it appeared to have more side effects (i.e. electrolyte imbalances). Limitations include this being the largest cohort of assessing early systematic EN in children. There was also an absence of data in children under 4 years old.

Application

This paper helps show shorter hospitalizations and GVHD occurrence in EN use. The paper also shows a standardization in use. The paper shows PN can have side effects such as electrolyte imbalance. It also suggested PN use in more severe GVHD.

Bicakli, D. H., Yilmaz, M. C., Aksoylar, S., Kantar, M., Cetingul, N., & Kansoy, S. (2012). Enteral nutrition is feasible in pediatric stem cell transplantation patients. *Pediatric Blood & Cancer*, *59*(7), 1327–1329. https://doi.org/10.1002/pbc.24275

Summary

The study aimed to demonstrate is EN is feasible in daily practice of HSCT. In this retrospective study only 5% of patients could not tolerate EN and PN was required. 68% of patients gained or maintained their weights. EN was started in 71% of patients prior to initiation of HSCT. In the beginning of their study patients were already malnourished with 24% of patients under the 3rd percentile and 26% above the 50th percentile. Overall, it was found to be feasible option.

Analysis

Limitations of this study include only using weight measurements for evaluation of nutritional status. The study also used a retrospective design. The feasibility and tolerance of EN may have been contributed to adequate emesis control and timing of EN initiation, as it was started in a majority of patients prior to the start of HSCT. This study suggests that EN is less likely to experience infections, frequency of GVHD, a better nutritional response, and more likely to go home early.

Application

This study displays that when initiating EN promptly (before HSCT or as soon as possible) the outcomes are better and weight is gained or maintained. The study also may suggest that if emesis is controlled, the patient may have better nutritional outcomes, which could be helpful in improving quality of care of patients. The patients also had less infections and frequency of GVHD, which is a positive outcome.

Evans, J. C., Hirani, S. P., & Needle, J. J. (2019). Nutritional and Post-Transplantation Outcomes of Enteral versus Parenteral Nutrition in Pediatric Hematopoietic Stem Cell Transplantation: A Systematic Review of Randomized and Nonrandomized Studies. Biology of Blood and Marrow Transplantation. *Journal of the American Society for Blood and Marrow Transplantation, 25*(8), e252–e259. https://doi.org/10.1016/j.bbmt.2019.02.023

Summary

The purpose of this systematic review was to determine the efficacy of EN and PN during admission of HSCT through randomized and observation studies. The systematic review also looked at the efficacy in relation to nutritional parameters and post-transplant parameters. The study found that En was tolerated with 70% to 100% of EN groups maintaining exclusively on EN. Overall there were conflicting results on EN and PN for interventions, nutritional intakes, biochemical anthropometric changes, mortality, infections, admission length, and neutrophil engraftment. EN was found favorable in benefits of GVHD and platelet engraftment. EN was found to maximize gut microbiome, prevent mucosa atrophy, and reduce the risk of bacterial translocation. There were inconsistent reporting of nutritional intakes and anthropometric measurements. PN had more hypoalbuminemia. The study did not find more infections with PN.

Analysis

This systematic review was able to look at multiple studies of EN and PN use in HSCT. There were not more infections identified with PN, this could be because studies had a short time period. The study mentions that there needs to be a standardization of nutritional measurement in children, as there was inconsistent reporting of anthropometric measurements. This makes understanding nutritional status difficult. Additionally, a limitation is that some studies has moderate to serious risk of bias from the absence of baseline parameters, retrospective design, selection bias, randomization, and control groups.

Application

This study shows that EN helps with rates of GVHD and platelet engraftment, which is a positive outcome in HSCT patients. PN was shown to have more episodes of hypoalbuminemia. However, there was shown to be no admission length difference in EN and PN groups. The paper did find the need for a standardization of measuring nutritional measurement.

Evans, J., Green, D., Gibson, F., O'Connor, G., & Lanigan, J. (2023). Complications and outcomes of gastrostomy versus nasogastric tube feeding in paediatric allogeneic bone marrow transplant: A prospective cohort study. *Clinical Nutrition ESPEN, 55*, 58–70. https://doi.org/10.1016/j.clnesp.2023.02.022

Summary

This study aimed to compare enteral tube complications, nutritional, and clinical outcomes between children with gastronomies (g-tubes) and NGT throughout HSCT. This study found that g-tube use was relatively safe and complications were minor, as 87% of g-tube patients had complications and 97% of those patients had minor complications. Mechanical issues were most common in g-tube use. The most common complication of NGT was dislodgement. There was no admission or survival difference between EN and PN. Anthropometric measures generally declined or stabilized despite total calorie intake in EN and PN groups.

Analysis

This was a prospective study that suggested that when NGT tubes could not be tolerated to use g-tubes. Limitations in the study include no randomization, small sample size, single center study, food diary accuracy was poor, and nutritional intake was measured 3 days monthly from months 2-6.

Application

G-tubes are a relatively safe option and can be an alternative to NGTs if they are not tolerated. The study findings did not mention a significance in admission and survival rate.

Evans, J., Needle, J. J., & Hirani, S. P. (2019). Early outcomes of gastrostomy feeding in paediatric allogenic bone marrow transplantation: A retrospective cohort study. *Clinical Nutrition ESPEN*, *31*, 71–79. https://doi.org/10.1016/j.clnesp.2019.02.014

Summary

The study aimed to compare PN use between gastronomy and non-gastrostomy fed children during admission for HSCT. The secondary objective was to compare further nutritional and post-transplantation outcomes including weight and albumin changes, incidence of GVHD, positive blood cultures, and survival between the two groups. It was found that there was no difference of PN duration between the groups. No difference was found in the hypoalbuminemia, as it is common following HCST. More children with gastrostomies required EN at discharge than those without gastrostomies. EN only had shorter admission than EN with PN and less GVHD grade III and IV, and faster platelet engraftment. There was also no difference in weight loss >10kg in each group.

Analysis

Limitations include the absence of randomization and a control group, the retrospective design, and possible selection bias. This study was able to look at early outcomes, but long-term impact of gastrostomy feeding tube post-discharge was not evaluated. This study showed that patients with gastrostomies needed PN less or PN was initiated later.

Application

This study showed that gastrostomy feeding may be a feasible choice for EN. Gastrostomy feeding may be an option if NGT was not feasible for patients. However, it was seen that those with gastrostomies had more incidences of going home with EN. This study will be useful in discussing the lower incidences of GVHD and faster platelet engraftment as well.

Gonzales, F., Bruno, B., Alarcón Fuentes, M., De Berranger, E., Guimber, D., Behal, H., Gandemer, V., Spiegel, A., Sirvent, A., Yakoub-Agha, I., Nelken, B., Duhamel, A., & Seguy, D. (2018). Better early outcome with enteral rather than parenteral nutrition in children undergoing MAC allo-SCT. *Clinical Nutrition, 37*(6 Pt A), 2113–2121. https://doi.org/10.1016/j.clnu.2017.10.005

Summary

This paper looked at the effects of early administration of EN versus PN. EN had a greater day 100 overall survival rate verses PN. EN also had a lower rate o non-relapse mortality. There were lower incidences of GVHD in EN, but difference in mucositis. Platelet engraftment was better in EN, however there was no difference in neutrophil engraftment. Additionally, there was no difference in bacterial and viral infections. It is also mentioned that EN use was shorter and had a greater weight loss in this group.

Analysis

The paper did not discuss the amount of EN and PN delivered in each patient. The study was also biased as it only included EN patients from a single center. The paper was a retrospective study. However, this study supports that EN has a better overall survival rate, hospitalization was shorter, lower incidences of GVHD, and platelet engraftment. The greater loss could potentially be attributed to less fluid retention.

Application

This paper displays overall quicker recovery in the EN group than EN and PN. This is usually in mentioning the benefits of EN. The paper does not support infection control. The paper also discusses less incidences of GVHD in EN.

Hastings, Y., White, M., & Young, J. (2006). Enteral nutrition and bone marrow transplantation. *Journal of Pediatric Oncology Nursing: Official Journal of the Association of Pediatric Oncology Nurses*, *23*(2), 103–110. https://doi.org/10.1177/1043454205285866

Summary

This was a retrospective study that evaluated the efficacy of EN feeing in meeting nutritional and energy requirements in patients undergoing HSCT. The secondary aim was to document the complicated associated with the HSCT process and ability to maintain enteral feedings. The patients in this study were able to tolerate enteral feedings well and only one patient needed PN due to gastrointestinal toxicity causing vomiting, diarrhea, and mucositis. These were also symptoms in other patients, but it was not severe enough to stop EN in those patients. At discharge 80% of patients were above the 50^{th} percentil for weight for age. Additionally, 32% of daily energy requirements were met with NGTs.

Analysis

The study had a small sample size and was a retrospective study. Additionally, at admission 87% of patients were above the 50^{th} percentile for weight for age and at discharge only 80% of patients were. This paper questions the assumption that weight is an accurate indicator of nutritional status because of possible fluid overload. This paper discuses that EN is an option and although there are complications it does not affect the delivery of nutrition through EN.

Application

This paper is helpful for addressing the feasibility of EN even in patients who are having vomiting, diarrhea, and mucositis because although they had these symptoms, it was not severe enough to stop. The population also had an outcome of 80% of patients remaining above the 50^{th} percentile, although the admission rate was 80%. The paper addresses the question of using weight for nutritional status. This is helpful because it solidifies that there is not a gold standard for nutritional status evaluation in pediatrics and further identifies the need for one. This paper also discusses that EN can deliver daily energy requirements to patient via EN, however this study only was able to deliver about 32% of daily energy requirements.

Muratore, E., Leardini, D., Baccelli, F., Venturelli, F., Cerasi, S., Zanaroli, A., Lanari, M., Prete, A., Masetti, R., & Zama, D. (2023). The emerging role of nutritional support in the supportive care of pediatric patients undergoing hematopoietic stem cell transplantation. *Frontiers in Nutrition*, *10*, 1075778. https://doi.org/10.3389/fnut.2023.1075778

Summary

This study aimed to comprehensively review evidence on nutritional support for pediatric HSCT patients to discuss the relationship between HSCT and nutritional status between phases of transplant and to address the clinical outcomes of nutritional supports. The review found that children who are overweight before allo or auto HSCT have a reduced probability of survival than compared to ideal weight children. Those with a BMI less than 5^{th} percentile at the time of transplant was associated with significant increased incidence of electrolyte disorders. Those with EN had a lower incidence of GVHD. There was faster platelet engraftment for the EN group. This paper also identified feasibility in use of gastrostomy for EN resulting in lower rates of PN.

Analysis

Limitations of this paper include data on pediatric patients are few and identified that more specific studies are warranted. The paper discusses that malnutrition prior to transplant can impact nutrition post-transplant negatively with increased incidence of electrolyte disorders. The paper also identified the importance of standardized nutritional evaluation.

Application

This paper helps support the that nutritional status prior to transplant is an important factor for nutritional status post. The paper also supports that EN has lower incidences of GVHD and faster platelet engraftment. The paper also mentions the feasibility of gastrostomy for EN resulting in lower rates of PN.

Oratz, T., Bate, C., Smith, A., Bryson, E. W., Justice, C., & Cherven, B. (2022). Nutritional support: Enteral nutrition pathway for children undergoing hematopoietic stem sell transplantation. *Clinical Journal of Oncology Nursing*, *26*(6), 651–658. https://doi.org/10.1188/22.CJON.651-658

Summary

This paper completed a study on implementing a pathway for tube placement in patients undergoing HSCT. The paper evaluated the safely and feasibility of implementing such pathway. The pathway was found safe; however, the feasibility was limited because of inconsistent placement and dislodgement of the NJT. Patients also often refused tube replacement or experienced mucositis.

Analysis

This paper provides context for the need of an EN EBP pathway for tube placement. However, feasibility was limited due to dislodgement, patient refusal for replacement, and limited amount of replacement attempts. The sample size was small, which also limits the study.

Application

This paper will help provide context to complications revolving EN feeds. This paper discusses complications for placement, which ultimately can delay EN administration, or cause patients to receive PN. The paper also discusses further need for an EBP pathway for tube placement.

Papadopoulou, A., Williams, M. D., Darbyshire, P. J., & Booth, I. W. (1998). Nutritional support in children undergoing bone marrow transplantation. *Clinical Nutrition*, *17*(2), 57–63. https://doi.org/10.1016/S0261-5614(98)80306-3

Summary

The aim of this study was to compare EN and PN in respect to maintaining weight, improving overall wellbeing, and reversing nutritional deficiencies in pediatric HSCT patients. This study found no significant deterioration in anthropometrics. There appeared to be multiple electrolyte imbalances with the PN group. EN was tolerated well and had an overall better nutritional response.

Analysis

This paper was a prospective study, which is a strength. However, limitations include the lack of randomization and smalls sample size. The paper supports the use and overall better tolerance of EN.

Application

This paper helps support the overall tolerance of EN. This paper discusses no significant deterioration in anthropometrics. The paper also suggests electrolyte imbalances with PN. These findings support the overall feasibility of EN.

Ringwald-Smith, K., Hillman, H., Gibbons, K., & Epperly, R. (2023). Nutrition management of pediatric patients undergoing hematopoietic stem cell transplantation: Guidelines, gaps, and research. *Nutrition in Clinical Practice, 38*(4), 731–747. https://doi.org/10.1002/ncp.11018

Summary

This literature review highlighted the gaps in current guidelines and research regarding nutrition management in HSCT pediatric patients. The paper provided recommendations for NGT placement. It suggests that the tube should be replaced before the first signs of mucositis, as this can reduce the need for PN. It discusses that PN should be used when patients are unable to meet their nutritional needs by oral or EN. It also mentions that EN has a shorter length of stay, mortality rate, and severity of GVHD, and less blood stream infections.

Analysis

The paper provides a great overview of nutrition recommendations and further research needed in HSCT pediatric patients. Limitations include small sample sizes, guidelines from general pediatric nutrition or adult HSCT guidelines.

Application

This paper supports the use of EN and give recommendations for when to place NGT and start EN. The paper also supports the use of EN and that there is less severe GVHD in patients that utilize EN.

Soussi, M. A., Besbes, H., Mellouli, F., Drira, C., Lazreg, O., Belghith, A., Zouari, B., Zaouali, S., Bejaoui, M., & Razgallah Khrouf, M. (2019). Parenteral Nutrition Complications in Children Undergoing Bone Marrow Transplantation. *Journal of Pediatric Hematology/Oncology*, *41*(7), e473. https://doi.org/10.1097/MPH.0000000000001560

Summary

The aim of this study was to report and describe PN related complications in children undergoing HSCT. In this study those with PN had various different electrolyte imbalances with hypokalemia being the most common. The children with PN also had episodes to line infections and tolerated treatment well. However, there were a couple cases of sepsis.

Analysis

Limitations of this study include the overestimated PN complications and the retrospective design. The helped identify the need for nutritional protocols in HSCT patients to help prevent complications.

Application

The paper helped identify the need for a nutritional protocol. The paper also mentions several complications that arose from PN. This helps support that PN is not as feasible as EN and can have more risk associated with it.

Woods, T., Tariman, J. D., & Lee, Y.-M. (2019). Enteral and parenteral Nutrition: An integrative literature review on nutrition in pediatric recipients of hematopoietic stem cell transplantation. *Clinical Journal of Oncology Nursing*, *23*(4), 351–354. https://doi.org/10.1188/19.CJON.351-354

Summary

This integrative review evaluated the effectiveness of EN versus PN to meet nutritional and energy needs of pediatric HSCT patients. The paper mentioned that EN is recommended over PN due to the preservation of the GI tract. It was found that EN has been shown to limit complications, minimize length of hospital stays, and promotes better quality of life in this population.

Analysis

This paper was able to provide application to practice in the integrative review. The paper only had two papers that had a sample size greater than 100 participants. There was only one randomized blind study.

Application

This paper can help support the use of EN. The paper mentions that additional research is needed to establish standard of care regarding nutrition in pediatric HSCT patients.

Zama, D., Muratore, E., Biagi, E., Forchielli, M. L., Rondelli, R., Candela, M., Prete, A., Pession, A., & Masetti, R. (2020). Enteral nutrition protects children undergoing allogeneic hematopoietic stem cell transplantation from blood stream infections. *Nutrition Journal*, *19*(1), 29. https://doi.org/10.1186/s12937-020-00537-9

Summary

The aim of this study was to evaluate the role of EN regarding clinical and nutritional outcomes in pediatric HSCT patients. In this study, the EN group had less blood stream infections, platelet engraftment was shorter, and duration of fever was shorter. There was no difference in neutrophil engraftment. Statistically there was no difference in nutritional outcomes, however PN was seen to have a greater reduction in BMI during oral realimentation. Furthermore, there was no difference in the BMI scores from admission to discharge.

Analysis

Limitations include the small sample size of the study. The paper does a good job at identifying the benefits of EN and PN. The paper focuses on nutritional outcomes. However, the paper does identify that no study exists in the literature evaluating how long EN should be administered to induce a protective microbiome.

Application

This study helps identify more complications of PN, which could potentially prolong hospital stay. Complications such as blood stream infections were identified that could have potentially been caused by the increased use of lines in the PN group, and potentially increase the overall hospital stay in the PN group. Although there was no difference in nutritional outcomes, once oral nutrition was reintroduced to the PN group, they had lower BMI.