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Review of the Effectiveness of Enteral Feeding in Pediatric Oncology Patients

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Abstract

Enteral supplementation for nutritional support in pediatric oncology patients remains nonstandardized across institutions and between providers. Pediatric oncology patients frequently fail to meet their growth curve percentiles, lose weight, and/or are malnourished due to both the oncologic process as well as side effects from chemotherapy and radiation treatments. Methods of increasing weight include enteral feeding (nasogastric, nasoduodenal/jejunal, or gastrostomy), parenteral intravenous feeding, and oral supplementation. Indications for feeding and feeding protocols are highly variable, in part due to parental and familial choices, and in part due to the lack of guidelines available for providers. This article provides a comprehensive literature review of 8 published studies regarding the effectiveness and safety of enteral feeding in maintaining or increasing weight in pediatric oncology patients to help inform practice. The review concludes that enteral feeding in pediatric oncology patients is an effective and safe method to affect weight positively. However, further research is needed for developing treatment guidelines, including establishing a timeline for initiation of feeding, and determining which patients are most likely to benefit from enteral feeding.

Keywords

nutrition, pediatric, oncology, evidence-based practice

Introduction

Cancer is the leading cause of disease-related death in children younger than the age of 14 years (Robinson, Loman, Balakas, & Flowers, 2012). Ladas, Sacks, Brophy, and Rogers (2006) state that the rate of "malnutrition in children with cancer ranges between 8%-60%" (p. 339). Cancer-related malnutrition is due to a variety of factors, including poor oral intake, abnormal metabolism of nutrients, and adverse effects from chemotherapy and radiation, including nausea, vomiting, anorexia, and mucositis (Jones, Watling, Wilkins, & Pizer, 2010). Generally speaking, peptide hormones produced by malignant tumors may lead to decreased intake, anorexia, and, ultimately, weight loss (Andrassy & Chwals, 1998). Reducing mortality in children with cancer requires advancements in chemotherapy and biotherapeutics, as well as improvements in supportive care measures such as nutrition.

Malnutrition is defined by the World Health Organization (2016) as "deficiencies, excesses or imbalances in a person's intake of energy and/or nutrients." Ultimately, malnutrition can complicate the child's course of medication treatment, leading to dose delays or reductions (Andrassy & Chwals, 1998). These delays can, in turn, lead to worse outcomes and poorer long-term survival (Ladas et al., 2006).

Methods of determining nutritional status remain highly variable from institution to institution, as well as between providers (Robinson et al., 2012). In a survey of physicians, dieticians, and nurses in the Children's Oncology Group, Ladas et al. (2006) revealed that nutritional screening was not uniform and institutions utilized various methods of monitoring weight changes without the use of any standardized nutritional support guidelines.

The purpose of this review is to evaluate current evidence regarding the use of enteral feeding in pediatric oncology patients in order to inform practice. Specifically, this review will assess the effects of enteral nutrition on weight in pediatric oncology patients, both independently and as compared with parenteral nutrition and oral supplementation. For the purposes of this literature review, enteral nutrition refers to nutrition supplied by nasogastric, nasoduodenal/jejunal, or gastrostomy tube. Although oral nutritional supplementation can be considered to be

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a form of enteral nutrition, it is discussed separately in this review.

Evaluating the effects of enteral nutrition is important because there exists wide variance in common practices among pediatric cancer centers . The lack of evidence-based practice may lead to poorer outcomes (Ladas et al., 2006). Outcomes evaluated include the impact of enteral feeding on weight and comparisons of the effectiveness of different types of feeding (enteral, parenteral, and oral).

The population of interest was pediatric patients with an oncologic diagnosis, aged 0 to 18 years, all races, ethnicities, and both genders. Oncologic diagnoses include the most common childhood cancers: leukemias, lymphomas, and solid tumors (Children's Oncology Group, n.d.). An age range of 1 to 18 years was utilized because infants under the age of 1 year with a diagnosis of cancer often have comorbid feeding disorders based on their young age at diagnosis. The patient values and preferences of this age group (0-18 years) often involve autonomy in decisions over one's own feeding and eating schedules, as well as respect for parents' independent decisions regarding family food choices, cultural and ethnic considerations, and family eating norms.

History and Review of Literature

Studies that met the aforementioned criteria were selected. Search terms included "enteral," "nutrition," and "pediatric oncology." Studies published after the year 2000 were included for review. Qualitative research studies were excluded from this literature review because of the focus on measurable effectiveness of enteral feeding with pediatric oncology populations.

The initial literature search was done by searching PubMed and the Cumulative Index of Nursing and Allied Health Literature (CINAHL). Based on the search terms, the first search attempt identified 314 articles. Based on the title, 229 articles were immediately eliminated as they did not fulfil the inclusion criteria, and 24 duplicate articles were eliminated. Sixty-one abstracts were then evaluated and additional studies were excluded based on outcomes that did not fit with the purpose of this study (24 articles), lack of proper intervention (ie, medication used to increase appetite; 16 articles), study design (6 articles), wrong population (5 articles), study reported in a language that could not be readily interpreted (1 article), and poster abstract but no full study published (1 article; see Figure 1). As the search progressed, a search of the Cochrane database was carried out and revealed one review updated in 2012; however, it primarily reviewed studies published prior to 2000 and was, therefore, not included. Eight results were organized into 2 categories: the effects of independently delivering enteral nutrition on weight in pediatric oncology patients (6 articles) and enteral feeding as compared with parenteral nutrition and oral supplementation (2 articles). Independently delivering enteral nutrition refers to employing enteral nutrition as a single therapeutic agent without other interventions (eg, parenteral nutrition and oral supplementation).

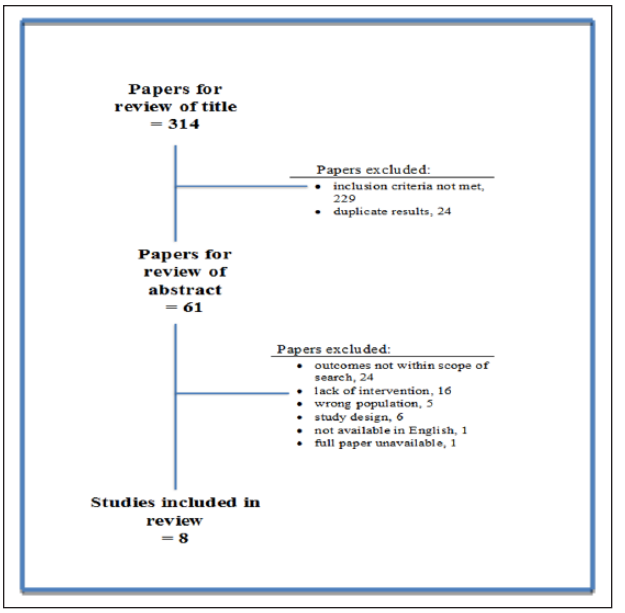

Figure 1. Literature search results flow chart.

The Effects of Independently Delivering Enteral Nutrition in Pediatric Oncology Patients

Barbosa, Pedrosa, and Cabral (2012) evaluated enteral nutrition in 71 hospitalized pediatric oncology patients from 1 month to 18 years of age. This cohort study evaluated the frequency and efficacy of enteral feeding and found that enteral nutrition significantly increased weight in malnourished patients (body mass index [BMI]/age at the beginning = −3.29, SD = 0.74, and mean BMI/age at the end = −2.44, SD = 1.29, $P < .05$). However, no statistically significant changes were found in the cohort with adequate nutritional status at the beginning of the study, while the overweight cohort had statistically significant losses throughout the study (mean BMI/age at start = 1.53, SD = 0.60, and mean BMI/age at the end = 1.01, SD = 0.95, $P < .05$). A strength of this study was the analysis of both height and weight in relation to age, as well as the stratification of cohorts based on initial nutritional status. Weaknesses of the study included the use of a convenience retrospective sample, frequent initiation of feeding when the patient was already medically compromised

(31% of patients were ventilated), and the short amount of time that feeding efficacy was evaluated (5-10 days). Additionally, this study was performed in Brazil and may not translate well to care in the United States.

In a 2015 prospective cohort study, Brinksma et al. evaluated BMI and percent fat mass (% FM) at 0, 3, 6, and 12 months after diagnosis in pediatric patients (aged 0-18 years) with solid and hematologic malignancies (N = 133). Enteral tube feeding statistically significantly increased BMI between 0 and 3 months (estimate of slope interaction tube feeding/time = −0.07, 95% confidence interval [CI; −0.25, −0.00], $P = .047$), but not during 3 to 12 months. Diminished activity level on the Lansky Play Performance Scale (Lansky PPS) was the only factor statistically significantly related to an increase in % FM throughout all months (estimate of slope interaction Lansky PPS/time = −0.001, 95% CI [−0.002, −0.0002], $P = .018$). A strength of this study was the analysis of various factors related to weight changes (ie, Lansky PPS, corticosteroid dosages, etc), as well as the longitudinal analysis (12 months). One limitation of the study was the lack of randomization.

Hastings, White, and Young (2006) evaluated enteral feeding in a retrospective study of 2- to 15-year- olds who had a bone marrow transplant (BMT) patients (N = 15). Fourteen of the patients had been diagnosed with leukemia (acute lymphoblastic and chronic or acute myeloid), and one of the children was diagnosed with Glanzmann syndrome (Hastings et al., 2006). On admission to the hospital, 87% of the patients' weights wereabove the 50th percentile for their age. Enteral feeding was the main source of nutritional supplementation for the pediatric patients during the entire hospitalization (mean length of stay = 24 days) for the BMTs (Hastings et al., 2006).

Although most of the patients experienced toxicity side effects (diarrhea, nausea, and mucositis) related to the BMT treatment, the relationship between these side effects and feeding was not measured in this study. Gut toxicity was treated with antinausea medications and analgesia. Enteral feedings continued even during maximal gut toxicity. Findings demonstrated that 80% of the patients were able to maintain weight above the 50th percentile at the time of discharge (Hastings et al., 2006). A strength of this study was the unique and specific population, as well as the observation of BMT-related toxicities and the effectiveness of feedings. Weaknesses of this study included the small number of subjects, the lack of standardization of the intervention, and the lack of statistical analysis comparing feeding with toxicity.

A pilot study utilizing voluntary interventions evaluated proactive enteral tube feeding (initiated within the first 2 cycles of chemotherapy) in 69 pediatric patients ages 1 to 20 years who were undergoing chemotherapy (Sacks et al., 2014). Those who received proactive feeding as compared with those who eventually received enteral nutrition experienced significantly less weight loss based on age (>0.5 weight/age Z score loss, $P = .037$). Occurrences of bloodstream infections were also evaluated and were not determined to be statistically significant between the 2 groups (no statistic, $P = .112$). Weaknesses of this study included lack of randomization, small sample size, selection bias (families were able to determine whether they wanted to be in the treatment group or control group), and the predominant number of younger children in the cohort receiving early initiation of enteral feeding. A strength of the study was that it evaluated the impact of the timing of initiation of feeding.

In a retrospective chart review, Schmitt et al. (2012) evaluated the efficacy and safety of percutaneous endoscopic gastrostomy (PEG) feedings in pediatric oncology patients as compared with neurologically impaired children aged 6 months to 18 years (N = 131). The study found statistically significant increases in weight-for-height following PEG placement ($Z = +0.8$, $P < .05$). The only statistically significant complication was a higher rate of peritubar wound inflammation in the oncologic group (29 vs 10, $P = .049$). Relapse and disease-related deaths were also analyzed, and while lower in the group treated with enteral nutrition, it was not statistically significant. Weaknesses of this study included the retrospective method and the inherent differences between comparison groups. A strength of this study was the long length of time that enteral feeding were administered (5-24 months), as well as the evaluation of the impact of feeding on both height and weight.

Skolin, Hernell, Larsson, Wahlgren, and Wahlin (2002) evaluated effects and complications of PEG feedings in 18 pediatric oncology patients aged 6 months to 14 years, retrospectively. Statistically significant increases were seen in weight-for-age (WFA) at 1 month (mean = 0.03, 95% CI [−0.96, 0.67], $P = .04$), and 2 months (mean = 0.11 95% CI [−0.66, 0.92], $P = .04$) post placement. Weight changes at other time points were not statistically significant. Complications included peristomal infections and inflammation. Weaknesses of this study included the small number of patients evaluated and the various timing of PEG placement during treatment. A strength of this study was the evaluation of weight at different time points following PEG placement.

Enteral Feeding as Compared With Parenteral Nutrition and Oral Supplementation

Bakish, Hargrave, Tariq, Laperriere, and Bouffet (2003) looked at patients' charts retrospectively and evaluated the percent of weight change following nutritional intervention in pediatric oncology patients (N = 103) with newly diagnosed medulloblastoma or supratentorial

primitive neuroectodermal tumor. The authors found that enteral feeding resulted in statistically significant weight gain at 1 month, with a median weight change of +4.78% (95% CI [−0.80%, 7.19%], $P = .0055$), and a change of +11.73% (95% CI [8.3%, 14.75%], $P < .001$) at 3 months. Parenteral nutrition was statistically significantly associated with weight gain at 1 month with a median weight change of +2.67% (95% CI [−1.22%, 9.20%], $P = .031$), but not at 3 months. Oral supplementation did not result in a statistically significant weight gain at any time point. Enteral nutrition was supplied by gastrostomy and nasogastric tubes, with 25 episodes of complications. Two patients had major complications involving peritonitis and an abdominal wall abscess. Strengths of this study were the utilization of a population at high risk for malnutrition due to their disease process (medulloblastoma and supratentorial primitive neuroectodermal tumor patients) and the direct comparison of feeding methods. A weaknesses was the lack of long-term follow up, as the study only evaluated end-points at 1 and 3 months.

Parbhoo, Tiedemann, and Catto-Smith (2011) evaluated WFA and BMI for age following PEG placement in 14 pediatric patients, aged 6 months to 19 years, with malignancies in a retrospective case review. They found that PEG placement statistically significantly reversed weight lost, and further, weight continued to improve at 6 months following removal of the PEG (mean WFA at removal = 1.04, SD = 1.38, vs mean WFA 6 months later = −0.53, SD = 1.11, $p < .05$). Complications occurred in 50% of patients and included wound infections (n = 5) and tube migration (n = 2). Peristomal infections were statistically significantly more likely to occur in malnourished patients (mean BMI/age = −2, relative risk = 3.5, 95% CI [1.02, 11.96], $P = .04$). One weakness of this study included the small sample size. A strength was the analysis of outcomes 6 months following removal of the tube.

Discussion

The studies reviewed examined the effectiveness of enteral nutrition on weight in pediatric oncology patients, both independently as a single intervention, and as compared with parenteral nutrition and oral supplementation. Seven of the 8 studies evaluated concluded that enteral nutrition positively benefited weight in pediatric oncology patients (Table 1). Additionally, these studies often examined short-term outcomes rather than long-term effects and the extent of sickness and age range of study participants varied among samples. Brinksma et al. (2015) and Schmitt et al. (2012) were the only investigators to explore outcomes at 1 year or greater, with most studies evaluating outcomes 1 to 3 months following the initiation of feeding.

Four out of the 8 studies also discussed the safety of enteral feeding. Hastings et al. (2006) evaluated pediatric BMT patients for gastrointestinal toxicities following nasogastric feeding and found many occurrences of Grades 2 and 3 gastrointestinal toxicities. These effects were similar in patients who did not receive enteral nutrition and were likely a result of the BMT regimen or symptom side effects (e.g., the occurrence of graft-versus-host disease). Three studies evaluated the safety of PEG placement and feeding (Parbhoo et al., 2011; Schmitt et al., 2012; Skolin et al., 2002). Together, the investigators found frequent occurrences of peristomal inflammation and infection; however, no events were life-limiting, few required tube removal, and PEG placement and feeding was thought to be safe with the appropriate monitoring for side effects.

This literature review informs the current state of the science with regard to enteral nutrition and feeding in pediatric oncology patients. The review supports the consideration of enteral nutrition as an effective feeding option for the pediatric oncology population. Benefits include weight stabilization, weight gain, and safe placement. Furthermore, enteral feeding can be a more cost-effective method when compared with parenteral feeding. For example, DeSwarte-Wallace, Firouzbakhsh, and Finklestein (2001) found a total cost savings of $111,690 when 25 hospitalized pediatric oncology patients were prescribed nasogastric feedings rather than parenteral nutrition (median length of stay = 40 days). The participants had either received or were currently receiving chemotherapy during the study. Enteral feedings cost an average of $50 per day compared with an average of $135 per day for total parenteral nutrition (DeSwarte-Wallace et al., 2001).

Barriers to enteral feeding include patient, parent, and provider preferences and body image difficulties encountered in association with nasogastric feeding (Schmitt et al., 2012; Williams-Hooker et al., 2015). Both parents and patients tend to prefer parenteral nutrition over enteral, citing reasons such as the fear of discomfort during and after nasogastric tube placement and body image concerns (Montgomery et al., 2013; Williams-Hooker et al., 2015). Parents believe there is less harm to their children with parenterally administered nutrition while healthcare providers believe enteral approaches provide more nutritional benefits with less risk of severe infections and sepsis (Williams-Hooker et al., 2015).

The discordance between research findings and current practice demonstrates the importance of ongoing research and, particularly, the importance of assimilating empirical evidence into the knowledge base that underpins clinical practice. While this review found that enteral nutrition improves weight outcomes in pediatric oncology patients, the limited data lack generalizability, and

Table 1. Literature Summary of Effectiveness of Enteral Feeding in Pediatric Oncology Patients.

Author (Year)	Population	Outcome(s)	Notes
Bakish et al. (2003)	Newly diagnosed pediatric patients (0-18 years) with medulloblastoma or primitive neuroectodermal tumors (N = 103)	Statistically significant weight gain with enteral nutrition at 1 month and 3 months	Greater weight gain with enteral feeding than parenteral or oral supplementation
Barbosa et al. (2012)	Hospitalized pediatric oncology patients (aged 1 month to 18 years) (N = 71)	Enteral feeding statistically significantly improved weight in malnourished patients only, no statistical impact on well-nourished patients	Evaluated patients who were very ill at the time of initiation of feeding and examined short durations of feeding
Brinksma et al. (2015)	Pediatric patients (0-18 years) with solid and hematologic malignancies (N = 133)	Body mass index statistically significantly increased with enteral feeding during 0 to 3 months, not at other time points. Increase in % fat mass statistically significantly associated with decrease in activity level on Lansky Play Performance Scale.	Evaluated outcomes at 0, 3, 6, and 12 months following diagnosis
Hastings et al. (2006)	Pediatric (2-15 years) bone marrow transplant patients (N = 15)	No statistical analyses comparing toxicity side effects and feeding types	Safety—Grades 2 and 3 gastrointestinal toxicities
Parbhoo et al. (2011)	Pediatric patients (6 months to 19 years) with malignancies following percutaneous endoscopic gastrostomy (PEG) tube placement (N = 14)	Weight statistically significantly increased following PEG placement	Safety—Statistically significantly more complications, such as wound infections, in malnourished patients
Sacks et al. (2014)	Pediatric patients (1-20 years) undergoing first 2 cycles of chemotherapy (N = 69)	Statistically significantly less decrease in weight in proactive enteral feeding cohort	Evaluated impact of early initiation of feeding No randomization.
Schmitt et al. (2012)	Pediatric oncology patents (6 months to 18 years) compared with pediatric neurologically impaired children (N = 131)	PEG feeding statistically significantly increased weight for height	Safety—Higher rate of peritubar infections in cohort with oncologic diagnoses
Skolin et al. (2002)	Pediatric oncology patients (6 months to 14 years) (N = 18)	PEG feeding statistically significantly increased weight-for-age at 1 and 2 months post PEG placement	Safety—Occurrences of peristomal inflammation and infection (no statistical analyses).

validity is circumspect due to the absence of randomized controlled trials.

Further research is needed to determine the most effective and least disruptive means of feeding children with cancer. Longitudinal, randomized controlled trials with large samples would help determine the most effective and least invasive method of feeding and substantiate long-term benefits and hazards. However, given the population of interest, it may be difficult to ethically justify randomization, as any benefit from a particular intervention could not be withheld from an individual. Cohort studies may provide adequate data, provided they have large enough sample sizes and standardized interventions. A stronger design than a cohort study would be the use of a quasi-experimental design. These designs include clearly identified inclusion/exclusion criteria and allow the researcher to examine differences in weight gain in clinical settings that routinely employ multiple enteral feeding interventions in the same population of pediatric patients. Future qualitative research studies should include parents', pediatric patients', nurses', and other health care providers' perspectives about different feeding options (Williams-Hooker et al., 2015). The examination of health outcomes relevant to pediatric oncology practice, such as long-term survival and maintenance of growth curves, are needed to bridge the gap between science and knowledge.

Summary

The existing, limited research-based literature, provides recommendations for nurses, advanced practice providers, and physicians practicing within the field of pediatric

oncology. These recommendations include preferentially choosing enteral feeding over parenteral and oral supplementation, as it leads to greater weight gain and positively affects growth curves, including height (Bakish et al., 2003; Parbhoo et al., 2011; Schmitt et al., 2012). This recommendation is most beneficial to those patients who present malnourished, as compared with those who are adequately nourished or overweight (Barbosa et al., 2012). Enteral feeding appears to have the greatest positive impact on weight in the first 3 months of enteral feeding (Bakish et al., 2003; Brinksma et al., 2015; Skolin et al., 2002), but a definitive length of feeding cannot yet be recommended. Additionally, it is advised that nurses monitor closely for adverse events if utilizing gastrostomy tube feedings (Parbhoo et al., 2011; Schmitt et al., 2012).

The evidence from this literature review allows for the following recommendations for practitioners: (*a*) enteral feeding was effective in positively affecting weight in pediatric oncology patients and (*b*) initiating feedings early on in the treatment course appears to be most beneficial in preserving growth, particularly in young patients, patients who present for treatment already malnourished, and patients who have diseases and treatments that commonly lead to malnutrition (ie, Wilm's tumor, medulloblastoma, rhabdomyoscarcoma, neuroblastoma, and some leukemias; Andrassy & Chwals, 1998).

Unfortunately, any recommendations for clinicians must be tempered due to the limitations of the reviewed studies. These limitations were (*a*) feeding was evaluated in limited populations for short durations, (*b*) feeding was initiated after the patient was already malnourished, and (*c*) the use of retrospective chart reviews rather than randomized controlled trials. Therefore, further research is needed in order to obtain more information about (*a*) the population that is most likely to benefit from enteral feeding, (*b*) the kind of enteral feeding (nasogastric vs PEG) that is most effective and nondisruptive, (*c*) the length of feeding necessary for positive weight outcomes, and (*d*) the ideal time at which to initiate feedings.

Nurses need to be supportive of ongoing research while also utilizing the information provided by the studies currently available to encourage the greatest degree of health possible for their patients. They can help to establish evidence-based guidelines for enteral feeding, as well as help to encourage improved nutrition with each of their patients on a daily basis. Providers should initiate discussions with parents about enteral feedings early on in the treatment course and utilize shared decision making to discuss the potential benefits and harms of enteral and parenteral feedings with parents and, where age-appropriate, include the patient in this discussion. Together, parents, children, nurses, dieticians, and providers should collaborate with the primary goal of improving the nutritional status of pediatric oncology patients and improving their long-term health outcomes.

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