Published in final edited form as:

Semin Oncol. 2011 June ; 38(3): 439–442. doi:10.1053/j.seminoncol.2011.03.020.

PARENTERAL NUTRITION IN PATIENTS WITH ADVANCED CANCER: MERGING PERSPECTIVES FROM THE PATIENT AND HEALTHCARE PROVIDER

Jessica Mitchell, RN, CNP¹ and Aminah Jatoi, MD¹

¹Division of Medical Oncology, Mayo Clinic

Abstract

The decision to utilize parenteral nutrition in patients with advanced cancer is difficult. There are variable opinions in the literature. Those who routinely care for cancer patients often confront the challenges of discussing these interventions with patients and their families. We review results from previous randomized controlled trials, published guidelines, and recent work that describes the emotional challenges patients and families face as they make such decisions with their healthcare provider.

GUIDELINES ON PARENTERAL NUTRITION

Most data point to the same conclusion: healthcare providers should not prescribe parenteral nutrition to patients with advanced, incurable cancer. A meta-analysis summarized findings from 15 clinical trials¹. Parenteral nutrition led to inferior survival (relative risk 0.81; 95% confidence interval 0.62, 1.0), lower tumor response rates, (odds ratio 0.68; 95% confidence interval 0.40, 1.1), and increased infections (odds ratio 4.1; 95% confidence interval 2.4, 6.9). The increased infection rate persisted even after catheter-related sepsis was excluded. The latter observation raises the possibility that parenteral nutrition itself leads to circumstances conducive to the growth of bacteria and other organisms. This observation bolsters recommendations from recent, guidelines that suggest parenteral nutrition may not be in the best interest of patients with advanced, incurable cancer.

The European Society of Parenteral and Enteral Nutrition, the American Society of Parenteral and Enteral Nutrition, and the German Association for Nutritional Medicine have all recently published guidelines on the use of parenteral nutrition in advanced cancer patients^{2–4}. These guidelines overlap to some extent, but mostly suggest the limited value of parenteral nutrition in this setting.

These guidelines suggest that parenteral nutrition should rarely be prescribed to patients with advanced cancer during chemotherapy, although two of these guidelines make this statement more strongly than others. For instance, the American Society of Parenteral and Enteral Nutrition guideline states, “Nutrition support should not be used *routinely* as an

© 2011 Elsevier Inc. All rights reserved.

ADDRESS FOR CORRESPONDENCE: Aminah Jatoi, MD, 200 First Street SW, Rochester, Minnesota 55905 USA, Phone: 507-284-3902; FAX: 507-284-1803, Jatoi.Aminah@mayo.edu .

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The authors have no conflicts of interest.

adjunct to chemotherapy.” Similarly, the German Association for Nutritional Medicine states, “The indications for parenteral nutrition (PN) during chemotherapy are not different from the general indications in malignant diseases. Routine PN therapy as an accompaniment to chemotherapy is not indicated.” However, the European Society of Parenteral and Enteral Nutrition poses the question, “Is there a benefit in supporting incurable cancer patients with weight loss and reduced nutrient intake with ‘supplemental’ PN?” This society responds with the following, “Probably yes. There is probable benefit in supporting incurable cancer patients with weight loss and reduced nutrient intake with ‘supplemental’ PN.” It should be emphasized that this recommendation is relevant to patients with a life expectancy of at least 6–12 months.

Given the fact that 2 of 3 of these guidelines do not support the routine use of parenteral nutrition in patients with advanced cancer and that one is slightly ambivalent, it is important to underscore that these divergent recommendations arise from the same group of trials. These trials suggest that parenteral nutrition is ineffective, and potentially even harmful, to patients with advanced cancer. However, these trials are now over 10 years old. Many investigators have taken the stance that without definitive up-to-date data, there may be a possibility that parenteral nutrition provides benefit to advanced cancer patients receiving chemotherapy and that the issue requires further study.

CONTROVERSIES

Are There Real Exceptions to the Guidelines of No Parenteral Nutrition in Advanced Cancer Patients?

Yes--exceptional circumstances arise. As David Letterman describes, “Traffic signals in New York are just rough guidelines.” Indeed, guidelines need not be rigidly adhered to, and the three examples below suggest how these nutrition guidelines should be viewed.

First, the use of parenteral nutrition appears much higher than what one would expect were the guidelines being carefully adhered to. Forty percent of patients on home parenteral nutrition have a cancer diagnosis⁵. In countries, like Sweden, the Netherlands, France, and the United Kingdom, these figures are variable but cited at 80%, 60%, 27%, and 5%, respectively⁵. Obviously, these figures and their variability indicate that factors other than clear-cut evidence of clinical benefit or objective guidelines are being used in clinical practice.

Second, a previously-published case report describes "Shirley," a 60-yearold woman who presented with previously-treated ovarian cancer and a nonsurgical bowel obstruction⁶. She received parenteral nutrition for several months. It appeared unlikely she would have lived beyond a few months without parenteral nutrition; in fact she lived beyond 16 months. In the paper's discussion, the authors described the following:

So how should a physician respond when a woman with an inoperable malignant bowel obstruction asks, "Doctor, does this mean I'm going to starve to death?" In the absence of clear data from randomized trials, we recommend the following approach: first, consider the overall condition. The majority of patients will have rapidly progressive disease, dysfunction of other organ systems, and poor performance status, and will be too ill for consideration of PN. In these cases, the doctor should answer, "No, you won't starve to death," noting that, in general, discussions about the appropriateness of parenteral feeding should avoid the "sloganism of starvation."

This case report illustrates that cancer patients with metastatic disease can, sometimes, derive benefit from PN. This report raises at least two other particularly salient points. The

first is that any attempt at prescribing parenteral nutrition under these circumstances should be preceded by an extensive discussion with the patient and family. Most patients are too ill for PN, will not benefit, and may even be harmed. Patients deserve to know the existing data, even if some suggest it may not be perfect. Secondly, it is important to point out to patients and their family members that death from cancer does not mean that they will starve to death. The decision to start PN should not become reactionary, or a fearful gesture to avoid starvation. The several-month survival benefit in metastatic cancer is notable, suggesting the possible role of parenteral nutrition in select groups in advanced-stage cancer.

Third, a retrospective study explored outcomes in metastatic cancer⁷. Despite their disease status, 52 patients treated at the Mayo Clinic in the period from 1979–1999 had received home parenteral nutrition. This group consisted of patients with the following diagnoses: carcinoid/islet cell tumor (n=10), ovarian carcinoma (n=6), amyloidosis/multiple myeloma (n=6), colorectal carcinoma (n=5), sarcoma (n=5), pancreatic carcinoma (n=4), gastric carcinoma (n=3), lymphoma (n=2), pseudomyxoma peritonei (n=2), and other (n=9). Although 5 months was the median time from parenteral nutrition to death, one with carcinoid lived 154 months, and 16 survived ≥ 1 year. Therapy-related complications included 18 catheter infections, 4 thromboses, 3 pneumothoraces, and 2 episodes of liver disease.

What does this study tell us about parenteral nutrition in advanced cancer? First, it reiterates the point that, although some patients benefit, most do not. Although the patients in this retrospective study were hand-picked -- those declining rapidly or in imminent danger of death were not prescribed home parenteral nutrition -- most of these carefully selected patients still did not derive benefit. Second, this study did not include data on quality of life. As a retrospective study, this shortcoming was unavoidable. Lack of data in this study should not obfuscate the importance of trying to obtain such information in future studies. Although clinical records may not be revealing, these patients likely grappled with multiple issues: hanging parenteral nutrition bags, maneuvering tubing, accessing intravenous access devices, bloods draws for frequent monitoring, noisy intravenous infusion pump during the day or night, and worry about cost-related issues. In this study, most of the time, the benefits were marginal, particularly when viewed in the context of associated risks and anxieties. The available information suggests a need to pursue prospective studies that generate accurate data on quality of life.

Does Parenteral Nutrition Actually Palliate Symptoms?

This question is highly pertinent. An emerging literature suggests that parenteral nutrition may not palliate patients' symptoms. A 32-patient study in a palliative care facility aimed at longitudinally monitoring patient-reported symptoms over a 12-month period provides important information⁸. Twenty of these patients (63%) had no symptoms of hunger and, only fleeting symptoms of thirst. Such symptoms could be palliated by small amounts of food or fluid or applying ice chips to the mouth or lubrication to the lips. This study did not focus specifically on cancer, but it does question the argument that parenteral nutrition is palliative and that other simpler interventions might not be equally effective. Based on this study, it appears that many patients are not hungry or thirsty at the end of life and that palliation with an invasive intervention might be unnecessary.

A growing body of literature has sought to understand hunger or its absence in advanced cancer patients. If healthy patients do not eat, they feel hungry after a few hours. In contrast, over 80% of patients with advanced, incurable cancer report anorexia, or loss of appetite, during their disease course⁹. The etiology of this anorexia remains unclear, but inflammatory cytokines, such as interleukin-1 beta, tumor necrosis factor alpha, and interleukin-6 have been implicated⁹. Such observations underscore the fact that lack of

hunger itself is part of the overall cancer disease process. To prescribe parenteral nutrition as a palliative intervention makes little sense if advanced cancer patients are not hungry and do not crave caloric supplementation. It appears difficult to claim that “palliative” parenteral nutrition is addressing any perceptible symptoms.

Does Parenteral Nutrition Address the Main Issues with which Advanced Cancer Patients and Their Families are Contending -- Namely, the Fears and Anxieties of Cancer?

Parenteral nutrition may be an attempt to treat various end-of-life emotions, like fear and anxiety, rather than any specific, real nutrition-based needs. Recent studies have begun to capture some of these emotions.

For example, one group interviewed parenteral nutrition-treated patients with advanced cancer and their caregivers¹⁰. A feeling of desperation that centered on poor appetite and weight loss is what seems to have prompted parenteral nutrition. Ironically, despite the highly technical aspects of administering parenteral nutrition, positive effects seem to have been derived from the therapeutic interactions between the home healthcare teams and the patients and their families. Perhaps what patients and their families need more than medical technology is compassion. Perhaps it is ultimately more beneficial -- and more therapeutic -- to establish patient-healthcare provider relationships conducive to open, honest communication about end-of-life-related issues, fears, and anxieties. This conclusion implies a need for less focus on the more invasive medical approaches entailed in parenteral nutrition.

Ironically, these emotions can sometimes clash and become difficult to interpret. Siew and others recently reported on a situation where a patient with gastric cancer was mistakenly diagnosed with an eating disorder¹¹. This patient was admitted to an eating disorders unit; and a physical examination revealed a palpable abdominal mass. The latter resulted in a malignant diagnosis. This case report suggests that some patients', family members', and healthcare providers' first inclination is to view a poor appetite as a malady in its own right. They shy away from relating anorexia to any real pathology, like cancer. It follows that, sometimes, it may be difficult to blame cancer for anorexia and instead irrationally view it as a volitional stance or psychological malady. This adjustment to circumstances often results in confusion and strife among the patient, family, and providers. A mixed methods approach probed into such issues, describing one cancer patient's response to the challenge of eating¹²: “Then I force myself -- I just stuff it in because if you don't there's going to be trouble, right?” No doubt, loss of appetite and weight can be emotionally challenging.

What can be done to help patients and family members better deal with such issues? The Macmillan Approach to Weight Loss and Eating Difficulties was the focus of a randomized phase II trial¹³. This intervention builds upon a framework of coping and adaptation, relying on a new psychological intervention to help cancer patients better cope with weight loss and eating difficulties. This intervention is also intended to help with family-associated strife. The potential value on this intervention is bolstered by the fact that there are no highly effective pharmacological interventions to help cope with loss of appetite and weight. Psychological interventions thus merit further study.

This study assigned 25 patients to an intervention arm supported by a clinical nurse specialist and assigned another 25 to a control group of routine supportive care. Data collection consisted of audio-interviews conducted before and after the intervention and patient-completion of visual analogue scales for weight and eating distress.

Eating- and weight-related distress appeared less in patients exposed to the active intervention arm compared to the control arm. Qualitative data also suggested that the

intervention group seemed to do better. For example, patients gained reassurance in learning that they could eat whatever they found easiest to consume. This shift away from a totally negative outlook towards food might better help patients cope and requires further investigation.

SUMMARY

Parenteral nutrition might sometimes appear to help sustain life in patients with advanced cancer. However, recent guidelines -- coupled with multiple randomized trials -- illustrate that parenteral nutrition is the exception rather than the rule in the management of patients with cancer-associated anorexia and weight loss. This proclivity for patients and family members to ask about nutritional interventions, like parenteral nutrition, should be viewed more as a signal to healthcare providers to work harder to help patients deal with end-of-life issues rather than a mandate for prescribing parenteral nutrition.

Acknowledgments

This work was supported in part by K24CA131099.

REFERENCES

1. McGeer AJ, Detsky AS, O'Rourke K. Parenteral nutrition in cancer patients undergoing chemotherapy: a meta-analysis. *Nutrition*. 1990; 6:233–240. [PubMed: 2152097]
2. Bozzetti F, Arends J, Lundholm K, et al. ESPEN Guidelines on parenteral nutrition: non-surgical oncology. *Clinical Nutrition*. 2009; 28:445–454. [PubMed: 19477052]
3. August DA, Huhmann MB. the American Society for Parenteral and Enteral Nutrition Board of Directors. ASPEN clinical guidelines: nutrition support during adult anticancer treatment and hematopoietic cell transplantation. *JPEN*. 2009; 33:472–500.
4. Non-surgical oncology -- guidelines on parenteral nutrition. *GMS German Medical Science*. 2009; 7:1–14.
5. Howard L. Home parenteral nutrition: survival, cost, and quality of life. *Gastroenterology*. 2006; 130:S52–S59. [PubMed: 16473073]
6. Whitworth MK, Whitfield A, Holm S, et al. Doctor, does this mean I'm going to starve to death? *J Clin Oncol*. 2004; 22:199–201. [PubMed: 14701785]
7. Hoda D, Jatoi A, Burnes J, et al. Should patients with advanced, incurable cancer ever be sent home with total parenteral nutrition? A single institution's 20-year experience. *Cancer*. 2005; 103:863–868. [PubMed: 15641035]
8. McCann RM, Hall WJ, Groth-Juncker A. Comfort care for terminally ill patients. The appropriate use of nutrition and hydration. *JAMA*. 1994; 272:1263–1266. [PubMed: 7523740]
9. Jatoi A. Weight loss in patients with advanced cancer: effects, causes, and potential management. *Curr Opin Support Palliat Care*. 2008; 2:45–48. [PubMed: 18685394]
10. Orrevall Y, Tishelman C, Permert J, Cederholm T. The use of artificial nutrition among cancer patients enrolled in palliative home care services. *Palliative Medicine*. 2009; 23:556–564. [PubMed: 19477887]
11. Siew L-C, Huang C, Fleming J. Gastric adenocarcinoma mistakenly diagnosed as an eating disorder: case report. *International journal of eating disorders*. 2010; 43:286–288. [PubMed: 19365820]
12. Strasser F, Binswanger J, Cerny T, Kesselring A. Fighting a losing battle: eating-related distress of men with advanced cancer and their female partners: a mixed methods study. 2007; 21:129–137.
13. Hopkinson JB, Fenlon DR, Okamoto I, et al. The deliverability, acceptability, and perceived effect of the Macmillan approach to weight loss and eating difficulties: a phase II, cluster-randomized, exploratory trial of a psychosocial intervention for weight- and eating-related distress in people with advanced cancer. *J Pain and Symptom Management*. 2010 (article in press but available electronically).