

NUTRITION NOTES

SECTION OF NUTRITION
METABOLIC SUPPORT TEAM

CEDARS-SINAI MEDICAL CENTER

Division of Gastroenterology
Department of Medicine

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Editors note: We wish to acknowledge Dr. Rahbar for his tremendous effort in researching and writing the new Guidelines in Cancer Patients. This article represents countless hours spent in the library and at the computer. We sincerely thank you.

GUIDELINES FOR USING TPN IN CANCER PATIENTS

Farshid Sam Rahbar, M.D.

BACKGROUND:

Controversy exists regarding the use of nutritional support in cancer patients. Although nutritional support can clearly improve host nutritional status and restore immune confidence, the efficacy of nutritional support to reduce morbidity and mortality associated with antineoplastic therapy is questionable.

There has been some concern regarding nutritional support contributing to tumor cell proliferation and distant metastasis. Although alterations of cellular kinetic studies have been shown in parenteral nutrition, objective measures of tumor growth, metastasis and tumor protein synthesis have not been affected by parenteral nutrition.

Cancer Anorexia is a major mechanism for progressive malnutrition in cancer patients. Humoral factors have been proposed as the underlying mechanism for such anorexia. Animal studies show increased levels of plasma free

tryptophan as a humoral factor for cancer anorexia. Such levels may be elevated even before clinical anorexia become apparent.

Relief of anorexia is central to both well-being and nutritional improvement of the cancer patient. Among the many pharmacologic strategies tested only Megestrol Acetate has been shown to be consistently well tolerated and effective, with significant improvement in appetite and food intake. Large-scale, randomized, controlled trials involving more than 600 cancer patients, have shown a dose-response benefit with increasing doses of Megestrol Acetate from 160 mg to 800 mg per day. The mechanism of action of Megestrol Acetate is believed to have behavioral and metabolic effects.

Cancer Cachexia is a complex metabolic syndrome resulting from inadequate food intake, as well as ineffective host utilization of nutrients. The manifestations of this syndrome may also include muscle weakness and organ dysfunction. Cancer cachexia may arbitrarily be divided to "obstructive cachexia" and "non-obstructive cachexia". Obstructive, cachexia, which is usually seen in patients with head, neck and esophageal cancer, is secondary to mechanical obstruction, and starvation, and often responds well to the use of TPN. Non-obstructive cachexia, which is seen in cancers such as lung, colon, ovaries, and metastasis, is secondary to humoral factors (cytokines) affecting intermediary metabolism, and would be unlikely to respond to TPN.

There is a definite correlation between weight loss and morbidity. There appears to be relationship between weight loss and the type of tumor. For some patients, for example lung cancer, weight

loss has been noted to be even a better predictor of death than performance status or tumor type. In a review of 3,000 cancer patients DeWys and colleagues identified significantly improved survival in those patients without weight loss compared with those who had lost 6% of their body weight.

Clinical trials of TPN in cancer patients have attempted to demonstrate the results on several Outcome Variables. These outcome variables have included efficacy of TPN in improving treatment tolerance, tumor response, survival rate, postoperative morbidity and mortality, and reducing treatment toxicity. These trials, generally, have not addressed outcome variables, such as symptom control, functional status, effect on food intake, physical performance, psychosocial benefits, or simply better quality of life. Also, most trials are limited by small number of patients, which may not allow a potential benefit to be demonstrated.

Ideally, the design and conduct of nutritional trials should be carried out by a multidisciplinary team. Most reliable trials are then considered those that are prospective randomized controlled (Phase III), and entertain many outcome variables including those that are meaningful to the patients. Until then, we would need to base our guidelines on the present information available in the literature.

Chemotherapy And Radiation Therapy Trials:

Available data discourage the use of routine parenteral nutrition in patients undergoing cancer chemotherapy. In identifying appropriate patients for TPN, attention must be focused on those with medically significant malnutrition associated with fatigue, malaise, and lower quality of life. Patients who would undergo prolonged periods of inadequate oral intake (e.g., those with obstructive tumors), and those who are severely malnourished on presentation are considered appropriate candidates for TPN.

In a prospective crossover controlled study performed on 43 patients by De Cicco, gastrointestinal and myelotoxicity were similar in control and TPN-related group. TPN appeared to be unable to reduce chemotherapy-related toxicity. Chemotherapy did not result in any impairment of the nutritional status in normally nourished cancer patients. There was no acceleration of the hematopoietic recovery in patients receiving TPN.

It appeared that TPN should be limited to severely malnourished cancer patients undergoing chemotherapy, because of its ability to prevent further impairment of nutritional status and to improve nitrogen balance.

Radiation therapy increases the likelihood of severe nutritional deficits; the severity of these deficits is related to the size and location of the tumor. Three TPN/radiation trials have not yielded significant survival differences between groups randomized either to receive or not receive TPN.

Surgery Trials:

Although trials of perioperative TPN have demonstrated improvements in nutritional status, effects on clinical outcome are much less defined. The majority of studies examining the impact of perioperative nutrition have focused on the use of preoperative TPN. The accumulated data suggest that patients with gastrointestinal cancer who are severely malnourished may benefit from preoperative TPN. TPN before resection of tumor in such patients may reduce postoperative complications and mortality rate. The data also show lack of benefit of TPN in borderline, mildly, or moderately malnourished patients.

Bone Marrow Transplantation (BMT) Trials:

Published data suggest that TPN is beneficial to patients undergoing BMT. In a controlled study of 137 patients by Weisdorf et al, TPN was started one week before BMT and was continued through the fourth week after the procedure. Caloric intake was significantly less in the controls than in the TPN-treated group. Median survival was significantly longer for the TPN-treated group than the controls (21 months vs. 7 months, $P=0.010$). The control group had a greater percentage of relapse 2 years after BMT than did the TPN-treated group. Notably, however, the incidence of bacteremia was 50% greater than that among controls.

A recent study by Zeigler et al showed that modification of the amino acid formulation of TPN with L-glutamine improved nitrogen balance, diminished incidence of infection, and shortened hospital stay compared to patients receiving standard TPN.

PRACTICAL GUIDELINES:

1. All patients admitted to the hospital for cancer management, chemotherapy or surgical intervention, and suspected of having malnutrition, should have formal nutritional assessment, shortly after admission, to determine presence and severity of malnutrition. Patients with severe malnutrition, specifically, should be identified and receive priority management.

2. Dietary assessment should be obtained so that based on the historical data, or actual supervised calorie count, patient's degree of anorexia and actual intake compared to his/her needs can be determined.

3. An assessment of the "integrity" of the digestive tract should be performed. In patients whose GI tract is considered to be functionally intact, or at least partially intact, every effort should be made to use this route of alimentation before one can proceed with TPN. Modification of enteral formulas in many instances may allow the complete use of the GI tract for alimentation purposes. Side effects such as diarrhea may be common, and by itself may not justify switching to TPN. In difficult cases, consultation with GI specialist should be considered to assess the cause of diarrhea and to optimize anti-diarrhea therapy

4. Special attention should be made to management of anorexia associated with cancer. For patients with anorexia, and otherwise reasonably intact gut, Megestrol Acetate should be considered as an appetite stimulant and tried first. Dietary counseling should focus on patient interview to determine palatability and desire for different foods and enteral supplements.

5. In patients who are able to maintain only a partial oral intake, despite above efforts, one should give serious consideration to nasoenteral feeding. Since many patients may show resistance to the idea of nasoenteral tube placement for the purpose of feeding, the health care provider should counsel the patient regarding the potential and important benefits of this approach. Such benefits may be summarized as follows:

- A. Minimal discomfort when done in expert hands with a small tube and local anesthetic.
- B. Minimal or no discomfort shortly after the tube is place.
- C. Allowing a more physiologic route for

nutrition.

- D. Less potential for metabolic abnormality.
- E. Less potential for infection.
- F. May have a protective effect as far as prevention of stress gastritis and gastroduodenal ulceration.
- G. Avoids complications such as hepatocellular abnormality, biliary sludge, and metabolic bone disease seen with TPN.
- H. Helps to prevent gut atrophy.
- I. Feeding may be intermittent, and oral intake remains possible.
- J. Can be stopped at any time.

6. Patient counseling, in regards to tube placement for feeding, should ideally be done by the primary care/attending physician who has already developed a rapport and a state of trust with the patient. Such counseling should include understanding of patient wishes, desires, and fears, as well as clearing of any pre-judgments that patient may have based on inadequate information.

7. If PICC line is being considered for the sole purpose of parenteral feeding, the placement of this line should be withheld until indication for TPN is clarified by virtue of falling in to one of the designated indications, or by granting justification through MST.

8. Patients who have developed mucolysis secondary to chemotherapy, and are unable to maintain adequate oral intake, are considered appropriate candidates for TPN.

9. Patients who are identified as severely malnourished, and in whom treatment toxicity (chemotherapy, radiation) is expected to preclude oral intake for more than one week, are considered appropriate candidates for TPN and should receive TPN at the onset of cancer therapy. In other words to qualify for TPN in such patients, they should meet the following criteria:

- A. Be severely malnourished based on nutritional assessment.
- B. Patient is expected to undergo therapy in the form of chemo or radiation.
- C. Treatment toxicity is expected to preclude oral intake for more than one week.
- D. There is documentation that patient has been counseled for nasoenteral feeding and as why

Of the 30 subjects, 9 reported minimal symptoms and were able to absorb lactose. The rest of the subjects who had lactose malabsorption tolerated 240 ml of milk a day, also with minimal symptoms. The results of the study brought the authors to the conclusion that lactose-digestive aids are not necessary when the lactose intake is limited to 240 ml or less per day.

provided by June Hata, R.D.

Dietary saturated fatty acids: a novel treatment for alcoholic liver disease.
Wanji AA, et al. *Gastroenterology*;109:547-554.

This article provides an excellent review of lipid peroxidation and its potential role in a simple treatment for alcoholic liver injury. It is a first step rat research study which compares 3 groups of wistar rats (5/group). Group 1 were fed a liquid rat chow with 35% fat content, via gastrostomy tube. The fat source was Menhaden fish oil and ethanol for 6 weeks only. Groups 2 & 3 were fed fish oil and ethanol for 6 weeks, then switched to a diet containing fish oil with dextrose (Group 2) or palm oil with dextrose (Group 3) for 2 more weeks.

Composition of each fat source was reviewed. α - and γ - tocopherol levels were reviewed and the effect on liver histology reviewed and compared.

The conclusion was that a diet rich in saturated fat from the palm oil reversed alcoholic liver injury. The effect may be explained by down regulation of lipid peroxidation.

In review, several issues can be noted:

1. The diets themselves were based on moderately low fat content, (35 % of calories).
2. The complete nutrient composition of the diet was not provided.
3. Lecithin may have a role in treatment of alcoholic fibrosis and cirrhosis but apparently was not determined in the diet.

Given the nutritional differences between rats and humans, we still do not fully know if this treatment would benefit human liver treatment. Further study is suggested. This provides an interesting and useful review for future treatment of alcoholic liver injury.

provided by Teresa Baczkowski, R.D.

Editor's note: The above articles represent an objective review of the available peer reviewed medical literature. Many questions remain to be answered regarding optimal nutritional intervention in this setting. Your comments are welcome. Please send to:

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**"Doctor - What Should I Eat?:
Discovering the Health Benefits of Food and Wine".
1996 Nutrition Symposium on Saturday, March 30:**

Noel Merz, M.D., CSMC:
"Reversing coronary artery disease with nutritional therapy"

Michael Criqui, M.D., UC San Diego:
"Cardiovascular benefits of red wine"

Ka Kit Hui, M.D., UCLA:
"Legitimate herbal interventions for organic disease"

KEYNOTE SPEAKER
**Isadore Rosenfeld, M.D., NY Hospital, Cornell Center,
author of the book "Doctor, What Should I Eat?"**

he/she would not qualify for this mode of therapy.

10. Preoperative TPN may be appropriate in patients who are severely malnourished, and enteral route can not be established, and are to undergo cancer surgery. In such patients preoperative TPN may be started 5-10 days prior surgery.

11. Bone marrow transplant patients are considered appropriate candidates for TPN. In these patients TPN can be started shortly before the transplantation, and continued until patient is able to resume his/her adequate oral intake.

The incidence of bacteremia is higher in these patients, but may be reduced by adding L-glutamine to TPN.

12. TPN is not routinely indicated for well nourished or mildly-malnourished patients undergoing surgery, chemotherapy or radiation therapy and in whom adequate oral intake is anticipated or an enteral route of nutrition can be maintained.

“Moderately” malnourished patients in whom an enteral route cannot be established, and on nutritional assessment are found to be highly stressed, may be appropriate candidates for TPN, and should be screened by MST.

13. TPN is unlikely to benefit patients with advance cancer whose malignancy is documented as unresponsive to chemotherapy and radiation.

SUMMARY OF GUIDELINES:

1. Does the patient have Mucolysis? Is the patient unable to take his/her nutritional needs by mouth? If yes, start TPN.

2. Is the patient Severely Malnourished? Anticipate inability to eat for one week or more? Nasoenteral feeding is not an option? Patient is to undergo chemotherapy? If the answer to above questions is yes, start TPN.

3. Is the patient Severely Malnourished? Is cancer Surgery anticipated? An Enteral route cannot be established? If the answer to above questions is yes, start TPN 5-10 days prior to surgery.

4. Is the patient planned to undergo Bone Marrow Transplantation (BMT)? Start TPN shortly before BMT and continue until he/she is

able to take nutritional needs by mouth.

5. Is the patient Moderately Malnourished? Nutritional Assessment shows high level of stress? Chemotherapy or Surgery is planned? An enteral route cannot be established for the next one week? If the answer to above questions is yes, the patient may be a candidate for TPN. Contact MST.

6. Is the patient Well Nourished or Mildly Malnourished? Chemotherapy or Surgery is planned? Patient may be able to eat in about one week? If the answer to above questions is yes, TPN is not indicated. Reevaluate Nutritional Assessment in one week, and follow earlier guidelines.

7. Does the patient have advanced cancer? Life expectancy is less than two weeks? Or, cancer is documented as unresponsive to chemotherapy or radiation? If the answer to above questions is yes, TPN is unlikely to benefit patient. Contact MST, if any questions.

(REFERENCES AVAILABLE UPON REQUEST)

SELECTED SUMMARIES

Editor's note: In an attempt to make Nutrition Notes more practical, useful and beneficial to its readers, we are beginning a new series in the newsletter. "Selected Summaries" will be an effort to provide the most useful of the peer-reviewed literature related to nutrition. Our goal is to assist in keeping us all up-to-date with the most recent knowledge of our profession. Your comments and suggestions are encouraged.

Current use and clinical outcome of home parenteral and enteral nutrition therapies in the United States. Howard L, et al, Gastroenterology 1995;109:355-65.

Home nutrition support is very costly. This review tried to evaluate usage and quality of therapy outcomes for patients receiving home parenteral and enteral nutrition support (HPEN) in the United States. The study reviewed data from Medicare HPEN use from 1089-1992 and

assessed use, growth and costs. A brief discussion of cost/benefit per disease was included in the discussion. National Registry information was utilized on 9288 patients to assess disease distribution and therapy outcome.

The data collection procedure was critically reviewed and limitations discussed. Despite limitations these three conclusions can be derived from the analysis:

1. Both home parenteral and enteral therapies are relatively safe. Fewer incidents of 'sepsis' were noted in home HPEN vs. in hospitalized settings.
2. Registry analysis emphasized the importance of the primary diagnosis in determining long-term survival and rehabilitation. Patients with Crohn's disease, ischemic bowel disease, motility disorder or radiation enteritis usually had lengthy survival rates. In contrast, patients with AIDS and active cancer had shorter survival rates. More in-depth studies were recommended to determine prognostic factors that identify which cancer and AIDS patients will have longer survival rates. Patients with CVA related dysphasia or neurological dysphasia had poorer outcomes and rehabilitation probably related to the course of the impairment.
3. The Registry data also reflected on the influence of age on therapy. The results make it reasonable to say that age per se should not disqualify anyone from HPEN, as long as the home situation is suitable and patient is stable enough for HPEN.

Although HPEN cost-benefit studies have not been performed in the United States, a cost-utility analysis on HPEN in Canada (Detsky, et al) concluded that long-term patients with severe bowel impairment are less expensive and have better quality of life when supported on PN at home compared with frequent rehospitalization for nutrition rehabilitation. Nutrition therapy at home, even with domiciliary nursing visits, is likely to be a cost savings compared to nutrition therapy in hospitals. Lastly the reduced complications at home suggest the possibility of increased safety with reduced nosocomial infections. The conclusion was that the major cost-benefit issue was not where to provide long-term nutrition support but when to provide it.

3 areas of further study were recommended:

1. Question whether in terminal patients with bowel obstruction HPEN is better than simple hydration or even anti-emetic and narcotic

therapy.

2. Role of short-term HPEN in patients who are not dying such as preoperative HPEN in malnourished patients and its relation on postoperative complications and length of hospital stay.
3. Question of appropriateness in patients who have no primary gastrointestinal disease yet have severe nutritional depletion because of inadequate oral intake, i.e. dementia and anorexia nervosa, or CRF or pulmonary and cardiac dyspnea.

In conclusion, the study asks why the use of HPEN increased so much over this 5 year period in relation to usage in other developed countries. With health costs reduction we need to critically review expensive medical technologies while preserving these rehabilitative options in treating disease which has well-established positive outcomes with HPEN.

provided by Teresa Baczkowski, R.D.

Comparison of symptoms after consumption of milk or lactose hydrolyzed milk by people with self-reported severe lactose intolerance. Suarez F.L., D.A. Savaiano, M.D. Levittx. New England Journal of Medicine, Vol.333, No.1:1-4.

Researchers of a randomized, double-blind, crossover trial comparing symptoms after consumption of milk or lactose hydrolyzed milk have reported that some people mistakenly believe they are lactose intolerant. The results of this trial have brought them to the conclusion that it is not necessary for those with self-reported lactose malabsorption to buy lactose-digestive aids or avoid milk completely.

While it is known that the majority of people with lactose malabsorption suffer from gastrointestinal distress after ingesting a large dose of lactose (50 grams in 1 liter of milk), it is uncertain whether smaller doses of lactose such as the amount of milk with coffee or cereal (240 ml of milk) have a similar effect.

Thirty subjects ranging in age 18-50 with self-reported lactose intolerance were assessed for their ability to digest lactose. During a period of one week they received either 240 ml of lactose hydrolyzed milk or the same amount of 2 percent fat milk with aspartame for breakfast.