TITLE: Nutritional Considerations for Head and Neck Cancer Patients
SOURCE: Grand Rounds Presentation, UTMB, Dept. of Otolaryngology
DATE: March 26, 2003
RESIDENT PHYSICIAN: Glen T. Porter, MD
FACULTY PHYSICIAN: Anna M. Pou, MD
SERIES EDITORS: Francis B. Quinn, Jr., MD and Matthew W. Ryan, MD

"This material was prepared by resident physicians in partial fulfillment of educational requirements established for the Postgraduate Training Program of the UTMB Department of Otolaryngology/Head and Neck Surgery and was not intended for clinical use in its present form. It was prepared for the purpose of stimulating group discussion in a conference setting. No warranties, either express or implied, are made with respect to its accuracy, completeness, or timeliness. The material does not necessarily reflect the current or past opinions of members of the UTMB faculty and should not be used for purposes of diagnosis or treatment without consulting appropriate literature sources and informed professional opinion."

INTRODUCTION

Cancer patients often present to their physicians in a poor nutritional state. Their nutritional deficits have a significant impact on mortality, morbidity and quality of life. Head and neck cancer patients are no exception. The literature indicates that up to 57% of patients with head and neck cancer present with significant malnutrition (manifest by greater than 10% weight loss from baseline body mass). Alcohol and tobacco use frequently exacerbates this problem. Alcohol provides a large amount of simple carbohydrates without essential vitamins, proteins, and fats. These “empty calories” may actually contribute to cancer growth and further nutritional decay. Tobacco is an appetite suppressant. Moreover, head and neck cancers may cause significant trismus, odynophagia, dysphagia, and aspiration. Large tumors can actually obstruct the aerodigestive system. Treatment options for head and neck cancer include surgery, chemotherapy, and radiation therapy. Each of these interventions have side effects that contribute to malnutrition. Thus, it is especially important that patients with head and neck cancer undergo pretreatment nutritional evaluation, appropriate nutritional supplementation, and continued attention to this detail during and after treatment.

Malnutrition

Malnutrition is generally divided into two types—marasmus and kwashiorkor. The former is characterized by normal serum protein levels and total calorie deprivation from all food sources (starvation). Kwashiorkor is caused by a decrease in protein intake. Serum levels of protein are reduced. Most head and neck cancer patients present with protein-deficiency malnutrition. Thus, diminished nutrient intake, or diminished appropriate nutrient intake is one etiology of cancer malnutrition. As previously discussed, cancers of the head and neck can physically impede the intake of nourishment or cause trismus and odynophagia that limit oral intake. Alcohol and tobacco use, commonly seen in this patient group, add to the problem by providing “empty calories” devoid of essential nutrients, and suppressing appetite. Patients who consume excessive amounts of alcohol have also been shown to have a much decreased intake of fresh fruits and vegetables. A diet low in essential vitamins and minerals has been associated with increased risk of head and neck cancer. The treatment regimens for head and neck cancer

often result in side effects that decrease oral intake. Surgical treatment can alter the anatomy such that chewing and swallowing can be temporarily or permanently dysfunctional. Radiation therapy and chemotherapy commonly result in mucositis, dysgeusia, anosmia, xerostomia, nausea, and vomiting. Poor dentition may also contribute by increasing difficulty with mastication. Radiation-induced dental disease can further exacerbate this.

The other factors that can lead to a malnourished state include increased nutritional losses, increased nutritional demand, and tumor-induced metabolic dysfunction. Increased nutritional losses are most commonly seen with vomiting and diarrhea, but can be caused by enterocutaneous fistulae or gastrointestinal malabsorption. Increased nutritional demands result from surgery, radiation, and chemotherapy. Pneumonia, wound infections, and sepsis can further increase nutritional demands. These demands often correspond to the time that oral nutrition is impossible or very limited, i.e. the early postoperative period, or during daily radiation treatments. The nutritional demands during this acute phase result in catabolism of stored glycogen (exhausted during the first 24 hrs) and proteins in the muscles and tissues. Energy stored in fat does not appear to be mobilized to meet the nutritional needs of this phase. After 3 to 7 days the body begins to slowly return to normal metabolism.

Finally, specific tumor-induced anorexia and metabolic dysfunction contribute to malnutrition. Anorexia of cancer is thought to result from alterations in neurotransmitters (possibly serotonin) and possibly from learned food aversions. Alterations in metabolism are profound. Most solid tumors derive their energy from glucose. They are unable to use amino acids or fat to create energy. Tumor factors (thought to include tumor necrosis factor, and interleukins IL-1, and IL-6) result in catabolism of muscle and tissue proteins which are converted to glucose in the liver and used for cell replication by cancer cells. Fat is also catabolized. Elevated levels of plasma free fatty acids are thought to be secondary to hepatic neoketogenesis and are responsible for a relative insulin insensitivity by normal body tissues. This results in a decreased ability for normal tissues to take up amino acids and further fuels gluconeogenesis which feeds the tumor.

Impact of Malnutrition

The impact of malnutrition on patient outcomes is great. Mick, et al. studied a group of patients with stage III/IV head and neck cancer treated with multiple modalities. The strongest independent predictor of survival was pretreatment weight loss. Brookes, et al. showed that head and neck cancer patients have a significant 2-year survival if they are malnourished at presentation (7.5% vs. 57%). Finally, Bertrand, et al and Van Bokhorst-de Van der Shuer showed that 7-10 days of preoperative nutrition resulted in a significant improvement in postoperative quality of life, and led to a 10% decrease in postoperative infectious complications. Patients that have lost 12-20% of their ideal body weight are at increased risk of postoperative sepsis. Malnourished patients have depressed immune systems with a particular decrease in cell-mediated immunity. This is thought to be the reason for the anergy often seen in cancer patients. It is also proposed to be the reason that malnourishment coincides with tumor size and prognosis—that a decrease in the immune system leads to unimpeded tumor growth. Cachectic patients are also frequently unable to tolerate antineoplastic therapies which results in treatment delay and higher costs.

Diagnosis

Because of the associated risks, it is important to be able to diagnose malnutrition in head and neck cancer patients. Malnutrition has been defined as weight loss greater than 10% of ideal body weight that is associated with loss of muscle. However, there have been multiple systems for assessing malnutrition proposed. A complete history and physical in combination with the 10% "rule" is probably the most commonly used method of evaluating nutritional status. The best muscles to assess for wasting are the quadriceps femoris and the deltoid muscles. Cheilosis, stomatitis, and dry scaling skin can be indicative of vitamin deficiencies. Other parameters include anthropomorphic measurements (tricep skin fold, upper arm diameter), skin testing (for anergy), laboratory values, total lymphocyte count (patients with TLC<1700 have 5X risk of wound infection), and weight as a percentage of baseline weight. Laboratory values include albumin, prealbumin, transferrin, and retinol binding protein. Albumin is often used to evaluate nutritional status, but is handicapped by a long half-life (20 days) whereas the prealbumin, retinol binding protein, and transferring are more indicative of the present nutritional state (half life of 8 days). The creatinine-height index, prognostic nutritional index (PNI), and subjective global assessment (SGA) are all methods of identifying nutritionally deficient patients using one or more of the above parameters. Once high-risk patients are identified, immediate intervention can result in a much improved outcome.

Treatments

Patients with difficulty eating secondary to pain and anorexia can be offered medical treatment. Mucositis is common in patients receiving radiation therapy and chemotherapy. Treatment is generally with topical medications (analgesics, antifungals, coating agents, and antihistamines), and gentle local care. Dental care can address pain of dental origin and frequent sips of water, synthetic saliva, and pilocarpine can address problems of xerostomia. Chemotherapy-related nausea and vomiting have been significantly ameliorated with newer generation antiemetics such as Ondansetron and Granisetron. Patients who suffer from cancer-associated anorexia have shown good response to progestogens such as megestrol. Other agents under investigation include THC, thalidomide, melatonin, and pentoxifylline. The dysgeusia experienced by patients who undergo radiation therapy and chemotherapy usually resolves within a year of treatment. Pain management is important as maximal medical therapy may not be able to completely alleviate the pain associated with these disorders.

Once a patient has been evaluated and his risk of malnutrition identified nutritional counseling should be offered. Patients who appear to be healthy should be counseled in regards to their diet and encouraged to eat a balanced diet with emphasis on high-protein, high-calorie foods. Expectations for future treatments and their influence on nutrition should be discussed. Interestingly, patients who are counseled to avoid favorite foods during treatment periods seem to return to a normal diet quicker and have fewer food aversions. For patients with mild to moderate malnutrition who tolerate oral feeding, nutritional supplementation should be advised. The most complete nutritional supplementation is found in the commercially available enteral formulas. This can be fairly expensive, and is not necessary in patients who are able to chew and swallow effectively. These patients should be encouraged to eat a balanced diet with an effort to eat high-protein, high calorie foods. They might be counseled to use whole milk instead of fat-free, real mayonnaise instead of dressing, butter, eggs, meats, legumes, ice cream, and "instant

breakfast" powders. These changes can significantly increase caloric intake with little change in actual volume. The patient should be invited to stop drinking alcohol and smoking tobacco.

Consulting a dietitian is appropriate whenever one identifies a patient currently malnourished or at risk of malnutrition. Their input is especially helpful when deciding the total caloric needs of a patient and when exploring the options for nutritional supplementation in patients with other medical problems. A dietitian is able to provide nutritional counseling throughout the course of a patient's cancer treatment and give valuable treatment suggestions for the otolaryngologist—head & neck surgeon.

Patients who are judged at high risk and are unable to eat by mouth should be given enteral feeding. Placement of feeding tubes into the gastrointestinal system effectively bypasses the most common areas of feeding difficulty. Dysphagia, odynophagia, and aspiration are usually not issues once feeding is started through a nasogastric tube, gastrostomy or jejunostomy. The questions of when to initiate tube feeds and what type of tube is appropriate have been addressed by many authors. If the patient is cachectic or unable to satisfy his/her basic caloric needs by oral intake they are a candidate for supplemental tube feeds. Gastrostomy placement before XRT has been shown to prevent weight loss, treatment interruption, and dehydration. In general, a nasogastric feeding tube can be used if expected length of use is less than 30 days. These tubes irritate the nasal mucosa and are not well tolerated. They clog easily and typically require replacement every 10 days. The tip of the tube can be placed in the stomach or the small intestine. If the patient has a history of reflux, or if aspiration is a concern, the tube should be passed into the duodenum. The pyloric sphincter acts as an additional barrier to refluxing feeds. Enteral formula (hypertonic) can be instilled directly through this catheter and given in bolus form. Most authors feel that stomach feeds are more physiologic and are the first choice if aspiration risk is low.

If the patient is likely to require more than 30 days of tube feeds an enterocutaneous feeding tube is indicated. Enterocutaneous feeding tubes can be placed into the stomach or small bowel. They can be performed laporoscopically, open, under fluoroscopy, or endoscopically. When performed endoscopically, the tube can be "pushed" from the oral cavity into the stomach and through an incision in the stomach and skin, or "pulled" through a skin incision into the stomach. Complications are rare with any of the applications, though morbidity is somewhat higher for open procedures. There are case reports of cancer cells seeding the feeding tube site after endoscopic placement. This complication theoretically is avoided by "push," open, or fluoroscopic procedures.

No matter which type of tube is used, placement of the tip into the stomach is preferred. The stomach acts as a reservoir (allows for bolus feeds) and allows for hypertonic feeds. If the patient has delayed emptying time or other gastric dysfunction (often seen in the critically ill patient) a feeding tube placed into the small bowel may be more appropriate. Other indications for jejunal feeding include proximal fistula or leak, and severe reflux of gastric contents. Jejunal feeding is associated with a decreased rate of pneumonia in critically ill patients. This is thought to be a result of less reflux aspiration. When instilling enteral formula into the small intestine bolus feeds are contraindicated. Instead, a constant rate of up to 180cc/hr is well-tolerated. One study compared nasogastric tube placement with gastrostomy tube placement one day before surgery. Those patients with tonsil or laryngeal SCCA that received a gastrostomy tube spent a

significantly shorter time in the hospital (60+% reduction) (Gibson, et al.). Saunders, et al showed that patients tolerated gastrostomy tube placement long-term with high satisfaction levels. Scolapio, et al. followed patients who received a gastrostomy before starting radiation therapy. He reported a significant prevention of weight loss, treatment interruption, and hospitalization for dehydration. Enteral nutrition is well-tolerated and effective. It likely does not matter what tube is used to supply to formula, its effects are the same.

There are a wide variety of enteral formulas available. Most formulas provide 1-2 kcal/ml. In general, enteral feeding formulas can be separated into polymeric, monomeric, and disease-specific formulations. Polymeric contain carbohydrate polymers, complete proteins, and triglycerides. They can be used safely in the vast majority of patients. These formulas can be instilled in the stomach or small intestine. Monomeric formulations are essentially the breakdown products of the polymeric formula. As such, it contains carbohydrates in the form of oligosaccharides or maltodextrin, protein in the form of short peptide chains or free amino acids, and lipids as a mixture of short and long-chain triglycerides. Monomeric formulations are considered more appropriate for patients with poor absorption or other digestion dysfunction. There have been no studies to clearly confirm the benefit of their use. Disease-specific formulas are made specific to a patient's disease state. There are formulations for diabetes, renal insufficiency, pulmonary disease, hepatic dysfunction, and immunosuppression. Enteral feeding formulas rich in arginine, glutamine, omega-3 fatty acids, and polyribonucleotides are thought to alter immune function. This has resulted in their increased use for cancer patients. Although a met analysis of relevant studies failed to show any survival benefit in cancer patients, patients on this formula have been shown to have 50% fewer post-op infectious complications. One other important specialized enteral feeding formula is the medium-chain triglyceride formulation which is traditionally used in patients with post-operative chyle leaks (Lipisorb, Mead-Johnson, and Travasorb MCT, Clintec). Although there are formulas to calculate a patient's daily nutritional needs, metabolic needs are generally 35 kcal/kg/day for maintenance, and 45 kcal/kg/day to support an anabolic state.

Parenteral nutrition is the feeding option of "last resort," and should be employed only when enteral feeding is not possible or is contraindicated. Total parenteral nutrition (TPN) can be valuable when treating severely malnourished patients who need immediate treatment. This intervention is much more expensive, requires a central line, and is associated with significant complications. The formula is a hypertonic mixture of amino acids, dextrose, fat emulsions, vitamins, trace elements, and electrolytes. Insulin is often added to the formula to treat the hyperglycemia TPN can cause. This allows for automatic titration of the insulin to the amount of formula being administered. TPN requires daily electrolyte monitoring and composition adjustment. Complications include line-related problems, infection and sepsis, and metabolic complications. Patients should always be weaned off TPN before surgery as inadvertent hyper/hypoglycemia can result. Studies show improvement in postoperative morbidity in malnourished patients receiving TPN. Preoperative TPN seemed to provide the most significant improvement. When compared with enteral nutrition, TPN provided no added benefit over enteral feeds. PPN is peripheral parenteral nutrition and is a diluted form of TPN. It is generally used as an adjunct to enteral feeds.

Often, patients are noted to have aspiration or increased dysphagia with certain food consistencies. A growing number of companies now offer a full line of food products adapted to

these sorts of needs. Thickened water, juices, and pureed food lines are available if the patient wishes to pursue oral feeding. Long-term enteral nutrition with occasional pleasure eating by mouth is also an option. Patients who undergo surgical or radiation therapies may have long-term nutritional challenges as a result of treatment-related dysphagia and should be evaluated in cooperation with a skilled speech language pathologist.

Alternative Medicine

When discussing nutrition with patients it is important to recognize the role of alternative medical treatments. A growing number of Americans are turning to alternative medicine to either replace or supplement traditional western medicine (estimated at 1/3 of the American population). Much of the alternative or non-western approach is based on nutritional supplementation. Many of these supplements have been shown to be efficacious and useful. Others have little objective data to base judgments on. It is important to communicate that no treatments currently known to the scientific world can "cure" head and neck cancer outside of the modalities of surgery, radiation, and chemotherapy. Alternative interventions can, however, alleviate symptoms, and increase quality of life for patients with cancer. One study found that 15% of patients with head and neck cancer used alternative medicine. Interestingly, patients were usually well-educated and from high socioeconomic groups. Most patients used alternative medicine in conjunction with mainstream medical treatment. Chinese medicine (acupuncture and herbs), homeopathy, naturopathy, herbal medicine, Ayurvedic medicine, massage, mind-body medicine, chiropractic manipulations, and osteopathic manipulations are all forms of alternative medical practice that might be employed to treat a patient who presents with cancer. Low-dose ginger can be used as an antiemetic (may interfere with anticoagulation and cause hypoglycemia). Of all the alternative interventions, "mind-body intervention" seems to be the most successful. Many studies have shown treatment modalities that concentrate on "mind-body intervention" are effective in helping patients tolerate the side effects of medical therapies. One study comparing patients with melanoma treated with the standard of western medical care with and without mind-body treatments showed decreased recurrence and mortality in the group receiving alternative intervention. Recently, food compounds have been identified that may have an impact on health. Several of these are currently undergoing clinical trials. It is interesting that allopathic medicine is also investigating food nutrients for possible preventional value.

Looking to the Future

Preventing cancer by changing your diet is an emerging field. Some authors have started looking at food-related substances in an effort to identify what foods might offer a protective value against head and neck cancer. Low serum levels of vitamin A or B-carotene have been associated with cancer of the head and neck and cancer of the lung. Schantz, et al. showed an increased risk of head and neck cancer in patients who ate foods deficient in cryptoxanthin, lycopene, and Vitamins C and E. He postulated that these substances might act as free radical scavengers and thus "protect" DNA from mutation. Recently, studies looking at n-3 polyunsaturated fatty acids derived from fish oils have shown some effect in patients who are immunocompromised. This resulted in development of special enteral formulas which contain arginine, dietary nucleotides, and n-3 fatty acids. Studies have shown some improvement in

postoperative infection. A meta analysis of these studies, however, showed no added benefit when compared with regular enteral feeds.

Conclusion

Comprehensive care of head and neck cancer patients includes an evaluation of their nutritional status. Once a patient has been identified as suffering from malnutrition they should be assessed for their ability to take food by mouth, and their expected treatment course reviewed. Appropriate supplementation should then be provided. Enteral feeding is very successful in bypassing disease states of the upper aerodigestive system and results in improvement in treatment tolerance, post-treatment morbidity, as well as long-term quality of life and mortality. Alternative medical interventions may also be effective as adjuvant therapies. Scientists with hopes of identifying preventative substances for head and neck cancer may soon find that the best medicine we can take is the food we eat.

Bibliography

Asher, Benjamin F., et al. Complementary and Alternative Medicine in Otolaryngology *Laryngoscope* 111(8):1383-1389, Aug 2001.

Bertrand, Pauline Coti a, et al. Preoperative nutritional support at home in head and neck cancer patients: from nutritional benefits to the prevention of the alcohol withdrawal syndrome *Current Opinion in Clinical Nutrition & Metabolic Care*5(4):435-440, July 2002.

Bower R.H., et al. Postoperative enteral vs. parenteral nutrition. A randomized controlled trial *Archives of Surgery* 121(9):1040-1045, Sept. 1986.

Dudrick, Stanley J., et al. Nutritional Management of Head and Neck Tumor Patients Comprehensive Management of Head and Neck Tumors by Stanley E. Thawley, William R. Panje. W.B. Saunders Company, Philadelphia, PA. c1987.

Emberhardie, Chris Nutrition support in palliative care *Nursing Standard* 17(2):47-52, 54-55, Sept 2002.

Forbes, K. Palliative care in patients with cancer of the head and neck *Clinical Otolaryngology* 22(2):117-122, April 1997.

Gibson S., Wenig B.L. Percutaneous endoscopic gastrostomy in the management of head and neck carcinoma. *Laryngoscope* 102:977-980, 1992.

Mahan, L. Kathleen, Escott-Stump, Sylvia Krause's Food, Nutrition, and Diet Therapy W. B. Saunders Company, Philadelphia, PA, 1996.

Mantovani, Giovanni, et al. Managing Cancer-Related Anorexia/Cachexia *Drugs* 61(4):499-514, 2001.

Mick, R., et al. Prognostic factors in advanced head and neck cancer patients undergoing multimodality therapy. *Otolaryngology Head & Neck Surgery* 105:62-73, 1991.

Reilly, James J. Nutritional Management of Patients with Head and Neck Cancer Cancer of the Head and Neck by Eugene N. Myers and James Y. Suen. Churchill Livingston, New York, NY. c1989.

Saunders, JR Jr, et al. Percutaneous endoscopic gastrostomy in patients with head and neck malignancies. *Am J Surg* 162:381-383, 1991.

Schantz, Stimzon P., et al. Genetic Susceptibility to Head and Neck Cancer: Interaction Between Nutrition and Mutagen Sensitivity *Laryngoscope* 107:765-781, June 1997.

Schattner, Mark Enteral Nutritional Support of the Patient with Cancer: Route and Role *Journal of Clinical Gastroenterology* 36:297-302, Apr 2003.

Scolapio, James S., et al. Prophylactic Placement of Gastrostomy Feeding Tubes Before Radiotherapy in Patients with Head and Neck Cancer: is it Worthwhile? *Journal of Clinical Gastroenterology* 33(3):215-217, Sept 2001.

Sheldon, John M., Shike, Moshe Nutritional Management of Patients with Head and Neck Cancer Head and Neck Cancer A Multidisciplinary Approach by Louis B. Harrison, et al. Lippincott-Raven, Philadelphia, PA. c1999.

Sniderman, Carl H., et al. Reduced Postoperative Infections with an Immune-Enhancing Nutritional Supplement *Laryngoscope* 109(6):915-921, June 1999.