

Anorexia, Cachexia and Dysphagia

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Objectives

- Define Anorexia-Cachexia Syndrome
- Causes of Anorexia-Cachexia
- Conditions that Interfere with Eating
- Pathophysiology of Anorexia-Cachexia Syndrome
- Food-Related Conflicts
- Management of Anorexia-Cachexia
- Causes of Dysphagia
- Management of Dysphagia
- Approaches to Irreversible Dysphagia
- Counseling Patients/Families on Artificial Nutrition

Anorexia & Cachexia

Definitions

- **Anorexia** is defined as the loss of appetite or desire to eat, which is a common complication of advanced cancer and other terminal illnesses.
- **Cachexia** is characterized by involuntary weight loss, fat, and muscle wasting, fatigue, immune dysfunction, and a variety of metabolic and hormonal alterations.
- These terms are often described together and referred to as **anorexia-cachexia syndrome**.

Anorexia

- There are multiple causes, which may include endogenous cytokines, metabolic disturbances, and infections, as well as other reversible physical and psychosocial problems.
- Although lack of interest in food is a common symptom of depression, anorexia of advanced conditions is often caused by treatable symptoms and difficulties with the mechanics of eating.

Reversible Causes of Anorexia

- Aches and pains (abdominal pain)
- Nausea and gastrointestinal dysfunction
- Oral candidiasis
- Reactive --or organic-- depression
- Evacuation problems (constipation)
- Xerostomia
- Iatrogenic (radiation, chemotherapy, or drugs)
- Acid-related problems (gastritis, GERD, peptic ulcers)

AAHPM Primer of Palliative Care, 3rd Edition, 2004

Conditions that Interfere with Eating

- Dentures that fit poorly
- Poor dental hygiene
- Taste disorders
- Weakness or neuromuscular problems
- Stress and tension
- Dry mouth caused by radiation, drugs, or disease
- Dryness caused by systemic hydration
- Oral candidiasis
- Bacterial or viral infection
- Reflux esophagitis
- Mucosal damage
- Diffuse esophageal spasm

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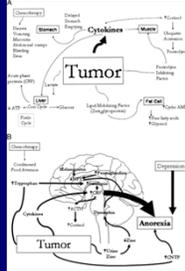
Cachexia

- Occurs in up to 80% of cancer patients; the incidence is highest in GI and lung cancers.
- It is not correlated with food intake or the stage of the tumor.
- Abnormal weight loss (more than 5-10% of pre-morbid weight) results in significant physical and psychological morbidity and is an independent risk factor for early mortality.

Anorexia-Cachexia Syndrome

- Clinical features include:
 - Marked weight loss
 - Anorexia
 - Weakness
 - Fatigue
- Associated physical features include altered taste sensation, loose dentures causing pain and difficulty eating, pallor (anemia), edema (hypoalbuminemia), pressure sores, increased skin folds, decreased turgor, and ill-fitting clothing.

Anorexia-Cachexia Syndrome: Pathophysiology



Food-Related Conflicts

- Family and caregiver response to loss of appetite could be to focus concerns on the patient's eating habits.
- Families may prepare unwanted foods and become distressed when these feedings are refused.
- Conflicts can occur even when the patient accepts decreased appetite as part of the dying process.

Management of Anorexia-Cachexia Syndrome

Resolving Food-Related Conflicts

- These conflicts can be diffused by suggesting other measures, such as:
- Providing patient/family education about the natural progression of advanced illness and its effects on appetite
 - Anorexia is part of the disease process
 - The patient is not starving to death
 - Forced feeding may cause discomfort and put the patient at risk for aspiration
 - Artificial feeding usually does not prolong life and may shorten it
 - Patients can live comfortably for a long time on very little food
 - Providing sensible dietary advice
 - Involve the patient/family in menu planning
 - Offer small portions of the patient's favorite foods – "pleasure feeds"
 - Avoid foods with strong odors
 - Offer easy-to-swallow foods, such as semi-liquids, puddings, or soft or pureed foods
 - Helping family members identify alternative methods of expressing their love for a patient

Nonpharmacological or Noninvasive Interventions

- Avoid routine weighing
- Educate about physical changes (new bony prominences and importance of skin care)
- New clothing –if affordable– for quality life and enhancing self esteem
- Durable medical equipment to help maintain patient's independence

Appetite Stimulants

- Pharmacological stimulation of appetite is not always successful, but some patients may benefit from appetite stimulants.
- If the previously mentioned interventions do not relieve anorexia, a short trial of appetite stimulants maybe appropriate.
- If the patient does not experience any benefit within a week, either increase the dose or discontinue the medication to avoid unnecessary side effects or expense.

Appetite Stimulants

- First line treatment, short term
 - Prednisone
 - Dexamethasone
- First line treatment, long term
 - Megestrol
- Second line treatment
 - Dronabinol
- Third line treatment
 - Cyproheptadine
 - Remeron

Appetite Stimulants (cont'd)

When appetite stimulants are appropriate, consider:

- **Megestrol** (160-800mg daily) can be effective in patients with cancer or HIV
- **Prednisone** (10-20mg daily) and **dexamethasone** (2-4mg qd-tid) are helpful for patients who have a shorter prognosis or other indications for steroid use.
- **Dronabinol** (2.5mg qd initial, then 2.5-10mg bid) is especially effective in young patients with HIV who cannot tolerate megesterol.

Other Appetite Stimulants

- **Progestogens** are expensive and should be used selectively. The effect of progestogens may be enhanced by concurrent use of ibuprofen (1200mg/day), or another NSAID.
- **Antihistamines** (cyproheptadine) may cause sedation, dizziness, and dry mouth but alleviate itching and rhinitis.
- **Mirtazapine** (15-45mg qd) is helpful in patients with concurrent insomnia or depression. Remember that lower doses are more sedating, higher doses more effective for depression.

Megestrol Acetate (Megace)

Clinical trials have demonstrated that megestrol is:

- Equally efficacious to dexamethasone as an appetite stimulant.
- Superior to dronabinol in appetite stimulation and non-fluid weight gain.
- Effective, when used concurrently with radiation therapy in lung or head and neck cancer to reduce treatment associated weight loss.
- Associated with fewer side effects than corticosteroids.

Megace (cont'd)

- Despite these apparent benefits, available data suggest that weight gain is largely adipose tissue (not lean muscle) and only one study has demonstrated a quality of life benefit.
- No study has shown a survival advantage.
- Overall, only 20-30% of advanced cancer patients will have a significant response (weight gain > 5%), with a median time to response of 6-8 weeks.

Megace: Dosing

- Dosed orally, once daily
- Increasing dose/response curve from 160-800mg/day; doses above 800mg daily have no additional benefit
- Can be dosed in an elixir form
- 60-80% excreted in the urine; no renal dosing guidelines available

Megace: Side Effects

- Side effects are mild but can include thromboembolic events (use with caution in patients with history of thromboembolism), adrenal suppression with insufficiency upon abrupt discontinuation, HTN, hyperglycemia, breakthrough uterine bleeding, and skin photosensitivity.
- On retrospective study showed that megestrol treatment of elderly nursing home residents with significant weight loss was associated with a significant increase in all-cause mortality without a significant increase in weight.
- Other retrospective studies have demonstrated an association between the use of megestrol and DVT among nursing home residents.

Mirtazapine (Remeron)

- A Phase II trial of mirtazapine for cancer-related anorexia and cachexia has the potential for treatment with 24% of patients gaining at least 1 kg after 4 weeks of therapy (versus 0.4 kg with dexamethasone and increase in 10% of baseline weight with megestrol – in 10% of patients– after 4-8 weeks of therapy)
- However, the attrition rate was high in this particular study due to poor clinical condition and death.

Mirtazapine (cont'd)

- The result is promising but further research is required to substantiate these findings.
- Mirtazapine is associated with weight gain. Patients taking this medication report a voracious appetite, with intense cravings for carbohydrates.
- The exact mechanism by which mirtazapine induces weight gain is not clear, but there are several hypotheses in the literature.

Artificial Nutrition

- Often times, families request that NG, PEG, or IV feedings be given when patients become thin and weak.
- These families should be reminded that these interventions could be more burdensome than beneficial.
- There is a considerable amount of evidence to guide decision-making, and education is key here!

Dysphagia

Neurological Causes of Dysphagia

- Stroke
- Motor neuron disease (ALS)
- Parkinson's disease
- Poliomyelitis
- Multiple sclerosis
- Myasthenia gravis
- Myopathies

Non-Neurological Causes of Dysphagia

- Head and neck cancer
- Mucosal injury
- Medications
 - KCI
 - NSAIDs
 - Antibiotics (doxycycline, trimethoprim-sulfa)
 - Anticholinergics
 - ACE-inhibitors
 - Antihistamines

Non-Neurological Causes of Dysphagia (continued)

- Dry mouth caused by radiation, drugs, or disease
- Dryness caused by systemic hydration
- Oral candidiasis
- Bacterial or viral infection
- Reflux esophagitis
- Mucosal damage
- Diffuse esophageal spasm

(as seen in earlier slide "Conditions that interfere with eating")

Non-Neurological Causes of Dysphagia

- GERD
- Post chemotherapy or radiation
- Esophageal cancer
- Achalasia
- Scleroderma

Management of Dysphagia

- Dry mouth caused by radiation, drugs, or disease
 - Pilocarpine 5-10mg tid (5mg bid for med causes)
 - Saliva substitute or oral gel q1-2h or gum
 - Pilocarpine combined with a saliva substitute
 - Avoidance of glycerine swabs or lemon juice
 - If caused by medication, reduce dosage or change medication
- Oral candidiasis
 - Nystatin suspension
 - Clotrimazole 10mg troche 1 dissolved in mouth 5 times daily
 - Fluconazole 100mg qd-bid x 10-14 days

Management of Dysphagia

(continued)

- Bacterial infection
 - Adequate oral hygiene and an antibiotic
 - Chlorhexadine gluconate 0.12% 30mL swish and spit bid may help with periodontal infection
- Viral infection
 - Acute: Acyclovir 400mg 5 times daily x 7-10 days
 - Chronic suppression: Acyclovir 800mg tid daily
- Reflux esophagitis
 - Proton pump inhibitor or H2 blocking agent
 - Place of patient in a more upright position

Management of Dysphagia

(continued)

- Mucosal damage
 - Chlorhexadine gluconate or oral lavage with 5mL of sodium bicarbonate to 0.95L of water
 - Combination mouthwash containing 2-3 of the following: diphenhydramine, lidocaine topical, loperamide, nystatin, tetracycline, hydrocortisone
 - Lidocaine 2% 2-5mL q4-8h (can be diluted or flavored if desired); 50/50 mixture with famotidine will cause better adherence to tissues; can cause aspiration if used before meals
 - Sulcrafate suspension 5mL swish & swallow tid-qid
 - Doxepin oral rinse (5mg/5mL) up to q4h
 - Topical or parenteral opioids

Management of Dysphagia

(continued)

- Dryness caused by systemic hydration
 - Increase in oral liquid intake, if possible; try frozen juice, flavored ice, or popsicles
 - Ice chips, atomizer, or sips of water
 - As death approaches, have family members use moist sponge sticks or few drops of water from a syringe to keep patient's mouth moist
- Diffuse esophageal spasm
 - Anticholinergic medications

Irreversible Dysphagia

- When the dysphagia is caused by esophageal obstruction or if it is irreversible and progressive, the team should consider if the patient is an appropriate for more invasive measures, such as:
 - Surgical resection or laser ablation of obstructing lesion
 - Palliative radiation therapy
 - Esophageal dilatation
 - Placement of an esophageal stent

Irreversible Dysphagia

(continued)

- If esophageal stenting or dilatation are not feasible or do not provide sustained relief, and the prognosis is weeks or months, it may be appropriate to consider gastrostomy tube placement, especially if the patient is hungry and desires ongoing nutritional intake.
- A nasogastric tube is easier to insert but is not tolerated well in the long term and plugs up easily.

Risk of Aspiration

- Dietary evaluation/modifications
- Patient and family counseling/anticipatory guidance
- Precautions: monitor feeds, chin tuck while swallowing, head elevated 90 degrees, focus/concentration while eating

Artificial Nutrition

Supplemental Information

Educational Points on Artificial Nutrition

The medical literature is quite clear:

- Attempts to treat anorexia with enteral or parenteral feeding have demonstrated limited efficacy, at the price of increased morbidity.
- Tube feedings and forced feedings in terminally ill patients have never been shown to prolong life.
- Total parenteral nutrition (TPN) for cancer chemotherapy patients has been shown by a meta-analysis of 12 randomized trials to be associated with decreased survival, decreased response to chemotherapy, and an increased rate of infection.
- The American College of Physicians could not identify any subgroup in which such treatment appears to be beneficial.

Educational Points on Artificial Nutrition (cont'd)

- TPN for patients with HIV mostly increases body fat and has not been shown to improve survival.
- NG or PEG tube feedings, especially in the elderly, are associated with a high incidence of aspiration pneumonia, self-extubation, use of restraints, and symptoms such as nausea, rattling respiratory secretions, and diarrhea.
- The observations of many experienced hospice professionals indicate that artificial nutrition does not increase the comfort in terminally ill patients.

Practical Issues

- When making decisions about artificial nutrition, the following practical issues should be considered:
- NG tubes are uncomfortable and unattractive. Gastrotomy tubes require surgery, a procedure that involves some risk and discomfort.
 - The fragile veins of most terminally ill patients make it difficult to insert an IV needle, and IV sites may need to be changed frequently.
 - Artificial nutrition and hydration may increase secretions, ascites, or effusions, which then require additional intervention.
 - Appetite stimulants and treatment of impediments to eating may be more efficacious and less invasive.

Parenteral Nutrition

- PN is a controversial and expensive treatment that is sometimes considered to assist with nutrition in advanced cancer patients.
- Weight loss in advanced cancer is frequently due to insufficient caloric intake, as well as cancer-mediated hypermetabolism and hypercatabolism.
- These latter problems are caused by catabolic proinflammatory cytokines and eicosanoids and are responsible for much of the accelerated muscle wasting (cachexia) seen in advanced cancer.

The Role of Parenteral Nutrition (PN)

PN is usually considered outside the standard of care for most patients with advanced cancer. This is based on clinical research findings and other observations:

1. With a few specific exceptions (such as head and neck cancer patients undergoing radiation therapy), caloric supplementation of any kind has not been shown to benefit advanced cancer patients, and – if indicated – can almost always be achieved enterally.
2. There is no physiologic basis to assume the PN would affect the inflammatory and catabolic aspects of cachexia.
3. PN brings potential risks and burdens: laboratory testing, indwelling IV lines, infections, metabolic derangements, liver and pancreatic dysfunction.

Parenteral Nutrition Guidelines

There does remain a small subset of advanced cancer patients for whom PN may be an appropriate therapy to improve quality and/or length of life, such as cases in which:

1. Enteral nutrition is not an option or there is a specific benefit expected from PN (patients for whom a nonfunctional GI tract, and not cachexia itself, is the major problem).
2. Death is probably from starvation or malnutrition earlier than anticipated from disease progression.
3. The patient has a life expectancy of at least several months to allow a proper trial of PN (Karnofsky Score of $\geq 50\%$)

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