

# Management of Non-Pain Symptoms

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# Palliation of Dyspnea

# Dyspnea: ATS Definition

- “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity. The experience derives from interaction among multiple physiologic, psychological, social, and environmental factors, and may induce secondary physiologic and behavioral responses.”

# Advanced Chronic Obstructive Pulmonary Disease: Innovative Approaches to Palliation

- Rucker et al Journal of Palliative Medicine
- 2007;10:783-797

# COPD

- 12 million in US in 2001
- 24 million in US with impaired lung function
- 4<sup>th</sup> leading cause of death
- smoking

# Challenges for palliative care

- Unpredictable disease trajectory
- Episodic exacerbations/incomplete recovery
- Patients/caregivers unaware disease is terminal
- More likely to die in ICU
- More likely to die with greater symptoms

# Increased Risk of Death in Next Year

- FEV1 < 30% predicted
- Increasing dependency on caregivers
- Activity: a few steps without rest
- Depression
- No spouse
- Recurrent hospitalization
- Comorbidities

# **Interventions for Alleviating Cancer-Related Dyspnea: A Systematic Review**

- Ben-Ahron, I et al. Journal of Clinical Oncology
- 2008;26:2396-2404



# Dyspnea

- > 50% of terminally ill CA pts
- Increases as function declines
- Neural pathways still not well understood

# Results

- 18 trials included in meta analysis
- Good evidence for morphine to relieve dyspnea, with minimal side effects
- No evidence that oxygen was beneficial except in hypoxemic patients
- One trial showed added benefit by adding midazolam to morphine
- Nursing led nonpharmacologic interventions, some effect

# Clinical Utility

- Morphine remains the first line drug for dyspnea in Cancer patients
- It is both effective and well tolerated
- Oxygen offers little benefit in the absence of hypoxemia

# Dyspnea

- Fan
- Bronchodilators
- Oxygen
- Opiates

# Opioids and Dyspnea

- A Systematic Review of the use of Opioids in the Management of Dyspnea. Jennings et al Thorax 2002;57:939-944
- May see effect with low doses 1 mg q 4 h
- Oral and parenteral not nebulized
- No effect on ABGs

# Mechanism of Action

- Decreased central perception of dyspnea
- Decreased anxiety
- Decreased sensitivity to hypercapnea
- Decreased O<sub>2</sub> consumption
- Improved cardiovascular function

# **Midazolam as Adjunct therapy to Morphine in the Alleviation of Severe Dyspnea Perception in Patients with Advanced Cancer**

- Navigante et al. Journal of Pain and Symptom Management. 2006;31: 38-47

# Results

- No change in oxygen saturation at 24, 48 hrs and baseline
- **At 48 hrs:**
- **Mo** 69% reported relief, 12.5% no relief
- **Mi** 46% reported relief, 26% no relief
- **MM** 92% reported relief, 4% no relief
- Less breakthrough med in **MM**
- Side effects,(somnolence) greatest in **Mo**
- No difference in deaths



# Implications

- Anxiety may be an appropriate target for Rx in patients with dyspnea
- Benzodiazepines may add to dyspnea relief in patients with advanced cancer

# **Oxygen for Relief of Dyspnoea in Mildly or Non-hypoxaemic Patients with Cancer: a Systematic Review and Meta- analysis**

Uronis HE et al. British Journal of Cancer  
2008;98:294-99

# Results

- 5 studies were blinded, randomized and controlled crossover trials
- Cancer patients
- Oxygen was not effective in controlling dyspnea

# Oxygen

- \$250 per month
- Fall risk
- O<sub>2</sub> sat
- 48 hour trial ?

# Pulmonary Rehab

- Documented benefit but less evidence for end-stage patients

# Noninvasive Ventilation

- Relieve dyspnea
- Buy time
- Can be withdrawn when it does not meet patient's goals

# Cough Suppressants

- Central: ie opiates,,: good evidence for efficacy
- Peripheral: ie benzonatate (Tessalon): good evidence for efficacy

# Palliation of GI Symptoms



# Nausea

- Unpleasant sensation
- Precedes vomiting

# Vomiting

- Forceful contraction diaphragm, abdominal muscles
- Expulsion of stomach contents

# Retching

- Forceful contraction diaphragm, abdominal muscles
- Without expulsion of stomach contents

# Advanced Cancer

- 40-70% report nausea or vomiting
- Distressing
- Results from disease or treatment
- Also in CHF, AIDS

# Vomiting

- Efferent pathways
  - Phrenic nerve to diaphragm
  - Spinal nerves to intercostal and abdominal muscles
  - Vagus nerve to larynx, pharynx, esophagus, stomach

# Vomiting

- Stomach plays a minor role
  - Pylorus contracts
  - Fundus and GE sphincter relax
- Diaphragm, abdominal wall muscles contract
- Soft palate elevates
- Glottis closes, respiration inhibited

# Vomiting Center

- Medulla
- Input from:
  - Chemoreceptor trigger zone (CTZ)
  - GI tract afferents
  - Vestibular system
  - Higher cortical centers

# Chemoreceptor trigger zone

- Floor of fourth ventricle
- Little blood brain barrier
- Most medications act here



# Receptors

- Vomiting center
  - Histamine type 1
  - Acetylcholine (muscarinic)
  - 5 HT2
- CTZ
  - Dopamine type 2
  - Serotonin (5 HT3)
  - Neurokinin type 1
- Vestibular
  - Histamine type 1
  - Acetylcholine (muscarinic)
- Gut
  - Serotonin (5 HT3)
  - Stretch receptors

# History

- Medication use (chemo, opioids, digoxin, d/c of steroids)
- Bowel function
- Must rule out constipation
- Provocation
  - Movement?
- N, N+V, V only

# Physical examination

- Abdomen
  - Signs of obstruction
- Rectal
  - Impaction
- Eyes
  - Papilledema

# X-Ray

- Plain film
  - High impaction

# Lab

- When appropriate
  - Dig toxicity
  - Uremia
  - Hypercalcemia

# Medications/metabolic

- Act at CTZ
- Treat with D-2 receptor antagonist
  - Haloperidol
  - Prochlorperazine
  - PromethazineAlso 5 HT3 agent
- Chemo acts at 5 HT3 receptors and NK1

# Gastric stasis

- Causes
  - Medications, ascites, hepatomegaly, ulcers, gastritis
- Treat with agents to increase motility
  - Metochlopramide

# Serosal distention

- Liver metastases
- Treatment
  - Steroids to reduce edema



# Increased intracranial pressure

- Metastases
- Bleeding
- Projectile vomiting
  - Not a sensitive or specific indicator
- Treatment
  - Steroids

# Management of Nausea

- Start with D2 *antagonist*
- *Treat GERD if needed*
- *Add second agent, don't stop first*
- Antihistamine/Anticholinergic
- 5HT3 antagonist (mirtazapine)
- adjuvants

# Route

- Subcutaneous
- Rectal
- Oral
- **NOT Transdermal (gels)**

# Adjuvants

- Steroids(esp with chemo,bowel obstruction,increased ICP)
- Cannabinoids
- Benzodiazepines
- H 2 blockers
- ?IV Fluids

# Non-pharmacologic Rx

- Reduce Odors
- Cool carbonated drinks
- Relaxation techniques

# Bowel Obstruction

- Ovarian Cancer
- Colon Cancer
- Adhesions
- Motility Disorder(pseudo-obstruction)

# Bowel Obstruction

- High mortality with surgery unless early in illness
- Venting gastrostomy

# Bowel Obstruction

- Colic
- Continuous pain
- Nausea and vomiting



# Colic

- Anticholinergic

Scopolamine(acts centrally so decreases nausea but increases side effects)

# Pain

- Opiates

# Nausea and Vomiting

- Realistic goals
- Reduce Secretions
- Anti-emetics

# Reduce Secretions

- Anticholinergics
  - Scopolamine
  - Hycocyamine
- Octreotide

# Anti-emetics

?5 HT3 antagonists in ovarian CA

Antihistamines

Anticholinergics

?Dopamine antagonists

Steroids

# Hiccups

- Gastric Distension
- Diaphragmatic irritation
- Uremia
- Infection
- CNS Tumor

# Treatment

- Pharyngeal Stimulation
- Baclofen 5 mg bid to 20 mg tid
- Phenothiazines
- Haloperidol
- Benzodiazepines