

# Palliative Management of Symptoms: Part 1

## Focus on Respiratory Issues

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# Objectives

- √ Discuss the definition of dyspnea and its prevalence in patients with life-threatening illness
- √ Identify the components of a comprehensive symptom assessment
- √ Discuss both pharmacological and non-pharmacological management of dyspnea

## Mrs. P

- √ 58 year old hispanic female with history of COPD
- √ Newly diagnosed with advanced non-small cell lung cancer status post radiation therapy
- √ Social History: Divorced, 2 adult children, recently unemployed, lives in 3 story walk up

# Dyspnea: Definition

- v "A subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity. The experience is a combination of physiological, social, and environmental factors that potentiate physiological and behavioral response."  
(ATS, 1999)
- v "An uncomfortable sensation or awareness of breathing...patients may describe the feeling of shortness of breath, inability to get enough air or suffocation."  
(Thomas JR & von Gunten CF, 2003)
- v From the Greek  
dys = hard, pnoia = breathing

# Dyspnea: Definition

- v Similar to pain, dyspnea is a subjective symptom...it's intensity known only to the person experiencing it.  
(Quill TE, 2010)
- v Intensity ratings may not correlate with pulmonary dysfunction as evaluated by objective tests such as pulse oximetry, X-rays, or pulmonary function tests  
(Ries AL, 2006; GOLD, 2006)
- v "Breathing is one of the most primal biological drives, like thirst, hunger, and pain. It has greater immediacy than most primal drives—a few minutes without air means death."  
(Gilman & Banzett, 2009)

# Dyspnea: Prevalence

<u>Disease</u>	<u>Prevalence of Dyspnea</u>
COPD	95%
CHF	61%
CVA	37%
ALS	47 – 50%
Dementia	70%
Lung Cancer	90%
Terminal Cancer	45 – 70%
Advanced AIDS	68%

(Ripamonti, 1997; Claessens, 2000; Greenberg, 2000; McCarthy, 1996, Addington-Hall, 1995; Voltz, 1997; Reuben, 1986)

# Dyspnea: Prevalence

- √ Nearly all patients with COPD in the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT) had dyspnea during the last 3 days of their lives

(Lynn, 1997; Claessens, 2000)

- √ 1986 National Hospice Study:
  - 24% of the patients who complained of dyspnea did not have evidence of pulmonary or cardiac impairment.

(Reuben & Mor, 1986)

# Dyspnea: Pathophysiology

- √ Poorly understood and remains elusive
  - Increase in respiratory effort
  - Increase in the proportion of respiratory muscles needed to maintain a normal workload
  - Increase in ventilatory requirements
  - Numerous mediators
    - √ Culture, religion, environment, life experiences and psychological state may amplify symptom intensity

(Bookbinder & McHugh, 2010)

# Dyspnea: Pathophysiology

- v Dyspnea develops when there is a mismatch between central respiratory motor activity and incoming afferent information from receptors in the airways, lungs and chest wall structures
- v The longer the symptom continues, the more likely it is that psychological factors, such as fear, anxiety, depression and frustration, will influence the patient's perception and the intensity of the symptom

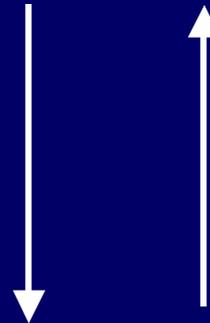
(Bookbinder & McHugh, 2010)

Factors Affecting Perception

- Psychological
- Social
- Cultural/religious
- Environmental

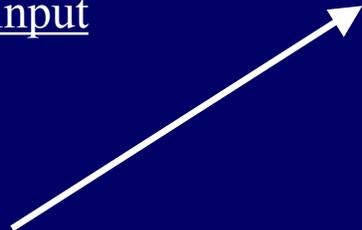


Cerebral Cortex



Brainstem Respiratory Center  
(located in the pons and medulla)

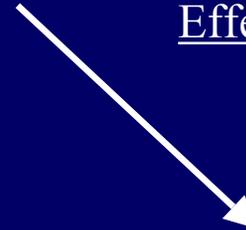
Afferent Sensory Input



Sensors

- Central & peripheral chemoreceptors
- Pulmonary C fiber receptors
- Airway irritant receptors
- Intrapulmonary stretch receptors
- Chest wall & muscle mechanoreceptors
- Proprioceptors in muscles & tendons
- Baroreceptors

Efferent Motor Neuron Output



Effectors

- Muscles of Respiration
- Diaphragm
  - Intercostal muscles
  - Abdominal muscles
  - Accessory muscles



(Adapted from Spector & Klein, 2001)

# Dyspnea: Etiology

- √ Pulmonary
- √ Cardiovascular
- √ Hematological
- √ Metabolic
- √ Neuromuscular
- √ Psychological
- √ Spiritual

(Thomas & von Gunten, 2003; Campbell 2004; Bruera, 1998)

# Dyspnea: Etiology

B ronchospasm

R ales

E ffusions

A irway obstruction

T hick secretions

H emoglobin low

A nxiety

I nterpersonal issues

R eligious concerns

(Storey, 1994; Gleeson & Spencer, 1995)

# Dyspnea: Assessment

- ♣ Patient's self-report is considered the gold standard
  - √ Onset
  - √ Frequency
  - √ Severity
    - Tools: VAS, Borg
  - √ Associated Symptoms
  - √ Exacerbating or Alleviating Factors
  - √ Impact on Mood, ability to perform ADLs, ability to sleep and eat

(Pan, 2003; Indelicato, 2007)

# Dyspnea: Assessment

- √ Meaning of symptom
- √ Patient/caregiver concerns related to specific therapeutic interventions
- √ Past and current therapies (both pharmacological and non-pharmacological) with history of allergies, dosing schedules, history of patient adherence, occurrence of side effects and amount of relief
- √ Patient's goals

(Pan, 2003; Indelicato, 2007)

# Dyspnea: Assessment

- √ Other assessment components:
  - Past medical history
  - Physical exam
  - Diagnostic studies
  - Social history
  - Smoking history
  - Advance directives
  - Psychological assessment
  - Environmental assessment

# Dyspnea: Assessment

## √ Physical Exam

– Based on patient's condition and goals of care

√ Heart

√ Lungs

√ Circulation

√ Psychological state

√ Signs/symptoms of infection

√ Lab data/diagnostic tests

# Symptom Management with a Palliative Focus

## √ General Principles

- Discuss goals of care and treatment options with the patient and caregiver and re-evaluate prn
  - √ Collaborate with team members to develop an appropriate plan of care
  - √ Treatment plan should include the patient's general condition, presence and severity of symptoms, expected survival and place of care
- Treat the underlying cause whenever possible and be consistent with the goals of care
- Attempt to avoid new problems when intervening
- Consider whether a treatment will be worthwhile for a patient and family
- Anticipate and prepare the family/caregiver
  - √ Prevent rather than react to a crisis

(Ahmedzai, 1999; Ferrell, 1998)

# Interventions: Pharmacological

- √ Opioid analgesics
- √ Benzodiazepines
- √ Phenothiazines
- √ Corticosteroids
- √ Bronchodilators
- √ Diuretics
- √ Methylxanthines
- √ Oxygen therapy

# Interventions: Opioid Analgesics

- √ Remain the mainstay of treatment
- √ Significant positive effect in the management of dyspnea in patients with COPD

(Jennings, 2002)

- √ 80-95% significant symptom relief in terminal cancer patients

(Bruera, 2005; Harwood, 1999; Mahler, 1990)

# Interventions: Opioid Analgesics

- √ Mechanism of action is unclear
  - Decrease perception of dyspnea
  - Decrease ventilatory drive
  - Decrease oxygen consumption & improve cardiovascular effects
  - Decrease anxiety

(Spector, Connolly & Carlson, 2007; Kubler, Andry & Davies, 2007)

# Interventions: Opioid Analgesics

- √ Suggested dosages

- √ Opioid tolerant: 25-50% increase in standing dose

- √ Opioid naïve:

- Mild: hydrocodone 5-10 mg po or codeine 30 mg po q 4h

- Severe: morphine sulfate 5mg po, oxycodone 5mg po or hydromorphone 1mg po q 4h

- Parental morphine 2.5-5mg subcutaneously or intravenously q 3-4 hours

(Bruera 1990; Dahlin 2006; Allard 1999)

# Interventions: Opioid Analgesics

- √ Depending on frequency of symptom, pt may benefit from around the clock, long acting formulations
- √ Titration will be based upon reassessment findings
  - Increase dose by 25-100% depending upon patient's response
- √ Patients with renal or hepatic failure as well as the elderly may require dose reductions of up to 50% or more
- √ Side effect management

# Interventions: Opioid Analgesics

## √ Hastening Death?

- Twycross (1994) and Wickham (2002) suggest that early use of morphine or another opioid, rather than hastening death in dyspneic patients, might actually prolong survival by reducing physical and psychological distress and exhaustion.
- 2001 systemic review by Jennings
  - √ 11 studies including blood gases or oxygen saturation after opioid administration
  - √ Only 1 study reported a significant increase in arterial partial pressure of carbon dioxide ( $\text{PaCO}_2$ ), but not above 40mmHg
- The development of clinically significant hypoventilation and respiratory depression from opioids depends on the rate of the change of the dose, the history of previous opioid exposure and possibly the route of administration. (Dudgeon, 2001)

# Interventions: Opioid Analgesics

## √ Nebulized opioids

- Remains controversial

- Rational for use:

- √ Opioid receptors are present on sensory nerve endings in the airways, therefore, if the receptors are interrupted directly, lower doses, with less systemic side effects, would be required to control breathlessness (Belvisi, 1988)

- No conclusive data regarding efficacy

- √ Jennings' 2001 systematic review: no evidence that nebulized opioids were any more effective than nebulized saline

- Patients may develop bronchospasm with morphine

# Intervention: Benzodiazepines

- √ Do not appear to reduce dyspnea directly
  - Reduces anxiety which can accompany dyspnea and contribute to its intensity
  - 2010 Cochrane review
    - √ No evidence for a beneficial effect for the relief of breathlessness in patients with advanced cancer and COPD
    - √ Justify use as a second or third line treatment within a therapeutic trial when other measures have failed  
(Simon, 2010)
  
- √ Metabolized in the liver
  - Short acting drugs (lorazepam) preferred in the elderly or patients with hepatic insufficiency

# Intervention: Benzodiazepines

## √ Suggested dosages:

### – Short acting formulations

- √ Lorazepam: 0.5-1 mg orally every hour until dyspnea is controlled with routine dosing q 4-6h thereafter
- √ Midazolam: 0.5mg IV q 15 minutes until dyspnea is controlled, then maintenance with a continuous subcutaneous or intravenous infusion

### – Long acting formulations

- √ Diazepam: 2-10 mg orally every hour, then routinely q 6-8hours
- √ Clonazepam: 0.25-2mg orally every 12 hours

(Thomas & von Gunten, 2003; Wickham, 2002)

# Interventions: Phenothiazines

- √ May be beneficial in controlling dyspnea and reducing anxiety
- √ Additionally, possess anticholinergic properties
  - Reducing respiratory secretions
  - Controlling nausea
- √ Dosing:
  - Chlorpromazine 10mg po q 4-6hrs and as needed
  - Promethazine 12.5mg po q 4-6hrs and as needed
- √ Side effects
  - Hypotension
  - Extrapyrarnidal effects

(Kuebler, 2007; Woodcock, 1981; McIver, 1994)

# Interventions: Corticosteroids

- √ Highly effective in treating dyspnea r/t
  - Carcinomatous lymphangitis
  - Superior vena cava syndrome
  - Tracheal obstruction
  - Bronchospasm r/t COPD and asthma
- √ Dosing
  - Prednisolone 30-60mg/day
  - Dexamethasone 4-8mg bid to qid
- √ Side effects
  - Muscular weakness, hypertension, fluid retention, hyperglycemia, suppression of immune response

(Ahmedzai, 1999 & LeGrand, 1999)

# Intervention: Bronchodilators

- √ Management of bronchospasm and patients with airflow obstruction
- √ Short acting agents
  - Albuterol sulfate, levalbuterol, pirbuterol acetate
- √ Long acting agents
  - Ipratropium bromide, salmeterol, formoterol, tiotropium, terbutaline sulfate
- √ Albuterol sulfate and ipratropium bromide are preferred
- √ Need for patient education r/t use of delivery devices and correct technique

(Congleton J, 1995; Croxton T, 2003; Manda W, 2003; Dahlin C, 2006; Kuebler K, 2005)

# Interventions: Diuretics

- √ Useful in the treatment of dyspnea r/t CHF or treating edema related to Superior Vena Cava Syndrome
- √ Standard dosing
  - Furosemide: 20-40 mg PO or IV bid

(Wrede-Seaman L, 1999)
- √ Side effects
  - Hypovolemia, electrolyte disturbances
- √ Nebulized furosemide (Shimoyama N, 2002)
  - 20mg qid
  - Decreased dyspnea, alleviation of tachypnea, reduced cough
  - Without an increase in diuresis or side effects
- √ Is the patient experiencing fluid overload?
  - Check IV hydration, PEG/NGT feeding rates

# Intervention: Methylxantines

- √ Aminophylline and Theophylline
  - Dilate the bronchi and improve diaphragmatic contractility
- √ Theophylline dosing
  - Between 200 and 400mg per day to maintain blood level of 8-12 mcg/ml
- √ Side effects
  - Vomiting, hypokalemia, hyperglycemia, tachycardia, dysrhythmias, neuromuscular irritability and seizures  
(Ahmedzai S, 1999; Kuebler K, 2005; Couser JI, 2001 )

# Intervention: Oxygen Therapy

- √ Controversial in the treatment of dyspnea
  - Cochrane review
    - √ Meta-analysis failed to demonstrate a significant improvement of dyspnea at rest when oxygen is compared with air inhalation (Cranston, 2008)
- √ Trial is recommended to ascertain benefit
- √ Humidified via nasal cannula is best tolerated
- √ 1-3l/min with titration up to 6l/min (Bruera E, 2003)

# Interventions: Non-Pharmacological

## √ Environmental

### – Positioning

- √ Usually upright position
- √ Keep compromised lung down in unilateral disease

### – Scheduling of activities

### – Room environment

- √ Cool, low humidity, dust free
- √ Increase air movement with use of fan directed towards patient's face
  - Physical stimulation of the V2 branch of the 5<sup>th</sup> cranial nerve
  - Avoid strong odors, fumes and smoke
- √ Use of durable medical equipment

(Kemp, C 1997; Quill TE, 2010)

# Interventions: Non-Pharmacological

- √ Breathing techniques
  - Pursed lip breathing
    - √ Promotes movement of air out of the lungs and increases airway pressure, keeping the airway open
    - √ Slow breaths decrease respirations, allowing for more efficient and less tiring breathing
    - √ Begin with relaxed neck and shoulders, close your mouth and inhale through your nose, “purse” your lips as if you were going to whistle and exhale slowly over a count of 3.
  - “Blowing bubbles”

(Warren, 2006; Harwood, 1999)

# Interventions: Non-Pharmacological

- √ Relaxation and distraction
  - May assist patient in coping with the emotional component of dyspnea (Renfroe KL, 1988)
  - Corner, 1996
    - √ Nurse practitioner clinic
    - √ Included counseling, breathing retraining, relaxation and coping strategies
    - √ Significant improvement in reports of dyspnea and ability to perform ADLs compared with control group
  - Don't attempt to teach an intervention in the midst of an acute episode of dyspnea

# Interventions: Non-Pharmacological

- √ Acupressure/acupuncture
  - RCTs support use of acupressure and acupuncture to relieve dyspnea in patients with moderate to severe COPD
  - Acupuncture provided marked symptomatic benefit in breathlessness and in respiratory rate in patients with cancer-related breathlessness
  - Acupuncture needles applied to sternal points provided improvements in breathing, ability to relax and a reduction in anxiety

(Jobst K, 1986; Maa SH, 1997; Filshie, 1996 )

## Mrs. P

- √ 58 year old hispanic female with history of COPD
- √ Newly diagnosed with advanced non-small cell lung cancer status post radiation therapy
- √ Social History: Divorced, 2 adult children, devout Catholic

# Palliative Care

“Palliative care is intensive care. It requires the same attention to detail as intensive care. The same careful dose titration, the same continual reassessment.”

(Waller and Caroline, 1996)