Managing Distressing Symptoms Near the End of Life

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DYSPNEA:
“...the most common severe symptom in the last days of life”

Davis C.L. *The therapeutics of dyspnoea* Cancer Surveys 2004
Dyspnea

**Definition**
- subjective
- uncomfortable awareness of breathing

**Impact**
- one of most frightening symptoms
Definition

0 The word dyspnea comes from the Greek "dys-", difficulty + "pnoia", breathing = difficulty breathing.

0 The American Thoracic Society (ATS) defines dyspnea as "a term used to characterize a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity."

0 (American Thoracic Society 1999)
Case Study – Mrs. P

Mrs P is a 72 year old patient with metastatic ovarian cancer.

Mets to pleura, peritoneum, and retroperitoneum

S/P multiple rounds of chemo, surgical resection, multiple therapeutic paracentesis

You are called to see her to discuss hospice care.

The staff tells you she has “lots of pain and SOB”
Mrs. P

On arrival to her hospital room you find:

- VS: 140/90, 108, 34, 98.6
- She is sitting in the chair, bent over wearing a face mask, and working hard to breathe.
- Has trouble answering your questions

Can you help her?

What do you want to know in order to help her?
Mrs. P

Current meds:
- Morphine 2mg IV q 6hrs prn – has had 6mg over past 24hrs
- Oxycodone 10mg PO q 4hrs prn – has had 30mg over past 24hrs
- Lorazepam 0.5mg IV q 6hrs prn anxiety – none given
Epidemiology

0 Found in:

0 50-65% of patients' with advanced cancer
   0 Worsens in last days of life (65% of patients in last 10 days of life)
   0 Cancer patients seen in ER for dyspnea symptom management had median survival of 12 weeks (lung = 4 weeks; breast = 22 weeks; concurrent tachycardia = 2 weeks).

0 > 50% of patients' with end stage COPD, CHF, AIDS, ESRD, end stage neuromuscular diseases
   0 Present for much longer than last days to weeks
Epidemiology

0 Prevalence and intensity increase with lung, pleural and mediastinal involvements in cancer patients (Reuben 1986) (Dudgeon 2001).

0 Low functional status (Karnofsky Performance Scale) is associated with an increase in severity and incidence of dyspnea (Reuben 1986) (Chang 2000) (Mercadante 2000).

0 Dyspnea is often unreported by patients and unnoticed by healthcare professionals (Roberts 1993) (Kutner 2001).
Symptoms Experienced in the last six months of life in patients with end-stage heart failure. European Journal of Cardiovascular Nursing 2003;2;213-17

- Breathlessness 88%
- Pain 75%
- Fatigue 69%
- Anxiety 49%
- Nausea 49%
- Edema 49%
Data from SUPPORT Study

- 1400 pts with advanced CHF
- 92 CHF patients who died during index hospitalization
- 63% severe dyspnea
- 41% severe pain in the 3 days prior to death
- 865 alive at one year, significant incidence of dyspnea and severe pain
Consequences - Overview

- Shortness of breath may be of more consequence to dying patients than even pain (Institute of Medicine 1997) (Weiss 2001) (Portenoy 1994).
- Dyspnea is associated with decreased quality of life and increased bio-psycho-socio-spiritual distress in patients with advanced illness.
Normal Breathing vs. Dyspneic Breathing

0 Breathing - special vital function
0 It is involuntary - but can be partially controlled voluntarily for a short duration.
0 You can control your breath rate for a short spell, but you cannot make your heart beat faster at will.
Pathophysiology

- Respiratory center (medulla and pons)
- Coordinates diaphragm, intercostal and accessory muscles of respiration
- Sensory input from chemoreceptors (pO2, pCO2)
- Mechanoreceptors (stretch, irritation)
Pathophysiology

- Work of breathing
  - Resistance (COPD, obstruction)
  - Weakened muscles (cachexia)

- Chemical
  - Hypoxemia, hypercarbia (small role in cancer)
Dyspnea Mechanisms

- Increased physiological deadspace
  - Impaired gas exchange
    - Ventilatory demands

- Increased airway resistance
  - Abnormal lung and chest wall mechanics
    - Reduced ability to respond to ventilatory needs

- Decreased lung compliance
  - Reduced ability to respond to ventilatory needs

- Hemodynamic, metabolic, & pulmonary parenchymal abnormalities
  - Reduced ability to respond to ventilatory needs

Dyspnea
Ventilatory supply is insufficient to meet ventilatory demand
Effects of Dyspnea On Physical Well Being

- Fatigue and tiredness correlates with intensity of dyspnea (Bruera 2000)
- In patients with symptomatic (advanced) COPD, dyspnea ratings are better predictors of general health status than physiologic measurements (Mahler 1992).
Effects Of Dyspnea On *Emotional Well Being*

- Perceived by patients and family as life threatening and anxiety provoking.
- Patients more likely to be anxious and depressed.
- Anxiety correlates with intensity of dyspnea.
- Depression, anger, helplessness, and loneliness.
- Frequently seek medical care, and are hospitalized more often and are at higher risk for dying in a institutional setting.
Effects of Dyspnea On Social Well Being

- Dyspnea, NOT lung function, correlates highly with disability.
- Dyspnea and decreased functional status prevent patients from activities, and in severe cases, even from eating, bathing and talking.
- Many feel hopeless, with strong sense of isolation and dependence.
Effects Of Dyspnea On *Spiritual* Well Being

Data collected from six home palliative care teams in Ireland indicated that the presence of dyspnea at referral was positively correlated with severity of patient spiritual distress (Edmonds 2000).
Effects of Dyspnea On Survival

- In cancer patients, the presence of dyspnea is a predictor of shorter lengths of survival.
- Lung cancer patients presenting to the ER with dyspnea have much shorter survival than patients with other malignancies.
- In a study of 227 patients with COPD by Nishimura, the 5-year cumulative survival rate was 73%.
- Intensity of dyspnea had a more significant effect on survival than disease severity based on FEV1.
- The physical symptom subscale score of the Memorial Symptom Assessment Scale (MSAS) significantly predicts survival and adds to the prognostic information provided by the Karnofsky Performance Scale and extent of disease (Chang 1998).
Dyspnea—Multiple Causes

- Obstructive airway process
  - tracheal obstruction—intrinsic / extrinsic
  - asthma / COPD
  - aspiration
- Parenchymal / pleural disease
  - diffuse primary or metastatic cancer
  - lymphangitic metastases
  - pneumonia
  - pleural effusion--malignant / other
  - pulmonary drug reaction
  - radiation pneumonitis
Dyspnea - Causes

- Vascular disease
  - pulmonary embolus
  - superior vena cava obstruction
  - pulmonary vascular tumor emboli

- Cardiac disease
  - congestive heart failure
  - pericardial effusion--malignant / other
  - arrhythmia
  - myocardial ischemia
Dyspnea - Causes

- Chest wall/ respiratory muscles
- Primary neurological disease (e.g. ALS)
- Malnutrition
- Other
  - Anxiety
  - Anemia
OK – It’s a No Brainer!
Assessment

- May be described as
  - Shortness of breath
  - A smothering feeling
  - Inability to get enough air
  - Suffocation

- Only reliable measure is patient self-report

- Respiratory rate, pO2, blood gas determinations DO NOT correlate with the feeling of breathlessness
The approach to evaluating dyspnea in terminally ill patients is different from other clinical settings. Almost all of patients in palliative care have known incurable advanced diseases which contribute to many of their symptoms including dyspnea. New or worsening dyspnea warrants looking for the causes with the aim of improving the patient's quality of life. The decision to pursue aggressive workups or interventions should carefully be weighed against the patient’s dying trajectory and the goals of care.
Evaluation - cont

- Intensity
  - In terminally ill patients can be assessed by bedside observation (e.g. unable to talk, or eat uninterruptedly for breath) and by caregiver reports.

- Objective
  - The American Thoracic Society's Functional Dyspnea Scale is useful.
  - Modified Borg Scale
  - Two potentially useful tools in terminally ill patients may be number counting and breath holding (Wilcock 1999) (Taskar 1995).
Functional Dyspnea Scale

0 0 - Not troubled with breathlessness except with strenuous exercise.
0 1 - Troubled by shortness of breath when hurrying on the level or walking up a slight hill.
0 2 - Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level.
0 3 - Stops for breath after walking about 100 meters or after a few minutes on the level.
0 4 - Too breathless to leave the house or breathless when dressing or undressing.

Most terminally ill patients have dyspnea at rest or on minimal exertion (functional scale level 4).

Dyspnea Treatment

Environmental

Psychosocial

Pharmacologic
Palliation to achieve maximal patient comfort is the main goal.

Simple things such as positioning in bed, opening the window, instituting oxygen therapy, and reassurance are often very helpful.

Look for simple, easily correctable problems such as oxygen on/off, kinked oxygen tubing or other cause.

Cool air flowing from a fan directed at the face have provided some benefit.
Oxygen and Dyspnea

- Pulse oximetry not helpful
- Potent symbol of medical care
- Expensive
- Fan may do just as well

Management - Psycho-Social Interventions

- Assess and treat for underlying anxiety and depressive disorders.
- Consider supportive counseling.
- Reassurance
- Non-pharmacological approaches such as cognitive behavior therapy, relaxation therapy, art therapy, massage therapy, guided imagery may be of benefit.
- Consider care-giver support as care-giver stress affects the patient and also influences the patient's site of death (increased emergency room visits and increased hospitalizations).
Management - Rehabilitative Measures

- Pulmonary rehabilitation should be considered in consenting patients who have a life expectancy of months to years.
- Breathing exercises if the patient is capable if the patient is able to cooperate.
- Rehabilitative measures may not be a feasible option in terminally ill patients with a life expectancy of days to weeks.
- Such patients should be encouraged to use a wheelchair and to rest.
- Patients who have not stopped smoking should not be pressured to stop as smoking may be one of the few remaining pleasures.
Management – Pharmacologic Measures

- Treatment of underlying disease process
  - i.e. corticosteroids, diuretics, nebulizers
- Opioids
- Benzodiazepines
Opioids and Dyspnea

- Alleviates the symptoms of breathlessness by acting directly on mu receptors in medulla.
- Decreases the ventilatory response to hypoxia and hypercapnea.
- Due to direct action on the blood vessels, decreases the tone of blood vessels and causes peripheral vasodilatation therefore reducing preload on heart.
  - Again due to vasodilatation, blood shifts from pulmonary to systemic circulation therefore relieving pulmonary congestion & edema.
- Decreases sympathetic drive therefore decreasing cardiac work.
  - Decreases oxygen consumption at rest and exercise.
- Produces an antitussive benefit.
Treatment: Opioids

- Dyspnea not responding to other interventions
- Opioids (oral and parenteral) are the drugs of choice for palliation.
- Often achieved with lower doses than required for palliation of pain.
- Start low and go slow, in opioid naive patients
- Higher doses will be needed for patients on chronic opioids (50% > baseline).
- IV opioids may be indicated for patients with acute dyspnea (e.g. morphine 0.5 to 1 mg IV Q 10-20min until relief or consider low dose continuous infusion).
Opiate Dosing

- Morphine as gold standard
  - Pain:
    - 0.1 mg/kg IV gives pain relief in half to 2/3rds of opiate naïve patients in severe pain
    - ex: 70 kg male = 7 mg IV morphine
  - Dyspnea: start with 1/3rd dose used for pain and titrate to effect
- Tolerance occurs in 72 hours
  - Side effects of respiratory depression & nausea diminish
- Titrate to response (if still in severe dyspnea or pain, increase by 50-100%)
Treatment: Opioids

- Relief not related to respiratory rate
- No ethical or professional barriers
- Small doses
- Central and peripheral action
- Morphine, hydromorphone
Opioids and Fear

- The fear of using opioids to ease distress of terminal dyspnea often leads to inadequate symptom control.
- Health professionals and the public often mistakenly equate use of opioids to ease terminal dyspnea with euthanasia or assisted suicide.
- Ethically, the use of these drugs are appropriate and essential, as long as the intent is to relieve distress, rather than shorten life.
Opiates Do Not Hasten Death...

- Chan et al reported that higher doses of opioids and benzodiazepines used in the withdrawal of life support were not associated with a decreased time from withdrawal of life support to death.

- Other studies found that survival time was unrelated to morphine dosage.

- Of 11 studies that provided information on arterial blood gases or oxygen saturation, only one study reported any significant changes in oxygenation after opioid administration.
  
    - The arterial carbon dioxide partial pressure increased with opioid use but not above a normal value of 40 mm Hg.
No justification for withholding symptomatic treatment to a dying patient out of fear of potential respiratory depression.

Understanding the patient's wishes for end-of-life symptom control and good communication with both family and other caregivers, nursing staff regarding why drugs to relieve distressing dyspnea are administered is essential to avoid misunderstanding.
The Vicious Cycle

Dyspnea → Anxiety → Dyspnea → Anxiety → Dyspnea
Anxiolytics

- Safe in combination with opioids but used as adjunct with opioids to decrease anxiety component of dyspnea
  - Oral Klonopin or Ativan prn
    - 0.25-2 mg po q 2-4 h prn until settled
    - then dose routinely q 6-8 h
  - Last hours with acute severe dyspnea:
    - Lorazepam 1-2 mg SC or IV q 5 to 15 minutes
    - Midazolam 5 mg SC or IV q 5 to 15 minutes
Pearls

- Dyspnea is a very common symptom in patients with advanced illness.
- There is poor correlation between oxygen saturation and the perception of dyspnea.
- Identify reversible causes and treat as appropriate.
- Interventions should be kept in line with goals of care with dyspnea relief as one of the therapeutic goals. Benefits and burdens must be carefully considered.
- Non-pharmacologic approaches are often useful, readily applicable, and inexpensive.
- Morphine is the mainstay of treatment for dyspnea in terminally ill patients.
So, What About Mrs. P?

Approach to terminal dyspnea

- O2, position, fan

- If Respiratory panic, SQ or IV is best

- Morphine 2.5 mg - 10mg, may repeat q20 to 30 minutes until relief, can then put on standing dose with titration by 50%.

- PRN might be best for COPD, CHF while continuous medications for persons with restrictive/infiltrative pattern

- Add an anxiolytic - 0.5-2.0 use PO/PR/Si/IV – scheduled is often necessary
EXCESS SECRETIONS

Respirations may become congested or gurgling, especially when death is imminent
- Caused by a decline in the gag reflex function and reflexive clearing of the oropharynx
- Secretions from the tracheobronchial tree accumulate and the patient is too weak or unable to swallow or expectorate the secretions
- Often the healthcare professionals and the family members are more affected by the noisy breathing than the patient
EXCESS SECRETIONS

Treatments
- Suctioning the patient is not recommended, as it is ineffective and often uncomfortable for the patient
- Turn the patient on his/her side
- Elevate the head of the bed
- Reassure the family of the patient’s comfort
- Educate the family about the etiology of the breathing
- Anticholinergics, such as scopolomine, glycopyrrolate and hyoscyamine can be useful in reducing secretions
## Treatment of Oral Secretions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade name</th>
<th>Route</th>
<th>Starting dose</th>
<th>Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyoscycamine</td>
<td>Scopolamine</td>
<td>Transdermal</td>
<td>1patch</td>
<td>12 hrs</td>
</tr>
<tr>
<td>Atropine</td>
<td>Multiple</td>
<td>Sublingual</td>
<td>1 drop</td>
<td>30 min</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>Robinul</td>
<td>Oral</td>
<td>1 mg</td>
<td>30 min</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>Robinul</td>
<td>SC, IV</td>
<td>.1 mg</td>
<td>30 min</td>
</tr>
</tbody>
</table>
AGITATION / DELIRIUM

Definition - An acute altered level of consciousness associated with:

- Reduced attention and memory
- Perceptual disturbances
- Incoherent speech
- Altered sleep-wake cycles
CAM

Feature 1
Acute onset and fluctuating course

Feature 2
Inattention

Feature 3
Disorganized thinking

Feature 4
Altered consciousness
AGITATION / DELIRIUM

- Hyperactive Delirium
  - Agitated, picking at clothes and bed covers, rambling and loud incoherent speech

- Hypoactive Delirium
  - Quiet, sleepy, little spontaneous movement, soft incoherent speech
Assessment of AGITATION / DELIRIUM

D – drugs
E – eyes and ears
L – low flow states
I – Intracranial
R – retention
I – infection
U – under – hydration/nutrition/sleep
M – metabolic and toxic
Delirium

- Imminent death

- Most patients will exhibit a hypoactive or hyperactive delirium in the days leading up to death.
Delirium--Assessment

Assess the overall goals of care—this will help you decide what if any level of testing is necessary to establish an etiology. If the goal is purely symptom relief until death, and death is felt to be imminent, then no or minimal diagnostics are necessary.
AGITATION / DELIRIUM

Treatment - Non-Drug

- Quiet, peaceful room
- Family member present to relieve anxiety
- Avoid physical restraints
- Assess for unresolved psychological or spiritual issues, unfinished business
- Holistic therapy
AGITATION / DELIRIUM

Treatment with Drug Therapy

- The primary drug class for terminal delirium are the major tranquilizers (e.g. haloperidol)
- Although benzodiazepines are commonly used, they may lead to paradoxical worsening of the delirium
- Dosing is similar to opioids for pain – give enough to reduce the target symptom, there is no maximum dose
  - Starting dose of haloperidol is 1-2 mgs, can be given every hour as needed to reduce symptoms until the patient has stabilized, then converted to a dose given every 6-12 hours
Atypical Antipsychotics

- Risperidone .25-1 mg taken BID to q 6 hrs
  - Caution with renal failure
- Olanzapine 2.5-10 mg taken daily
  - Not in CNS malignancy, hypoactive, over 70
- Quetiapine 12.5 – 50 mg taken bid
  - Dosing 4 pm and hs – most sedating
- Aripiprazole 5-15 mg taken q am
  - Useful for hyperactive – can cause insomnia
Delirium--Treatment

- Benzodiazepines
  - Use cautiously; watch for paradoxical worsening.
  - Additive CNS depressant effects with opioids.
- Barbiturates (Pentobarbital)
  - In rare cases, where escalating doses of major and minor tranquilizers fails to relieve agitation, barbiturates offer an excellent alternative, typically used in the final days of life.
Key Nursing Roles

- Patient advocacy
- Assessment
- Pharm tx
- Non-Rx tx
- Pt/family teaching
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