Dyspnea Assessment and Treatment at the End of Life
Hospice and Palliative Nurses Association (HPNA) Clinical Practice Forum – October 23-24, 2015

Dyspnea Assessment and Treatment at the End of Life
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Disclosures
Margaret Campbell has no real or perceived conflicts of interest that relate to this presentation.

Objectives
- Identify the prevalence of dyspnea
- Describe the most common tools for assessing dyspnea
- Describe the significance of cognitive impairment on dyspnea reporting
- Describe the RDOS
- Describe evidence-based interventions to reduce or eliminate dyspnea
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Definitions

• Dyspnea – a person’s awareness of uncomfortable or distressing breathing that can only be known through the person’s report

• Respiratory distress* – an observed corollary to dyspnea; the physical and emotional distress associated with respiratory dysregulation

* Campbell, Crit Care Clinics, 2004

Physiology/pathophysiology

• Phylogenetically ancient response
  • Developed when species moved from water to air respiration
  • Redundant brain areas respond to an asphyxial threat; survival is threatened
    • Blood gas abnormalities
    • Airflow alterations
    • Stretch receptors
  • Autonomic, cognitive and affective stimulation
    • Awareness of altered breathing; positive or negative
    • Emotional reactivity (suffocation fear)
    • Pulmonary stress behaviors

Prevalence of dyspnea across terminal Illnesses
(Solano et al. 2006)

<table>
<thead>
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<th>Diagnosis</th>
<th>Prevalence %</th>
<th># of studies</th>
<th>N</th>
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<td>10-70</td>
<td>20</td>
<td>10,029</td>
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<td>60-88</td>
<td>6</td>
<td>948</td>
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<td>90-95</td>
<td>4</td>
<td>372</td>
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<td>Renal disease</td>
<td>11-62</td>
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Trajectory of dyspnea by diagnosis

- Consecutive cohort study
  - n = 5862
  - Numeric Rating Scale measured at every clinical encounter
  - Average 86 days until death
  - Diagnoses
    - Lung cancer
    - Metastasis to lung
    - Heart failure
    - COPD

Results

- Dyspnea measured at 3 time points before death in days
  - 60-53
  - 30-23
  - 7-0
- Dyspnea was highest in non-cancer at all time points
- Dyspnea increased significantly in cancer

Patient (in)ability to self-report dyspnea when near death

- 89 patients near death from one or more of
  - Lung cancer
  - COPD
  - CHF
  - Pneumonia
- Asked “Are you short of breath?”
- Asked to point to a vertical VAS

Campbell, et al., J Pall Med, 2009
Results

• 48 of 89 (54%) could not respond to query
• 21 of 41 (51%) could not use the VAS
• Inability to self-report associated with
  o Consciousness (p<.01)
  o Cognition (p<.01)
  o Nearness to death (p<.01)
  o Hypoxemia (p=.07)

Cognitive skills necessary for symptom reporting

• Able to interpret sensory stimuli
• Able to pay attention to instructions and concentrate to form a report
• Able to communicate
• Able to remember previous report

Common dyspnea assessment tools

• Yes or No query: Are you short of breath?
• Numeric rating system – 0-10
• Visual analog scale – vertical or horizontal line anchored from 0-10 or 0-100 mm
• Modified Borg – category-ratio scale using descriptive terms to anchor responses to dyspnea after exercise
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Vertical Dyspnea Visual Analog Scale

A review of quality of dyspnea assessment

• Most instruments are one-dimensional
  • Quantify dyspnea at a particular moment
  • Numeric rating scale*
  • Visual analog scale
  • Modified Borg dyspnea scale
  • Quick and easy to administer
  • Not comprehensive
  • Require cognitive skills

  * Most suitable for palliative care

Mularski, Campbell, et al., Am J Respir Crit Care Med, 2010

Measuring respiratory distress in patients with cognitive impairment

• Gold standard instruments
  • Numeric rating
  • Dyspnea visual analog scale
  • Modified Borg

• Observation tools
  • Respiratory Distress Observation Scale
**Respiratory Distress Observation Scale**

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<th>0 points</th>
<th>1 point</th>
<th>2 points</th>
<th>Total</th>
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<td>Heart rate per minute</td>
<td>&lt;90 beats</td>
<td>90-109 beats</td>
<td>≥110 beats</td>
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<td>Respiratory rate per minute</td>
<td>11-15 breaths</td>
<td>16-30 breaths</td>
<td>&gt;30 breaths</td>
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<td>Restlessness: non-purposeful movements</td>
<td>None</td>
<td>Occasional, slight movements</td>
<td>Frequent movements</td>
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<tr>
<td>Accessory muscle use rise in clavicle during inspiration</td>
<td>None</td>
<td>Slight rise</td>
<td>Pronounced rise</td>
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<td>Paradoxical breathing pattern</td>
<td>None</td>
<td>Present</td>
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<td></td>
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<tr>
<td>Grunting at end-expiration</td>
<td>None</td>
<td>Present</td>
<td></td>
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<tr>
<td>Nasal flaring involuntary movement of nares</td>
<td>None</td>
<td>Present</td>
<td></td>
<td></td>
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<tr>
<td>Look of fear</td>
<td>None</td>
<td>Eyes wide open, facial muscles tense, brow furrowed, mouth open</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Reliability and Validity**

- Inter-rater reliability (r=1.0)\(^1\)
- Scale reliability (α = .78, .64, .85)
- Construct validity
  - RDOS - SpO₂
    - (r = .305, p < .01, n = 85)\(^2\)
    - (r = .688, p < .01, n = 210)\(^3\)
- Convergent validity
  - RDOS - patient report
    - (r = .740, p < .01, n = 210)\(^3\)
    - (r = .423, p < .01, n = 136)\(^2\)
- Discriminant validity
  - RDOS - pain (F\(_{2,207} = 119.84, p < .02\))\(^2\)
- Sensitive to change with treatment\(^2\)
- Intensity cut-points
  - RDOS 0-2 = none,\(^3\) ≥3 = any,\(^4\) 4-6 = mild-moderate,\(^4\) ≥7 = severe\(^4\)

4. Campbell, et al., unpublished
Assessment summary

1. Self-report should be elicited whenever possible using the simplest measure
   1. Yes or No response to query
   2. NRS or VAS
2. RDOS when patient is unable to self-report
3. Proxy opinion
   1. Clinicians
   2. Patient's family caregiver

Dyspnea Treatment

• Disease-modifying treatments when possible (consistent with goals of care)
  o Paracentesis, thoracentesis, diuresis
  o Antibiotics
  o Mechanical ventilation, invasive or non-invasive

• Maintain supportive treatments
  o Bronchodilators, anti-cholinergics
  o Inotropes, diuretics

Medications to treat dyspnea

• Opioids – immediate release
  o Morphine – all routes except nebulized
  o Fentanyl – all routes except nebulized and transmucosal

• Opioids – sustained release (preliminary evidence)
  o Morphine

• Benzodiazepines - adjunct
Opioids

• Potentμ agonist
• Routes
  - Oral, immediate and sustained release
  - Parenteral
  - Transdermal, transmucosal
• Indicated and approved for the treatment of severe pain
• Less often employed for dyspnea

Mechanisms of action in dyspnea

• Reduced O₂ and CO₂ effect on ventilation (ATS, Am J Resp Crit Care Med, 2012; Banzett et al., Am J Resp Crit Care Med, 2011)
  - Opioids trick the brain into not recognizing hypoxemia/hypercarbia


• Endogenous release during exertion in COPD (Mahler, et al., Europ Resp J, 2009; Mahler, et al., Chest, 2013)

Dyspnea: Opioids

• A systematic review of the use of opioids in the management of dyspnea (Jennings et al. Thorax, 2002)
  - 18 studies reviewed: double-blind, randomized, placebo-controlled trials
    • COPD = 14, ILD = 1, CHF = 1, Cancer = 2
  - Statistically positive effect of opioids by oral and parenteral routes
    • No statistically significant effect when nebulized
    • Insufficient evidence to rule out nebulized
  - All small, underpowered studies
### Doses
- High variability across studies
- Optimal dosing has not been established
  - Once daily sustained release (10mg titrated up to 30mg) is safe and effective for those who respond (Currow et al., J Pain Symptom Manage, 2012; Currow et al., J Pall Med, 2013)
- More dose studies are needed
- Recommended approach
  - Begin with immediate release formulation
  - 5mg (po) or 2 mg (IV)
  - Re-administer q30 (po) or q10 (IV) until relief
  - Titrate at 50-100% of initial dose until relief
  - Calculate total dose and prescribe/recommend accordingly
  - Prescribe/recommend prn when dyspnea is episodic

### Adverse effects in order of frequency
- Constipation – never abates, most common
- Itching – not an allergic response
- Nausea/vomiting – generally abates in 3 days
- Sedation
- Respiratory depression – not seen in any of the 18 studies in Cochrane review (Jennings, 2002); not seen in safety studies (Currow, 2011; 2013)

### Benzodiazepines and dyspnea
- Sedatives
- Indicated for sleep disturbance and anxiety
- Cochrane review (Simon et al., 2010)
  - 7 studies (RCT and CCT)
  - 200 patients with advanced cancer and COPD
  - No significant effect for relief
  - No significant effect as breakthrough
Midazolam as adjunct

  - Group 1 = ATC morphine with midazolam rescue
  - Group 2 = ATC midazolam with morphine rescue
  - Group 3 = ATC morphine and midazolam with morphine rescue
- Group 3 had best overall results
  - Does the benzodiazepine minimize fear associated with dyspnea?

Positioning

- Tripod positioning increases the space for air in the chest
- Tripod can be accomplished sitting in a chair, on the side of a bed, or in the bed, propped with pillows

Increase the flow of air

- Open a window, weather permitting
- Position a fan nearby blowing toward the face
- Use a bedside or small hand-held fan blowing toward the face

Bausewein, et al., BMC Palliative Care, 2010
Galbraith, et al., J Pain Symptom Management, 2010
**Oxygen benefits**

- Correct hypoxemia
- Reduce dyspnea
- Prolong life

**COPD and long-term oxygen**

- >15 hours/day
- Increased survival of patients with resting dyspnea
- $\text{PaO}_2 < 55 \text{ mm Hg}$
- $\text{SaO}_2 < 88$

Global Initiative for Chronic Obstructive Lung Disease, 2013

**Oxygen burdens**

- Decreased mobility
- Nasal drying
  - Nosebleed
- Feeling of suffocation
- Prolongs dying
  - Extends caregiver days
  - Increases health care costs
- Flammable
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Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnea: a double-blind, randomized controlled trial (Abernethy et al., 2010)

- 239 terminally ill patients with refractory dyspnea
  - Outpatient clinics in Australia, US, and UK
  - Life-limiting illness
  - Refractory dyspnea
  - PaO2 > 55 mmHg
- Nasal oxygen or medical air at 2l/min for 15 hours/day x 7 days
- NRS q morning and evening

Results

- No differences between oxygen and medical air
  - Clinically insignificant decrease in dyspnea
  - No differences in side effects
    - Drowsiness
    - Nasal irritation
    - Nosebleed

Oxygen is non-beneficial for most patients who are near death (Campbell, et al. J Pain Symptom Manage, 2013)

- Repeated measures, double – blinded, randomized cross-over, using the patient as his/her own control
- Patients who were near death and at risk of experiencing dyspnea
  - n = 32 (effect size 0.25, significance 0.05, power 0.80)
  - Near death – Palliative Performance Scale ≤ 30
- At risk for dyspnea but in no distress
  - COPD
  - Heart failure
  - Lung cancer
  - Pneumonia
Results

- 27 (84%) had oxygen flowing at baseline
  - Reason for oxygen not measured
- 29/32 (91%) patients experienced no distress during the protocol
  - 3 patients were restored to baseline oxygen
- 1 patient died during the protocol

Oxygen Conclusions

- Declining oxygen saturation is naturally occurring and expected
- Declining oxygen saturation may predict but does not signify respiratory distress
- The routine application of oxygen to most patients who are near death is not supported
- An n of 1 trial of oxygen is appropriate in the face of respiratory distress

Summary

- Objective assessment must be done to guide treatment
  - Yes or No query is simplest measure
  - NRS or VAS useful for trending
  - RDOS useful in cognitive impairment
- Opioids are the only evidence-based effective treatment for refractory dyspnea
  - Parenteral or oral routes
  - Morphine or fentanyl
- Nebulized opioids require further study
- Benzodiazepines require further study
- Oxygen is useful in awake patients with hypoxemia
  - Oxygen is not useful when death is imminent
**Case study**

- John is a 69 year old with a 100 pack/year smoking history, lung cancer, and COPD.
  - He has been on home oxygen for several years at 3l/min for most of the day/night.
  - He is restricted to the first floor of his home; too dyspneic to walk upstairs.
- Recent weight loss, decreased activity, and worsening dyspnea are the hallmarks of transition to the terminal stage.
- Spends most of the day/night in a recliner with a chair-side commode and urinal.
- Reports dyspnea at rest; 8/10 on a 0-10 scale.

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**Palliative Performance Scale**

<table>
<thead>
<tr>
<th>Item</th>
<th>Measures</th>
<th>Subitems</th>
<th>Score</th>
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<tr>
<td>Some activity</td>
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<td>11.0</td>
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<tr>
<td>Full time work</td>
<td>1.5</td>
<td>11.5</td>
<td></td>
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<tr>
<td>Ambulation</td>
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<tr>
<td>Reclining</td>
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<tr>
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<tr>
<td>Mild</td>
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</tr>
<tr>
<td>Moderate</td>
<td>1.0</td>
<td>11.0</td>
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<td>Severe</td>
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*Anderson, et al., J Pall Care, 1996*

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**Palliative Performance Scale**

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<th>Mean</th>
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<td>61.0</td>
<td>9.3</td>
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</table>

*Weng, et al., J Pain Symptom Manage, 2009*
**Refractory dyspnea treatment**

- John is optimized with his bronchodilator/anticholinergic regimen
- No evidence on physical exam for obstruction or pleural effusion or pulmonary edema
- Optimal position is upright which he has achieved by forgoing his bed for the recliner
- Balance rest with activity – he is already minimally active
- Oxygen at 3l/min produces an SpO₂ of 89-90%

**Global dyspnea treatment**

- Morphine immediate release 20mg/ml po
  - Begin with 5 mg
  - Wait 15-20 minutes for peak effect
  - Repeat with 5 mg every 15-20 minutes until relief
  - Calculate total dose and prescribe q4 hours
  - Use 5 mg dose for breakthrough dyspnea q1 hour
- Lorazepam 0.5mg po q6 hours prn anxiety
- Continue oxygen at 3l/min
- Add bowel regimen

**Case study continues**

- A week later
  - John is hypersomnolent, rouses briefly
  - Unable to give a dyspnea self-report
  - Wife reports infrequent use of breakthrough morphine, no use of lorazepam
  - Not eating, occasional sips of water
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Palliative Performance Scale

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<td>No</td>
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<td>Full</td>
</tr>
</tbody>
</table>

Global dyspnea treatment – near death

- Change MDI to aerosol delivery
- Change morphine to prn, teach wife buccal administration
- Evaluate need for oxygen
  - Turn oxygen off
  - Stand by to observe for respiratory distress
  - Resume oxygen if respiratory distress is noted
- Discontinue oral medications
Global dyspnea treatment – imminent death

• Three days later
  • John is unresponsive
  • Respirations are shallow, slow with periods of apnea
  • No intake
  • PPS = 10, median survival = 3 days
• Discontinue aerosol treatments
• Discontinue oxygen
• Continue morphine prn buccal space