Ethical Issues at EOL: Deciding When to Use Oxygen and Antibiotics
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Objectives

- Understand the evidence based use of supplemental oxygen at the end of life
- Apply the evidence in an ethical framework
- Identify the ethical framework of providing antibiotics at the EOL
- Develop new tools to discuss the use of oxygen and antibiotics with patients and families

To Palliate

Oxford Dictionary Online:
“Make (a disease or its symptoms) less severe or unpleasant without removing the cause”

Dyspnea

“Dyspnea is a complex symptom arising from the interaction and dependence of various signals and processes including an individual’s reactions and perceptions”, Can Thor Soc, 2011

Schematic representation of afferent pathways from respiratory muscle mechanoreceptors to the CNS. DRG = dorsal respiratory group; VRG = ventral respiratory group.
Mechanisms of Dyspnea

- “...the weight of current evidence suggests that hypercapnia is dyspnogenic in normal subjects and is dependent on the level of reflex stimulation of the respiratory centers; the source of the dyspnogenic signal, whether from the peripheral chemoreceptors, vagal C fibers, or central chemoreceptors, is unclear. Whether hypoxia is dyspnogenic per se remains uncertain.”

- Burki NK and Lee L-Y. Mechanisms of Dyspnea, Chest, 2010

Evaluation

- Dyspnea is a symptom; self-report is critical
  - \( \uparrow \text{RR} \neq \text{dyspnea} \)
  - \( \downarrow \text{SpO}_2 \neq \text{dyspnea} \)
- Dyspnea arises from varied mechanisms; need to identify the cause to alleviate the distress; N of 1 trials
  - In CHF, from fluid overload, pulmonary hypertension, deconditioning, therefore \( \text{rx} = \text{diuresis, pulmonary vasodilation, BiPAP} @ \text{night} \) can help too; ? High flow O2
  - In COPD, from inadequate ventilation due to loss of lung tissue, bronchospasm, airway obstruction, therefore treat with bronchodilators, anti-inflammatory, opioids for non-specific alleviation

COPD - Emphysema & Bronchitis

Benefits and Harms of Oxygen Treatment

Benefits
- Alleviate HYPOXIA, (sometimes)
- Increase mentation
- Reduce fatigue
- Increase exercise tolerance

Harms
- Dry mucosa, nose bleeds
- Discomfort from mask/plastic flanges
- Risk of tripping
- Flammable
- Bulky
- Socially isolating
- Noisy

When is Oxygen Indicated for Dyspnea?

ONLY in 2 conditions:
- Patient is hypoxemic \( \text{O}_2 \text{sat} < 90, \text{PaO}_2 < 55 \text{mmHg} \)
- Patient’s symptoms are relieved by oxygen

ASSESSMENT OF RESPONSE IS CRITICAL!!!
So why do so many patients “feel better” with oxygen?
Relief of dyspnea during the previous 24 h: Room Air v Oxygen. Pts reported their “relief of breathlessness over the previous 24 hrs” using 0-10 scale. Baseline is day −1 (dotted line).


What Works to Relieve Dyspnea? Opioids (+/-)

- Opioids, both endogenous and exogenous, may relieve dyspnea by altering central processing of efferent and afferent sensory information.

- Postulated mechanisms: reduced minute ventilation, increased ventilatory efficiency, reduced ventilatory responses to $pCO_2$ and $pO_2$, reduced bronchoconstriction, increased pulmonary vasodilation and modulation of central processing.

- No proven benefit to nebulized opioids


What Else Is Proven to Alleviate Dyspnea?

- Synchronized Chest Wall Vibration
- Neuromuscular Electrical Stimulation
- Management of Depression & Anxiety
- Heliox in COPD
- Inhaled bronchodilators (COPD)
- Inhaled Lasix
- Pursed-lip breathing
- Conservation of energy

How Do We Talk About This?

- “Mr. Kaplan, our goal is for you to feel better. In medicine, everything we do has both good and bad aspects, and I want to be sure that the balance is toward helping. I want to review all your treatments with you and together figure out what helps and what doesn’t.”

- “Now that we have reviewed your use of breathing treatments and medicines, let’s see about the oxygen.”
How Do We Talk About This?

- “What is problematic about using oxygen for you?”
- Blowing in my nose, nose bleeds
- Noise
- Tripping on cord
- Not as mobile
- Can’t smoke
- “What good things do you think the oxygen does for you?”
- Feel better
- “Why do you think that?”

- “If we found out that air or a fan made you just as comfortable as the oxygen, would you like to get rid of the ________ (problem(s) patient identified)?”
- “Right now, what is your level of breathing discomfort (1-10)? Your breathing rate is 30 and oxygen level is 92. First I want to put this fan in from of you and then I’m going to make some changes on your oxygen and we’ll wait 10 minutes and check these things again. Is that OK?”

Antibiotics: When and Why in Hospice Care?

- Decreased immune function
- Immobility
- Catheters
- Weak cough
- Urinary retention
- Aspiration
- Tumor fever
- High levels of IL 1, IL 6, TNF, Interferon alpha
- Medication induced fever
- DVT/PE
- Infection

Which Hospice Patients Get ABX in Last Week?

- Younger
- Longer time on service
- COPD (34%) > CA > Dementia > CVD > Debility (16%)
- Indwelling Foley
- Documented reasons:
  - Pneumonia 7%; UTI 4%; skin/ wounds 3%
Evidence of Palliation w/ Abx

Reinbolt RE, et al. JPSM 2005

Prospective 2 yr study, Advanced Ca pts, Home hospice, 1598 patients, 623 pts (39%) developed 685 infections, 633 were treated w/ abx

Complete or partial resolution of sx:

- UTI 79%
- Respiratory 43%
- Oral cavity 46%
- Skin/Soft tissue 41%
- Bacteremia/sepsis 0%

Evidence of Palliation w/ Abx

Thia V, et al. JPSM 2012

- 441 pts w CA, inpatient PC
- 40% developed a “clinical” or documented infection; 90% abx
  - Respiratory 43.7%
  - UTI 28.2%
  - Intrabdominal 16.5%
- When infections occurred in last 2-4 weeks, abx resolved sx < 50% of the time
- Survival in sepsis: 15 day vs 42 days, untreated < 1 d
- Survival in organ specific infection also improved with abx
- Survival with IV Abx was 6 days longer than po

Evidence of Life Prolongation with Antibiotics

- None in 3 studies
  - Reinbolt, JPSM 2005; White, JPSM 2003; Fabiszewski 1990
- Controversial in a 2, in which the authors felt that the longer survival was related to a higher proportion of long stay patients having an infection that was treated rather than the antibiotics prolonging survival
  - Vitetta, JPSM 2000; Chen, Support Care Cancer 2002
- Increased survival with sepsis in one study, IV>PO
  - Thia, JPSM 2012

How to Decide About ABX

- Beneficence: Does the treatment make the PATIENT feel better? Otherwise achieve patient’s goals?
  - Family?
  - Healthcare provider?
- Nonmaleficence: Does the treatment harm the patient?
- Justice: Does the treatment disproportionately harm others?

The Good and Bad of Abx

Good

- Lessen sx +/-
- Prolong life(?)

Bad

- Create sx
  - Diarrhea, associated caregiver distress, wound risk
- Thrush
- Nausea, anorexia
- Allergic reactions
- Prolong life (?)
- Cost (personal/ societal
- Pill burden
- Drug resistance

ML, Demented, Adv Dir, Hospice Patient

- 83 year old widow, clear advance directive stating not to prolong her time in end stage dementia but no specific discussion of antibiotics
- Develops pneumonia (fever, cough, accessory muscle use), no surrogate available
- How do you discuss with the surrogate?
- How would the discussion be different if there were no advance directive?
ML, Demented, Adv Dir, Hospice Patient

- 83 year old widow, clear advance directive stating not to prolong her time in end stage dementia
- Develops a wound infection. Next steps?
- Develops UTI. Next steps?
  - Do antibiotics reduce pain immediately?
  - Is there a medication that does relieve pain quickly in UTI?
- Develops sepsis. Next steps?
  - What is it like to die of sepsis?

PB, Demented, Adv Dir, Hospice Patient

- 83 year old widower, clear advance directive stating every moment of life is precious, regardless of quality
- Develops a wound infection. Next steps?
- Develops UTI. Next steps?
- Develops urosepsis. Next steps?

What Do We Need to Discuss in ACP re: Abx?

“Terminally ill folks are at higher risk of developing an infection than other people. If that were to happen to you, we will want to honor your priorities. Here are a few facts to help you decide whether or not to use antibiotics:

Antibiotics do not relieve symptoms right away and in more than half the cases, other than urinary tract infections, do not relieve them at all. Nevertheless, we have many other ways of increasing your comfort and we can give you both kinds of treatment at the same time.

There is no clear evidence that antibiotics will prolong your life.
Antibiotics can have side effects, as I imagine you have experienced during your life. These include diarrhea, thrush, nausea, poor appetite and, sometimes, allergic reactions.
There is no hurry to make any decision and you can always change your mind. I just wanted to bring this up so you can make informed choices if the situation arises.

Summary

- Oxygen is only indicated in the case of hypoxia and dyspnea that is relieved by oxygen; it is NOT a universal “comfort measure”
- Treatments tailored to the underlying pathophysiology, treatment of anxiety and depression (when present), opioids and nonpharmacologic measures are often effective
- The use of antibiotics should be thoughtful and be based on the patient’s goals of care and the individualized benefit burden balance. Overuse is also a societal burden.
- UTIs should probably always be treated. Pyridium is underutilized

Mechanisms of Dyspnea

- “Afferent information from reflex stimulation of the peripheral sensors (chemoreceptors and/or vagal C fibers) is processed centrally in the limbic system and sensorimotor cortex and results in increased neural output to the respiratory muscles. A perturbation in the ventilatory response due to weakness, paralysis, or increased mechanical load generates afferent information from vagal receptors in the lungs (and possibly mechanoreceptors in the respiratory muscles) to the sensorimotor cortex and results in the sensation of dyspnea.”
- Burki NK and Lee L-Y. Mechanisms of Dyspnea, Chest, 2010
fMRI showing cerebral activation during experience severe air hunger in healthy subjects. Strongest activation in anterior insula, (blue crosshairs), as shown in a number of studies. Other activation in anterior insula, anterior cingulate, supplementary motor area, prefrontal cortex, and cerebellum. Not visible in this figure, but reported in the same study was activation of the amygdala. Most of these regions fall in the category of limbic/paralimbic, and overlap with activation seen during pain, thirst, fear, and hunger.

Published in: Mark B. Parshall; Richard M. Schwartzstein; Lewis Adams; Robert B. Barcroft; Harold L. Manning; Jean Bourbeau; Peter M. Calverley; Audrey G. Gill; Andrew Harver; Suzanne C. Lareau; Donald A. Mahler; Paula M. Meek; Denis E. O'Donnell. Am J Respir Crit Care Med. 2012, 185, 435-452.