PALLIATIVE PEARLS
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Palliative Management of Bacterial Infections
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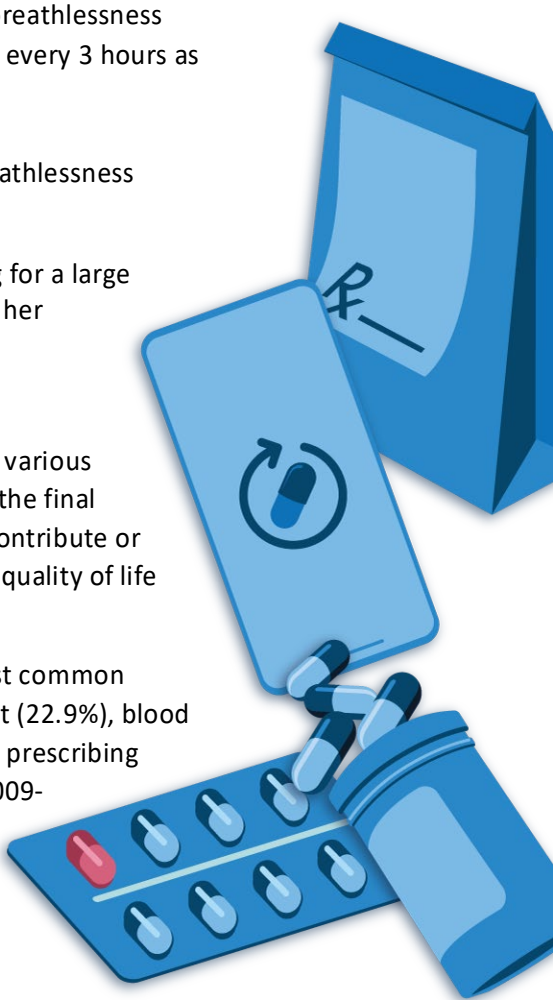
PATIENT CASE

KC is a 53- year-old female admitted to hospice last week with a primary diagnosis of congestive heart failure. Her co-morbidities include hyperlipidemia, hypertension, coronary artery disease and diabetes. She has no known drug allergies and currently resides with her daughter.

MEDICATIONS

- Advair Diskus 250/50mcg; inhale 1 puff twice daily
- Albuterol HFA inhaler; inhale 2 puffs every 4 hours as needed for breathlessness
- Morphine 20mg/ml oral concentrate; take 0.25ml (5mg) by mouth every 3 hours as needed for pain or breathlessness
- Dexamethasone 4mg; take 1 tablet by mouth twice daily
- Oxygen; inhale 2 liters per min via nasal cannula as needed for breathlessness
- Senna 8.6mg; take 2 tablets by mouth twice daily

KC's daughter reports to the hospice that her mom is feverish and sleeping for a large portion of the day and night with minimal oral intake and refusing most of her routine medications. How would you approach this case?



INSOMNIA OVERVIEW[1-4]

Research suggests that almost 50% of hospice patients may be affected by various infections during their length of stay with 25% receiving antibiotics during the final weeks of life.[1,2] These statistics beg the question, does antibiotic therapy contribute or deviate from the goals of hospice care that encompass comfort, improved quality of life and a dignified, peaceful passing?

In a retrospective study conducted in patients enrolled in hospice, the most common bacterial infection sites were the urinary tract (42.5%), the respiratory tract (22.9%), blood (12.5%), skin and subcutaneous tissues (12.5%) and eyes (10%).[3] Antibiotic prescribing was studied in patients discharged to hospice care over a 3-year period (2009-2011). In this study, antibiotics were most frequently prescribed for pneumonia (19.5%), urinary tract (18.9%), and gastrointestinal tract infections (17%).[4] A review of the literature on antibiotic use in this patient population revealed widespread use with mixed results:

- In a 2013 systematic review, symptom response after antibiotic therapy was studied among hospice patients. Urinary tract infections displayed greater symptom improvement (60-92%) compared to respiratory tract infections (0-53%). Moreover, patients with bacteremia had no observed symptom improvement.[1]
- A 2003 prospective study in patients with advanced cancer (prognosis was weeks to months), did not show any difference in survival prolongation between those who chose treatment with antibiotics compared to those who did not. The authors concluded that if prognosis is expected to be months to a year, antibiotics may prolong survival.[1]
- In a 2001 study, hospice patients could select either full antibiotic use, antibiotic use for symptomatic treatment only or no antibiotic use. Of the patients who chose antibiotic therapy, the majority with urinary tract infections improved, while fewer than half responded to infection treatment of the respiratory tract, mouth/pharynx, skin/subcutaneous tissues, or blood. The authors concluded, *"Patient survival in this study was not affected by the presence of infection or the use of antibiotics."*[5]
- From 2009-2011, 149 patients who received an outpatient prescription for an antibiotic on discharge from hospital to hospice care were studied to determine appropriateness of therapy. Only 9.7% of prescriptions specifically indicated that the antibiotic was prescribed for palliative reasons. Nearly 80% were continuing a course started in the hospital. In addition, only 50% of patients had an infection that was verified by culture data before discharge.[4]

Prognosis and patient/caregiver goals of care are major considerations when making decisions on antibiotic therapy. Discussion regarding the approach to treating infection is recommended early in the hospice length of stay, in preparation of future occurrences. It is recommended that both clinicians and patients/caregivers evaluate the risks and benefits of initiating antibiotic therapy closely, coming to a shared decision on therapy.[2]

A combination of nonpharmacologic and targeted symptom management therapies are reviewed below. Antibiotic therapies will not be covered here however useful articles on infectious diseases may be perused by accessing Medscape Drugs and Diseases: Infectious Diseases.[6]

BENEFITS OF ANTIBIOTIC THERAPY[2]

- Potential prolonged survival
- Symptom relief
- Psychological comfort for the patient/caregiver in knowing that the event is being addressed

RISKS OF ANTIBIOTIC THERAPY[2]

- Adverse drug events[7]
  - e.g., *Clostridioides (*formerly *Clostridium) difficile* infection (CDI) risk increases 7-10 times
  - Allergic reaction
  - Liver or kidney damage
  - Abnormal heart rhythms

- Drug interactions (with special consideration to pre-existing polypharmacy in this population)[7]
    - Ciprofloxacin used with theophylline may lead to theophylline toxicity
    - Ciprofloxacin or Bactrim® used with warfarin may increase INR levels
    - Macrolides (excluding azithromycin) used with warfarin may increase INR levels
    - Nitrofurantoin use in patients with creatinine clearance (CrCl) < 30ml/min or severe renal disease may lead to toxicity
    - Bactrim® used with an ACE inhibitor (e.g., lisinopril) or angiotensin receptor blocker (e.g., losartan) plus renal insufficiency may lead to hyperkalemia
- Antibiotic administered unnecessarily for a viral infection
- Multiple antibiotic therapy may lead to development of multi-drug resistant organisms
- Comprehensive assessment of an infection may be invasive (e.g., blood draws, chest x-rays)
- Unnecessary costs
- Parenteral route of administration (e.g., IM, IV) may contribute to significant discomfort
- Increased pill burden/duration of therapy that is not conducive with the patient's goals of care

MANAGEMENT

Non-pharmacological therapy[8]

- **Fever**
    - Elevated temperature (> 99.9^{o}F) may be associated with urinary tract, respiratory or systemic infection. In addition, patients suffering from a urinary tract infection (UTI), may present with chills or rigors, significant fatigue, or malaise beyond baseline.[9] Respiratory illness/pneumonia may also be characterized by fever, productive cough, respiratory distress, and sepsis.[10]
    - Managing fever may include cold baths, encouragement of clear liquid intake to prevent dehydration, maintaining a comfortable room temperature, and wearing of lightweight clothing.[11]
- **UTI symptoms**
    - Remove foley catheter if possible, increase water intake, and the use of cranberry juice and vitamin C supplementation.
- **Dyspnea and/or cough**
    - Shortness of breath, tachypnea and/or cough (with or without sputum production) may be symptoms of pneumonia or sepsis.[9]
    - Use fans, open windows if safe, breathing exercises, head and body positioning, limit strenuous activity, minimize stress, and employ relaxation techniques.
    - For cough, use chest physiotherapy, elevate head of bed, use a humidifier, water hydration, and smoking cessation.
- **Skin infections**
    - Reduce underlying edema by elevating affected area
    - Support stockings may reduce ankle swelling
    - Keep skin hydrated with emollients to prevent dryness and cracking
    - Odors in the room can be managed by using kitty litter or activated charcoal on a cookie tray

Pharmacotherapy[8]

- Fever: Acetaminophen, NSAIDs (e.g., ibuprofen)
- Urinary Pain: Phenazopyridine
- Urinary Spasms: Oxybutynin
- Dyspnea: Opioids, albuterol
- Skin Infections: Topical anti-infectives (bacitracin, triple antibiotic ointment, metronidazole tabs (crushed), metronidazole 1% paste or 5% powder, silver sulfadiazine 1% cream)
- Cough: Antitussives (e.g., guaifenesin, guaifenesin with dextromethorphan, guaifenesin with codeine)

CASE ASSESSMENT & RECOMMENDATIONS

The source of fever in KC may be a UTI or a respiratory infection. The hospice team and family discussed her goals of care, including the benefits and risk of antibiotic therapy. Multiple hospitalizations due to chronic health conditions had left KC weary and she expressly voiced her desire to come home and pass away peacefully. Considering KC's unresponsive status and limited routes of medication administration (sublingual, rectal, parenteral), her daughter recognized initiating antibiotic therapy would not be in line with her mother's goals.

Recommendation

Acetaminophen suppository 650mg, insert 1 suppository rectally every 6 hours as needed for fever.

SUMMARY

When goals include comfort only and not life prolongation, it is often best to forego antibiotic therapy. However, patients whose prognosis is longer, antibiotic therapy may be offered with careful consideration of associated benefits and risks. A useful antibiotic decision tree to aid clinicians in decision-making discussions with patients and caregivers can be found here.[12,13]

Manisha Juthani-Mehta, MD, an infectious disease physician, who authored the article, "Why Infection May be a Good Way to Die," aptly states, "*In American society, we have moved too far in the direction of doing more. There comes a point when doing less is more appropriate.*"[14]

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