Palliative Care and End of Life Issues: A Pharmacist's Perspective

LEAH HALL, PHARMD, BCPS, CGP
ASSISTANT PROFESSOR
UNIVERSITY OF CHARLESTON
SCHOOL OF PHARMACY

CPFI ANNUAL CONFERENCE
SPRINGMAID BEACH, SC

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Definition of Palliative Care

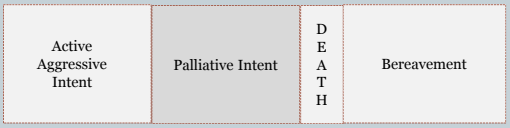
- WHO: "Palliative care is the active total care of patients whose disease is not responsive to curative treatment. Control of pain, other symptoms, psychological, social, and spiritual problems is paramount. The goal of palliative care is achievement of the best possible quality of life for patients and their families."
- NHPCO: "Treatment that enhances comfort and improves the quality of an individual's life during the last phase of life. No specific treatment is excluded…."
- "Hospice care" is palliative care provided to patients during the last months of life

World Health Organization. Definition of Palliative Care. Available at: http://www.who.int/cancer/palliative/definition/en/
National Hospice and Palliative Care Organization. What is Palliative Care. Available at: http://www.nhpco.org/about/palliative-care

Disclosure

- I do not have commercial or financial relationships to disclose relating to the content of this presentation.

Old Way of Thinking

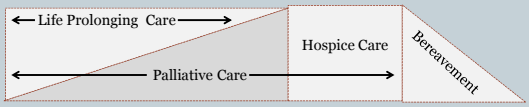


Adapted from: Frager G. Pediatric Palliative Care: Building the Model, Bridging the Gaps. 1996, Journal of Palliative Care, 12 (3):9-10.

Objectives

- Describe the roles and responsibilities of the pharmacist in palliative care
- Assess, recommend, and treat pain and common symptoms encountered in the palliative care setting
- Discuss advance directives commonly encountered in palliative care, and their effect on patient care
- Understand the concept of a "dignified death," and how the pharmacist can assist the patient and family in achieving optimal outcomes

New Way of Thinking



Adapted from: Frager G. Pediatric Palliative Care: Building the Model, Bridging the Gaps. 1996, Journal of Palliative Care, 12 (3):9-10.

ASHP Statement on the Pharmacist's Role in Hospice and Palliative Care

- Palliative care should be provided in **conjunction** with curative care at the **time of diagnosis** of a **potentially** terminal illness
- Palliative care alone may be indicated when attempts at a cure are judged to be futile
- Admissions to hospice and/or palliative care programs often come too late for optimal services to be provided
  - Length of stay
    - Mean: 50 days; Median: 25 days

American Society of Health-System Pharmacists. ASHP statement on the pharmacist's role in hospice and palliative care. *Am J Health-Syst Pharm*. 2002; 59:1770–3.

Symptom Management

- Pain
- Nausea and Vomiting
  - CINV
  - Generalized N/V
- Bowel Issues
  - Constipation & Bowel Obstruction
  - Diarrhea
- Anxiety
- Depression
- Delirium
- Oral Complications
  - Xerostomia and mucositis
- Dyspnea
- Death rattle/terminal secretions
- Insomnia
- Anorexia/Cachexia

The Pharmacist's Responsibilities

- Assessing the appropriateness of medication orders and ensuring the timely provision of effective medications for symptom control.
- Counseling and educating the hospice team about medication therapy.
- Ensuring that patients and caregivers understand and follow the directions provided with medications.

American Society of Health-System Pharmacists. ASHP statement on the pharmacist's role in hospice and palliative care. *Am J Health-Syst Pharm*. 2002; 59:1770–3.

General Approach to Symptom Management at End-of-Life

- Search for cause of symptom
  - History, physical, laboratory (as appropriate)
- Treat underlying cause (if reasonable)
- Treat the symptom
- Re-evaluate frequently

The Pharmacist's Responsibilities

- Providing efficient mechanisms for extemporaneous compounding of nonstandard dosage forms.
- Addressing financial concerns.
- Ensuring safe and legal disposal of all medications after death.
- Establishing and maintaining effective communication with regulatory and licensing agencies.

American Society of Health-System Pharmacists. ASHP statement on the pharmacist's role in hospice and palliative care. *Am J Health-Syst Pharm*. 2002; 59:1770–3.

Pharmacotherapy in Palliative Care

- Essential for many symptoms
- Non-symptom based drugs may be no longer appropriate or desired
- Data often limited
  - Pharmacokinetic/pharmacodynamic differences
  - Goals of treatment differ
- May need unusual routes of administration and/or dosage forms

Pain Management

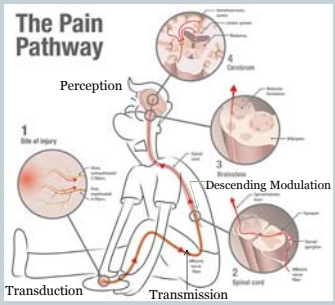
Pain Assessment

- P-Palliative, precipitating
- Q-Quality
- R-Radiating
- S-Severity
- T-Timing
- U-You

Pain Pathway

"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage

It's what the patient says it is!



Feeling Pretty Remarkable. Preventing Chronic Pain. Available at: http://www.feelingprettyremarkable.com/blog/preventing-chronic-pain

Pain Terms Defined

- Addiction
  - Continued repetition of a behavior despite adverse consequences
- Physical Dependence
  - Normal adaptive state that results in withdrawal symptoms if the drug is abruptly stopped or decreased
- Tolerance
  - Process by which the body continually adapts to the substance and requires increasingly larger amounts to achieve the original effects
- Pseudo-addiction
  - A drug-seeking behavior that simulates true addiction, which occurs in patients with pain who are receiving inadequate pain medication

Pain Management

- Types of pain
  - Nociceptive
    - Transient in response to noxious stimulus
  - Inflammatory
    - Tissue damage occurs despite nociceptive defense
  - Neuropathic
    - Spontaneous pain and hypersensitivity to pain, associated with damage to or pathologic changes in the periphery or CNS
  - Functional
    - Pain sensitivity due to an abnormal processing or functioning of the CNS in response to normal stimuli

General Approach to Treatment

- Effective treatment
  - Evaluate cause, duration, intensity
  - Selection of an appropriate treatment modality
- Two common approaches
  - Based on pain severity
  - Based on mechanism responsible for the pain
- Goal
  - Reduce peripheral sensitization, subsequent central stimulation and amplification associated with windup, spread, and central sensitization

Pain Treatment Paradigm

- Physical
  - Heat, cold, ultrasound, TENS, massage, exercise
- Behavioral
  - Imagery
  - Distraction
  - Relaxation
  - Cognitive behavioral therapy
- Pharmacotherapy
- Surgical
- Regional/Spinal Anesthesia

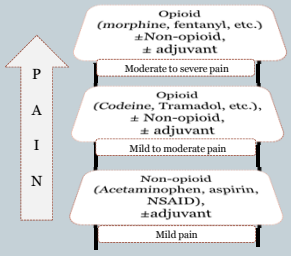
Critical Science. What Psychosocial Interventions Work. Available at: http://criticalscience.com/chronic-pain-psychosocial-interventions.html

Opioid Analgesics

- Classified by receptor activity (stimulate opioid receptors μ,κ, δ) in CNS), usual pain intensity treated, and duration of action
- Pure agonists
  - Three classes
  - Bind to μ receptor and have no "ceiling"
- Partial Agonists
  - Butorphanol, pentazocine, nalbuphine
  - Partially stimulate μ-receptor and anatgonize the κ-receptor
    - Reduced analgesic efficacy with a ceiling-dose
    - Reduced side effects at the μ-receptor
    - Psychometric side effects due to κ-receptor antagonism
    - Possible withdrawal in patients dependent on pure agonists

Pharmacotherapy

- Non-opioids
  - APAP & NSAIDs
- Opioids
  - Mu Agonists
  - Partial Agonists
  - Tramadol?
- Adjuvants
  - Topical Agents
    - Lidocaine
    - NSAIDs
  - Antidepressants
    - TCAs
    - SNRIs
  - Anticonvulsants
    - Gabapentin, Pregabalin



World Health Organization. WHO's Cancer Pain Ladder for Adults. Available at: http://www.who.int/cancer/palliative/painladder/en/

Classes of Opioids

Class I (Phenanthrenes)	Class II (Phenylpiperidines)	Class III (Phenylheptalamines)
Natural	Fentanyl	Methadone
Codeine	Meperidine	Propoxyphene (Disc)
Morphine		
Semisynthetic		
Hydrocodone		
Hydromorphone		
Oxycodone		
Oxymorphone		

Choosing Analgesics

- Type of pain
- Efficacy of analgesics for indication
- Route(s) available
- Renal and hepatic function
- Safety (NSAID vs. Cox-2
- Drug interactions
- Cost
- Patient and/or family preference

Self-Assessment

- The best opioid option for a patient with a true morphine allergy is?
  - A) hydromorphone
  - B) oxymorphone
  - C) oxycodone
  - D) fentanyl

Self-Assessment

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  - C) oxycodone
  - **D) fentanyl**

Opioid Chart Issues

- Unidirectional vs. bidirectional?
  - -A=B
  - But does B=A?
- Based on single-dose conversion data or multiple-dose conversion data?
- Pharmacogenomics
- Influence of age?

Opioid Switch

- Why switch?
  - Lack of efficacy
  - Development of intolerable side effects
  - Change in patient status
    - Inability to use specific dosage formulations
    - Transition of care
  - Other practical considerations
    - Availability of opioid, or dosage formulation
    - Cost or formulary issues
    - Patient, family preferences (morphobia)

Steps in Opioid Conversion

- Globally assess the patient and pain complaint
- Determine the total daily dose of the current opioid
- Decide which opioid to switch to (or formulation)
  - Consult an opioid conversion chart
- Individualize dose based on assessment info
- Patient follow-up and continued reassessment

Equianalgesic Doses of Selected Opioids

Equianalgesic Opioid Dosing

Drug	Equianalgesic Doses (mg)	
	Parenteral	Oral
Morphine	10	30
Buprenorphine	0.3	0.4 (sl)
Codeine	100	200
Fentanyl	0.1	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tramadol	100*	120

*Not available in the US

McPherson ML. *Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing*. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010. Copyright ASHP, 2010. Used with permission. NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

Setting Up Conversions

- Calculate total daily dose (TDD) of current opioids
- Set up conversion ratio between old opioid (and route of administration) and new opioid (and route of administration as follows:

$$\frac{\text{"X"}mg\ TDD\ new\ opioid}{mg\ TDD\ current\ opioid} = \frac{equianalgesic\ factor\ new\ opioid}{equianalgesic\ factor\ current\ opioid}$$

Or

$$\frac{\text{"X"}mg\ TDD\ new\ opioid}{equianalgesic\ factor\ of\ new\ opioid} = \frac{mg\ TDD\ current\ opioid}{equianalgesic\ factor\ current\ opioid}$$

Conversion Calculations

- Cross multiply, solve for "x"
- Three choices:
  - Reduce calculated dose due to lack of complete cross-tolerance
  - Begin with calculated dose
  - (Rarely) increase calculated dose
- Decide how many times per day you're going to dose the new opioid; divided by the appropriate dosing interval, and select a dosage that is available in that strength

Symptom Managment

Self-Assessment

- Convert Morphine 5mg IV every 4 hours + 0.5mg IV every 2 hours prn (used 6 doses in 24 hours) to oral oxycodone

Equianalgesic Opioid Dosing

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Morphine	10	30
Buprenorphine	0.3	0.4 (sl)
Codeine	100	200
Fentanyl	0.1	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tramadol	100*	120

*Not available in the US

McPherson ML. *Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing*. Asher Inc. of Health Systems Pharm, Bethesda, MD, 2010. Copyright ASHP, 2010. Used with permission. NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

Opioid Induced Constipation

- Tolerance does not develop
- Prevention is key!
  - Stimulant laxative cornerstone of therapy
  - Stool softener offers no benefit
- Golden rule
  - "The hand that writes for the long acting opioid, is the hand that writes for the breakthrough opioid, is the hand that orders the laxative"

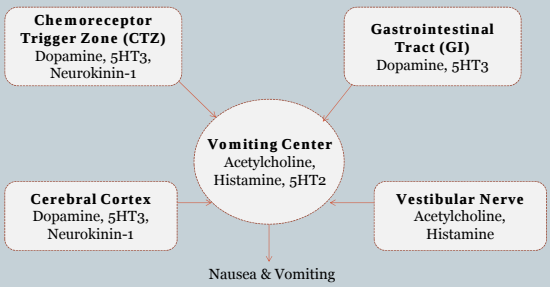
Self-Assessment

- TDD =33mg IV morphine

$$\frac{33mg\ IV\ morphine}{10mg\ IV\ morphine} = \frac{"X"mg\ oxycodone}{20mg\ oral\ oxycodone}$$

- X=66mg oral oxycodone
- Reduce by 25-50% for cross tolerance
  - 66mg x 0.75=49.5mg daily; 66mgx0.5=33mg daily
- Available as 5mg, 10mg, 15mg, 20mg, 30mg
- Dose: 5-10mg every 4 hours

Nausea/Vomiting



Adapted from: Chisholm-Burns MA, Wells BG, Schwinghammer TL, et al. Palliative Care. In: Pharmacotherapy Principles and Practice. 2013. 45.

11 M's of Emesis

- Metastases (cerebral, liver)
- Meningeal irritation
- Movement
- Mentation (anxiety)
- Medications (opioids, chemo)
- Mucosal irritation
- Mechanical obstruction
- Motility
- Metabolic (hypercalcemia, hyponatremia, hepatic/renal failure
- Microbes
- Myocardial

Education in Palliative and End-of-Life Care for Oncology. Self-Study Module 3p: Symptoms; Nausea/Vomiting. Available at: http://www.cancer.gov/cancertopics/cancerlibrary/epeco/selfstudy/module-3/module-3p-pdf

Managing N/V

- Mirtazepine
  - Antagonizes 5HT3 receptor
  - Refractory symptoms
- Olanzapine
  - Efficacy demonstrated in small case reports
- Cannabanoids
  - Efficacious for those with cancer and AIDS
  - Delirium and sedation, especially in older adults
- Lorazepam, diphenhydramine, haloperidol, metoclopramide (ABHR) suppositories/gels
  - No evidence to support efficacy

Managing N/V

Etiology	Pathophysiology	Therapy
Meningeal Irritation	Increased ICP	Steroids
Movement	Vestibular stimulation	Anticholinergics
Mentation (anxiety)	Cortical	Anxiolytics
Metastases • Cerebral • Liver	• Increased ICP • Direct Chemoreceptor Trigger Zone (CTZ) effect • Toxin buildup	Steroids Mannitol Anti-Dopamineric Antihistamine
Motility	GI tract, CNS	Prokinetic agents Stimulant laxatives

Goldstein NE, Morrison RS. Use of Medications to Prevent and Treat Nausea and Vomiting Unrelated to Chemotherapy. In: Evidence Based Practice of Palliative Medicine. 2013: 143.

Dyspnea

- Commonly seen in patients with heart failure and pulmonary issues
- Potential causes
  - Muscle wasting
  - Acid/base disturbance
  - Anxiety
  - Obstruction

Managing N/V

Etiology	Pathophysiology	Therapy
Metabolic • Hepatic/renal failure • Hypercalcemia	CTZ	Anti-dopaminergic Antihistamines Rehydration Steroids
Mechanical Obstruction	Constipation, tumor, fibrotic stricture	• Treat constipation • Reversible: surgery • Irreversible: Manage fluids; decrease oral intake; octreotide
Medications • Opioids • Chemotherapy	CTZ Vestibular effect GI tract	Anti-dopaminergic Antihistamines Anticholinergics Prokinetic agents Anti-5HT3 Steroids

Goldstein NE, Morrison RS. Use of Medications to Prevent and Treat Nausea and Vomiting Unrelated to Chemotherapy. In: Evidence Based Practice of Palliative Medicine. 2013: 143.

Treatment of Dyspnea

- Non-pharmacologic
  - Minimize need for exertion
  - Reposition upright
  - Avoid strong odors
  - Use fans or open windows
  - Adjust temperature/humidity
- Pharmacologic
  - Opioids
  - Benzodiazepines
  - Bronchodilators
  - Oxygen?

Self-Assessment

- True or False?
  - Opioids do not improve dyspnea through inhibition of the respiratory drive; rather, opioids improve dyspnea without causing significant deterioration in respiratory function.

Advance Directives

Document	Description
Substantive Directives • Living will • Five wishes • Personal wishes statement	Allows a patient to specify wishes for future care May include a section to designate a proxy decision maker
Process Directives • Health care power of attorney • Heath care proxy • Durable power of attorney for health care	Designates a surrogate decision-maker Does not specify wishes for care
Physician Orders for Life Sustaining Treatment	Physician orders regarding CPR, antibiotics and artificial nutrition/hydration Travels with a patient and is legally valid as an order in transit
Code status	Specifies whether to perform CPR in event of decompensation

Goldstein NE, Morrison RS. Effective Advance Care Plans and How they Differ From Advance Directives. In: Evidence Based Practice of Palliative Medicine. 2013: 259.

Self-Assessment

- **True** or False?
  - Opioids do not improve dyspnea through inhibition of the respiratory drive; rather, opioids improve dyspnea without causing significant deterioration in respiratory function.

POST

WV Center for End of Life Care. 2012 Post Form Revised. Available at: http://www.wvendoflife.org/MediaLibraries/WVCEOLC/Media/public/Post-Form-2012-rev-pink-SAMPLE.pdf

Advance Directives

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WV Center for End of Life Care. 2012 Post Form Revised. Available at: http://www.wvendoflife.org/MediaLibraries/WVCEOLC/Media/public/Post-Form-2012-rev-pink-SAMPLE.pdf

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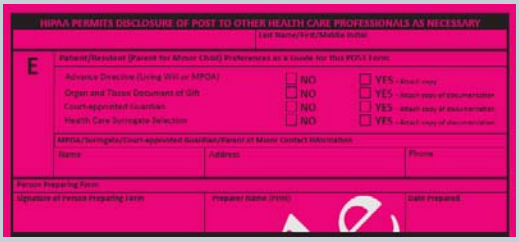

WV Center for End of Life Care. 2012 Post Form Revised. Available at: http://www.wvendoflife.org/MediaLibraries/WVCEOLC/Media/public/Post-Form-2012-rev-pink-SAMPLE.pdf

Self-Assessment

- Which of the following is false regarding most Physician Orders for Life Sustaining Treatment (POLST) forms?
  - They contain orders regarding CPR
  - They contain orders regarding artificial nutrition/hydration
  - They contain orders regarding antibiotics
  - **They contain orders regarding care of delirium**

POST

WV Center for End of Life Care. 2012 Post Form Revised. Available at: http://www.wvendoflife.org/MediaLibraries/WVCEOLC/Media/public/Post-Form-2012-rev-pink-SAMPLE.pdf

Honoring Patient Wishes and the "Dignified Death"

- Step 1: Prepare for the conversation
- Steps 2 and 3: Determine what the patient knows and wants to know
- Step 4: Deliver any new information
- Step 5: Notice and respond to emotions
- Step 6: Determine goals of care and treatment priorities
- Step 7: Agree on a plan

Goldstein NE, Morrison RS. Effective Advance Care Planning. In: Evidence Based Practice of Palliative Medicine. 2013: 264.

Self-Assessment

- Which of the following is false regarding most Physician Orders for Life Sustaining Treatment (POLST) forms?
  - They contain orders regarding CPR
  - They contain orders regarding artificial nutrition/hydration
  - They contain orders regarding antibiotics
  - They contain orders regarding care of delirium

5 Things to Say Before Death

- I love you
- Please forgive me
- I forgive you
- Thank you
- Good-bye

Boyock I. The Four Things That Matter Most: A Book About Living. 2004

Good-Bye For Now

- In my Father's house are many mansions: if it were not so, I would have told you. I go to prepare a place for you. And if I go and prepare a place for you, I will come again, and receive you unto myself; that where I am, there ye may be also. John 14: 2-3 (KJV)
- And God shall wipe away all tears from their eyes; and there shall be no more death, neither sorrow, nor crying, neither shall there be any more pain: for the former things are passed away. Rev 21:4 (KJV)

Questions?

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LEAH HALL, PHARMD, BCPS, CGP
ASSISTANT PROFESSOR
UNIVERSITY OF CHARLESTON
SCHOOL OF PHARMACY

CHRISTIAN PHARMACIST'S FELLOWSHIP
INTERNATIONAL-ANNUAL MEETING
SPRINGMAID BEACH RESORT
MYRTLE BEACH, SC

6-14-14