MANAGING PAIN, NAUSEA AND DYSPNEA WITH THE TERMINALLY ILL
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The Powerful Role of Nurse Practitioners As End of Life Approaches

Disclosures
Objectives

- At the end of this presentation, the participants will be able to verbalize:
  1. The unique and pivotal role Nurse Practitioners have in caring for their patients as their end of life approaches
  2. How to assess and treat dyspnea as end of life approaches
  3. The various contributors to nausea and pharmacologic options used to treat each
  4. The basics of how to assess and treat pain appropriately at the end of life using both opioid and non-opioid pharmacologic options
  5. The understanding of the role of Palliative Care/Hospice consultation for patients with GOC and symptom management needs.

Advance Practice and End of Life Care

- Hippocrates
  - To cure sometimes
  - To relieve often
  - To comfort ALWAYS

Dyspnea vs. Respiratory Distress

- **Dyspnea**: A person’s awareness of uncomfortable or distressing breathing that can only be known through the person's report.
- **Respiratory Distress**: Observed. The physical and emotional distress associated with respiratory distress associated with respiratory dysregulation.
Prevalence of Dyspnea across Terminal Illnesses
(Solano et al 2006)

1. COPD: 90-95%
2. Heart disease: 60-88%
3. Cancers: 10-70%
4. AIDS/Renal Failure: 11-62%

Assessment of Dyspnea

- Patient
- Self
- Report

Dyspnea Assessment

- “Yes/No”
- Numeric scale: 0-10 (vertical better than horizontal)
- Visual analog scale

Over 40 tools exist. The above tools are valid and reliable.
Challenge with Cognitive Decline
- Self report less valid
- **Respiratory Distress Observation Scale (RDOS) (0-16 scale) (Campbell 2013)**
- Quantifies observations when self-report cannot be provided
- Looks at the following 0-1-2 scoring
  - Heart rate/min: <90/90-100/>100
  - Respiratory rate/min: <18/18-30/>30
  - Restlessness/non-purposeful movements: none/occasional/frequent
  - Accessory muscle use: none/present
  - Paradoxical breathing pattern: none/present
  - Grunting: none/present
  - Nasal flaring: None/present
  - Look of fear: None/present

Palliation of Dyspnea
- **Disease Modifying Treatments:**
  - Consistent with the goals of care
  - Paracentesis, Thoracentesis, Diuresis, Antibiotics, Non-invasive Ventilation

Palliation of Dyspnea
- **Maintain Supportive Treatments**
  - Bronchodilators
  - Anti-cholinergics
  - Diuretics
  - Inotropes
Palliation of Dyspnea

- Medications used to treat dyspnea as end of life approaches

**Opioid's:** The ONLY MEDICATIONS that have evidence base for dyspnea relief.

- Morphine
- Fentanyl
  - Potent Mu agonist
  - Oral, parenteral, inhaled (not yet proved to show statistical significance although often used anecdotally)

  Works to decrease dyspnea by:
  - Reduced O2 and CO2 effect on ventilation (ATS, Am J Resp Care Med 2012)
  - Altered central perception (Pattinson et al, J Neuroscience 2009)

Opioids to Treat Dyspnea

- Dosing: Optimal dosing not yet established
- IR Morphine (5 mg oral/2 mg IVP) q 4 hrs with q 1 hr rescue available (Thomas and Van Guten Lancet Onc 2002)
- Currow et al, J Pain Symptom Management 2011 showed effectiveness of once daily dosing of Morphine (10-30 mg).
- **Adverse Effects:**
  - Constipation, pruritus, nausea, sedation
  - Respiratory depression NOT seen on Cochrane review of 18 major studies (Currow, 2011; Jennings 2002)

Benzodiazepine use to Treat Dyspnea

- Not heavily studied
- Navigante, et al J pain Symptom Management 2006 studies Midazolam as adjunct therapy with Morphine
  - ATC Morphine with Midazolam rescue vs ATC Midazolam with morphine rescue vs ATC Morphine and Midazolam with morphine rescue
  - Found that ATC Morphine AND Midazolam WITH Morphine Rescue was most effective
  - Hypothesis: Do benzodiazepines help alleviate the fear component of dyspnea
Furosemide Inhalation
• Mixed study results that are not strong enough yet to show statistical significance
• Further broad range studies needed
• Inhaled furosemide can protect against bronchospasm, decrease cough reflex, cause diuresis and possibly reduce dyspnea

Oxygen use to Treat Dyspnea Toward End of Life
• Global Initiative for Chronic Obstructive Lung Disease, 2013:
  • For patients who experience hypoxia with resting dyspnea, wearing O2 >15 hrs/day increased survival
  • Can correct hypoxemia, decrease dyspnea
  • O2 Burdens:
    Nasal dryness/epistaxis
    Flammable
    May prolong the dying process
  • O2 vs Medical Air (Abernathy et al, 2010)
    239 terminally ill patients with refractory dyspnea
    Nasal O2 or medical air at 2L/min for 15 hrs/day for 7 days
    NO DIFFERENCES in dyspnea relief between O2 administration and medical air

Oxygen at the End of Life
  • Declining O2 saturations is naturally occurring and expected
  • COPD, Heart Failure, Lung CA, PNA all were at risk BUT often without significant distress
  • Declining O2 sat may predict but does NOT signify respiratory distress often per RDOS
  • Routine administration of O2 to patients at the end of life is not supported
  • Can do a 1 hr trial of O2 use to re-perform RDOS and evaluated O2 appropriateness.
Summary/Dyspnea

- **Objective Assessment**: Self report or RDOS for cognitively impaired
- **Disease specific therapies**: (steroids, antibiotics, diuretics, procedures, and use of inhalers/nebs/anticholinergics to continue
- **Opioids**: Morphine Fentanyl studied
- **Benzodiazepines**: require further study )Ativan 0.5 mg po q 6 hrs prn)
- **O2** (humidified) for hypoxemia in setting of dyspnea but can try to turn off and RDOS re-assessment and resume O2 only if respiratory distress present
- **Non-Pharmacologic treatments**: Positioning, fans, cool room, pursed lip breathing

Nausea

- **Definition**: Feeling of sickness with sensation of needing to vomit
- **Initially portrayed as quite common in advanced cancer and life limiting illnesses, however recent research finds it less predominant than previously thought (Glare, et al, Clinical Int’l Aging 2011)
- **Cornerstone of assessment and treatment of Nausea and vomiting has been the “EMERG PATHWAY”.
- **Challenge is that often with patients with life-limiting illnesses, either it is difficult to ascertain and identifiable cause, or MULTIPLE causes are present

10/27/2014
Nausea

- In those with life-limiting illnesses, nausea is found most commonly with the following diagnoses:
  - AIDS: 43%
  - ESRD: 30%
  - Heart Failure: 17%
  - Cancer patients: CINV: 58%, disease related 6%


- 71% of all patients approaching the end of life experience nausea (Connil, et al. J Pain Symptom Management, 1997)

Nausea

Differential:

- Due to primary disease
- Due to Side effect of therapy
- Secondary to debilitation
- Caused by unrelated co-morbid condition

Nausea

- Anxiety/Anticipatory Nausea/Increased ICP
- Gastroparesis, Colitis, Chemotherapy
- Drugs/hypercalcemia
- Gastric stasis, Colitis, Chemotherapy
- Vestibular Neuritis/Meniere's

- Vestibular input (ACHM1, H1)
- Drum (binaural) Improved
- Meclizine: H1, Omeprazole
- Ondansetron: 4-8 mg tid
- Emend (NK1)
- Compazine: 10 mg tid
- Lorazepam: (Gaba)
- Oxazepam

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- Ondansetron: 4-8 mg tid
- Emend (NK1)
- Compazine: 10 mg tid
- Toloxolut (H1)
Other Agents to Treat Nausea

- Corticosteroids
- Hyoscine
- Octreotide
- Cannabinoids

**Corticosteroids**

- Chemotherapy induced nausea associated bowel obstruction, increased ICP (decreased permeability of Blood Brain Barrier to emetogenic substances)
- Dexamethasone 4-8 mg/day (may use up to 14-32 mg/day)

**Hyoscine**

- Anticholinergic
- Relax smooth muscle and reduce GI secretions and block muscarinic receptors therefore useful with malignant bowel obstructions
- Dose SQ/IV 0.6-2.4 mg cont.
- Hyoscine hydrobromide oral 0.1-0.4 mg q 6h
- Transdermal 3-5 mg q 3 days

**Octreotide**

- Malignant bowel obstruction especially with high output vomiting. Decreased secretion of fluids by intestine and pancreas, decrease GI motility and cause vasoconstriction
- Dose 100 ug tid SQ
- Or up to 600 ug/day cont. infusion

**Cannabinoids**

- Mostly studied for chemotherapy induced nausea and vomiting
- Limited evidence thus far
- Unclear mechanism of action
- Dronabinol
- Caution due to centrally acting effects and significant potential interactions
Other Modes of Nausea Control

- Avoidance of environmental stimuli (smells, sounds, fatty/spicy/highly salted foods, etc.). Avoid lying flat after eating, food modification, restricted intake, sips
- CBT: relaxation, distraction, guided imagery, progressive muscle relaxation
- Massage
- Ginger
- GI Surgical Interventions: G tube placement for decompression, stent placement, laser

Pain Management in the Setting of Life-Limiting Illness

- Total Pain: Physical, Spiritual, Social, Emotional
- According to the WHO, the undertreatment of pain in patients with advanced illness continues to be a prevalent problem. (Apolone, G et al Br J Cancer 2009)
- Prevalence of pain increases rapidly in the last few months of life regardless of the cause of death (Smith, A, et al 2010, Annals of Internal Med)
- Pain in the elderly: 70-80% have chronic pain with 30% stating pain is constant.
- Challenges today: Barriers, REMS, ACT 148, Prevention of diversion, Abuse/misuse
Pain Assessment

- Standardized tools:
  - Self report
  - Observation

Pain: Acute vs Chronic

- Acute pain: < 3 months
- Chronic Pain: > 3 months
- Baseline pain
- Incidental pain

Types of Pain

- Nociceptive
  - Bone: constant, deep ache
  - Visceral: Ache, cramp, difficult to isolate
  - Somatic: Easy to locate and describe

- Neuropathic
  - Burning, shooting, stabbing, numbing

- Functional
- Psychogenic
Principles of Pain Management

- **Assessment**: Physical exam, Studies, Assessment tools, Medical Record review
- **Non-Pharmacologic methods of management**: PT/OT/thermal/acupuncture/massage/CAM
- **Interventional and surgical options**
- **Pharmacologic options**
  - Non-opioids
  - Opioids
  - Adjuvant medications

Mild Pain Pharmacology

*Acetaminophen*
- Analgesic
- Antipyretic
- Minimal peripheral anti-inflammatory effect

**Acetaminophen overdose** is leading cause of acute liver failure in the US (King J, Am J Prev Med 40:593-598, 2011)

**Safe Dose**: No long term safety and efficacy studies.

- Suggestion is to limit to 3000 mg/day
- January 13, 2011: FDA asked that acetaminophen be limited to 325 mg/tablet and black box warning was added.

**BEWARE OF COMBINATION MEDICATION USE**

NSAIDS

- Analgesic
- Antipyretic
- Anti-inflammatory

**Toxicities Include:**
- **GI ulceration** (PPI's help prevent this), LGIB
- **Renal Failure, HTN** (higher risk if > 60, multiple myeloma, dehydration, DM, and other nephrotoxic substance administration (NCCN Clinical Practice Guideline Oncology: Adult Cancer Pain, Version 2, 2011)
- **Platelet aggregation abnormalities**
- **MI/CVA**
NSAIDs

- **Salicylates**: ASA, Choline magnesium trisalicylate
- **Propionic acids**: Ibuprofen, Ketoprofen, Naproxen sodium
- **Acetic acids**: Etodolac, Ketorolac, Indomethacin, Diclofenac, Nabumetone
- **Enolic acids**: Piroxicam, Meloxicam
- **Selective COX-2 inhibitor**: Celecoxib

- No clear evidence of superior efficacy of 1 NSAID over any other.
- Toxicities Differ however and if analgesia is achieved, but side effect limits use, try another class. If after trying 2, if analgesia or side effect prohibits use, DC the NSAID class. (Abernethy A, et al Evidence Based Practice Palliative Medicine 49-53, 2013)

Opioids: Moderate to Severe Pain

- “The data show no important differences between morphine, oxycodone and hydromorphone given by the oral route and permit a weak recommendation that any one of these 3 drugs can be used as the first choice opioid for moderate to severe cancer pain” (Lancet Oncol 2012; 13 e 58-68)

- Opioids… Each unique….
  - Morphine
  - Codeine
  - Oxycodone
  - Hydromorphone
  - Fentanyl
  - Methadone
  - Tramadol
  - Oxymorphone
  - Tapentadol
  - Buprenorphine

Principles of Opioid Use

- Start low and go slow
- Choose the appropriate route (oral/buccal/SL, transdermal, topical (poor bioavailability), SQ/IV, rectal, epidural, intrathecal)
- Titrate to relief
- Opioid switch when:
  - Intolerable side effects
  - Poor analgesia response despite aggressive titration (opioid induced hyperalgesia)
  - Drug-drug interaction
  - Change in clinical status
  - Financial or drug availability
Opioid Switching

Steps:
- Calculate the equianalgesic dose
- Dose reduce by 25-50%
- Consider additional increase or decrease of 15-30% based on medical and psychosocial characteristics
- FREQUENTLY reassess and titrate
- ENSURE YOU HAVE A RESCUE DOSE OF 5-15% OF THE 24 HR DOSE AVAILABLE


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Opioid Equianalgesic Chart

<table>
<thead>
<tr>
<th>Drug</th>
<th>Equianalgesic Dose (mg)</th>
<th>Parenteral</th>
<th>Oral</th>
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</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>40</td>
<td>0.3</td>
<td>0.4</td>
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<tr>
<td>Buprenorphine</td>
<td>100</td>
<td>0.1</td>
<td>NA</td>
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<tr>
<td>Codeine</td>
<td>100</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
<td>NA</td>
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<tr>
<td>Hydrocodone</td>
<td>30</td>
<td>50</td>
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<tr>
<td>Hydrocodone</td>
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<td>Hydromorphone</td>
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<td>Hydromorphone</td>
<td>950</td>
<td>1100</td>
<td></td>
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<tr>
<td>Hydromorphone</td>
<td>1000</td>
<td>1150</td>
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</tbody>
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Footnotes:
Opioids in the Setting of Renal Failure

- **Morphine**: should be avoided in renal failure due to metabolite accumulation (M3G, M6G with CNS effects/myoclonus)
- **Codeine**: should be avoided in renal failure due to metabolite accumulation
- **Hydromorphone**: IDG accumulates however is less neurotoxic than M3G.
  Monitor patients closely
- **Tramadol**: Metabolites accumulate and requires dose adjustment
- **Oxycodone**: Metabolites thought to be less neurotoxic than morphine and hydromorphone
- **Methadone**: appears to be safe in renal failure due to fact biliary excretion increases as renal excretion decreases.
- **Fentanyl**: Unknown metabolism effects. Appears to be safe in patients with renal failure

Opioid Side Effects and “Tolerance”
Manage Side Effects!!!!

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>Never</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>7-10 days</td>
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<tr>
<td>Pruritus</td>
<td>7-10 days</td>
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<tr>
<td>Sedation</td>
<td>36-72 hrs</td>
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<tr>
<td>Respiratory Depression</td>
<td>Extremely rare when dosed appropriately</td>
</tr>
</tbody>
</table>

Adjuvant (Co-Analgesic) Medications

- Medications originally developed to treat conditions other than pain but found to have pain relieving properties
- Various sites of action
- Many are very useful in the treatment of neuropathic pain
### Adjuvant (Co-Analgesic) Classes

<table>
<thead>
<tr>
<th>Options</th>
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<tbody>
<tr>
<td>Antidepressants (TCA, SSRI, SNRI)</td>
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<tr>
<td>Anticonvulsants (gabapentin, pregabalin, carbamazepine, clonazepam)</td>
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<tr>
<td>Steroids (dexamethasone)</td>
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<tr>
<td>Systemic Local anesthetics (lidocaine, mexiteline)</td>
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<tr>
<td>NMDA antagonists (ketamine, amantadine, dextromethorphan, methadone)</td>
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<tr>
<td>Bisphosphonates</td>
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<tr>
<td>External Beam Radiation</td>
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<tr>
<td>Radiopharmaceuticals</td>
</tr>
<tr>
<td>Complementary Alternative (CAM):</td>
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</tbody>
</table>

### Others
- Alpha 2 agonist
- Topicals (capsaicin, Lidocaine)
- Antispasmodics
- Antihistamines

### Antidepressants
- TCA's: Most documented efficacy but most side effect
  - nortriptyline, desipramine have less side effects than amitriptyline and doxipine (sedation, anticholinergic)
  - Trazadone: Good to assist with sleep
- SSRI's: Some data showing efficacy in pain
  - Paroxetine may be effective for neuropathic pain
  - Fluoxetine is only effective if depression is present
- SNRI's: shown efficacy in neuropathic pain
  - Duloxetine: Efficacy comparable to gabapentin and pregabalin
- Venlafaxine: diabetic neuropathy
- Side Effects: orthostatic hypotension, dry mouth, dizziness, constipation, nausea, sedation
Anticonvulsants

- Gabapentin (diabetic neuropathy and post-herpetic neuralgia as well as mood and sleep. 100-3600 mg/day)
- Pregabalin (similar to gabapentin with better kinetics and BID dosing. 150-300 mg/day)
- Carbamazepine (similar to TCA; trigeminal neuralgia use)
- Valproate
- Clonazepam
- Side Effects: fatigue, ataxia, dizziness, blurred vision, nausea, sedation

Steroids

- Primary effect is to decrease inflammation and raise the pain threshold.
- Secondary effects: tumor shrinkage, increased appetite, improved mood
- Preferred: Dexamethasone
  - Longer acting
  - Least mineralocorticoid effect
  - Dosing 4-20 mg/day
  - Side effects: immunosuppression, endocrine effects, psychosis, proximal muscle wasting after 4-6 weeks

Conclusion