

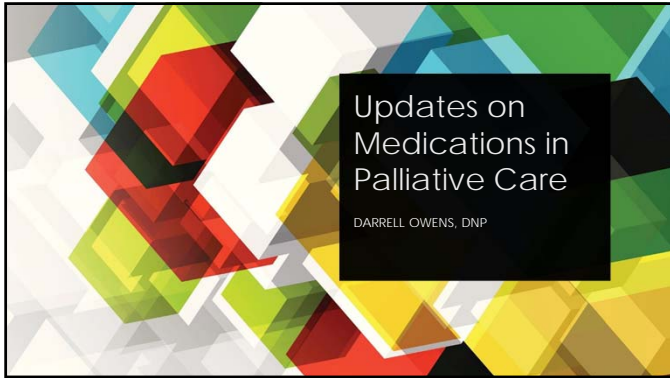
Adult/Geriatric Drug Therapy 2020

Updates on Medications in Palliative Care

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Objectives for Learning Outcomes:

1. Name the three most common symptoms in the palliative care population.
2. Identify three commonly used medications and their indications and SE in palliative care.
3. Identify three common misconceptions about sx management in palliative care.



Objectives



NAME THE THREE MOST COMMON SYMPTOMS IN THE PALLIATIVE CARE POPULATION.



IDENTIFY THREE COMMONLY USED MEDICATIONS AND THEIR INDICATIONS AND THEIR IN PALLIATIVE CARE.



IDENTIFY THREE COMMON MISCONCEPTIONS ABOUT SX MANAGEMENT IN PALLIATIVE CARE.

Growth in Palliative Care in the U.S.

- ▶ Over the past 16 years, the percentage of hospitals with > 50 beds with a palliative care program has tripled (Center to Advance Palliative Care, 2020)
- ▶ Availability varies by geography, hospital size and tax status
- ▶ Even in most hospitals with a palliative care program, only a small percentage of eligible patients are seen secondary to understaffing and under resourcing
- ▶ Predictors of palliative care programs within hospitals included region (New England, Pacific, and mid-Atlantic regions having the highest palliative care prevalence; the West and East South Central regions have the lowest) and tax status (not-for-profit hospitals and public hospitals were 4.3 times and 7.1 times, respectively, more likely to have a palliative care program as compared to for-profit hospitals).

Common Diagnosis Seen by Palliative Care

- ▶ When examined by medical specialty, palliative care reach is:
 - ▶ highest in surgery, followed by oncology and family medicine.
 - ▶ lowest in nephrology, followed by emergency medicine and neurology (Hughes and Smith, 2014)
 - ▶ Cancer, Cardiac, Pulmonary, Multi-morbidity (chronic illness, failure to thrive), Renal, Vascular, GI, Neurological

Most Common Symptoms in Palliative Care Patients

- ▶ Pain
- ▶ Fatigue
- ▶ Drowsy
- ▶ Loss of Appetite
- ▶ Nausea
- ▶ Depression
- ▶ Anxiety
- ▶ Dyspnea
- ▶ Constipation

Access to Palliative Care by People of Color

- ▶ Black and Hispanic patients with ESKD, receiving HD were less likely than Whites to receive a palliative care consultation (despite an average symptom burden of 9 bothersome symptoms)
- ▶ Hospitals with more minorities were less likely to provide palliative care compared with those with fewer minorities
- ▶ Larger hospitals compared with smaller hospitals (aOR 1.45, 95% CI 1.29 to 1.61, P<0.01) and urban teaching hospitals compared with rural nonteaching hospitals (aOR 1.60, 95% CI 1.30 to 1.96, P<0.01) had higher odds of palliative care utilization
- ▶ The odds of receiving palliative care for both white and minority stroke and cancer patients is lower in minority compared with white hospitals, suggesting system-level factors as a major contributor to explain race disparities in palliative care

Assessment

- Multiple etiologies for most symptoms in palliative care
- Treatments may vary based on etiology
- Non-pharmacologic interventions are often not included in treatment
- Without adequate assessment, adequate treatment is not possible

Medication Updates

- Majority (if not all) medication updates have nothing to do with clinical care
- Very few evidence-based medication changes in palliative care over the past 10 years
- Most changes or updates are based on formulary changes which are most often based on cost

Agitation Management

- First Line - Benzodiazepines
 - Mainstay - lorazepam 0.5 mg to 2 mg po PRN (may also be given PR, IM, SQ or IV)
 - Midazolam 1.0 to 2.0 mg PO PRN, standard dosing; 5-10 mg PO PRN (may also be given PR, IM, IN, SQ)
 - Diazepam (not readily available) 2-10 mg PRN (may also be given PR, IM, SQ)

Agitation Management

- No Relief, Second Line - Neuroleptics
 - Mainstay - Haloperidol 0.5 mg to 5 mg every 2-12 hours Olanzapine 2 to 10 mg po, IM, SQ, IV every 4-6 hours PRN (also available as ODT 10 mg rapid disintegrating tablet)
 - Ziprasidone 10 to 20 mg po every 12 hours PRN, when using IM dosing is 10 to 20 mg IM
 - Aripiprazole 10 to 20 mg PO QD
- It has been reported that first generation antipsychotics, e.g., haloperidol are falling out of favor, clinical practice does not support this statement (cost issue)

Agitation Management

- No Relief, Third Line - Ketamine
 - Low dose subtherapeutic dosing
 - Ketamine IV 0.25 mg per kg IV
 - Ketamine IM 0.5 mg per kg (IM dosing is generally twice the IV dose and may also be given SQ)
 - Full dose dissociative dosing regimens
 - Ketamine IV 2 mg per kg IV
 - Ketamine IM 4 mg per kg IM
 - Ketamine parental may be given po (25 mg to 50 mg tid); however, when given po, symptom relief may not be rapidly achieved

Anorexia

- ALWAYS assess cause
 - Is it anticipated / expected based on prognosis?
 - Cancer, dementia, prognosis of days to weeks
 - Does it need to be treated with medication?
 - Distressing to patients and families
 - Education and counseling is always first line
- Megestrol acetate 800 mg per day. Not proven effective in changing prognosis in people with dementia, can worsen cognition, increase fluid retention, risk of DVT, sexual dysfunction; contraindicated in hormone dependent tumors
- Dexamethasone 2 mg to 16 mg QD. MDD is not known, most people do well between 4 and 6 mg QD
- Cannabinoids (CBD) dose unknown, very effective in some, not at all in others.

Anxiety – Benzodiazepines (Dahlin, Coyne and Ferrell)

Generic Name	Approximate Daily Dose	Comment
Alprazolam	0.25 mg to 2 mg TID to QID	Short-acting
Clonazepam	0.5 mg to 2 mg BID to QID	Long-acting
Diazepam	5 mg to 10 mg BID to QID	Long-acting; rapid onset with single po dosage
Lorazepam	0.5 mg to 2 mg TID to QID	Short-acting; multiple routes, no metabolites
Bupirone (category Azapirones)	5 mg to 20 mg po TID	Extended time to peak effect similar to antidepressants

Anxiety – SSRIs (Dahlin, Coyne and Ferrell)

Generic Name	Approximate Daily Dose	Comments
Citalopram	10 mg to 40 mg QD	MDD 20 mg for elders
Fluoxetine	10 mg to 80 mg QD	Longest half-life among SSRIs
Paroxetine	10 mg to 60 mg QD	
Sertraline	50 mg to 200 mg QD	

Anxiety – Other Antidepressants (Dahlin, Coyne and Ferrell)

Generic Name	Approximate Daily Dose	Comments
Duloxetine	40 mg to 60 mg QD	
Venlafaxine	75 mg to 375 mg QD	
Mirtazapine	7.5 mg to 60 mg QD	Promotes sleep and appetite at low doses

Anxiety – Antipsychotics (Dahlin, Coyne and Ferrell)

Generic Name	Approximate Daily Dose	Comments
Olanzapine	5 mg to 15 mg QD	ODT available
Quetiapine	25 mg to 200 mg QD	Preferred for patients with PD
Risperidone	1 mg to 3 mg QD	
Haloperidol	0.5 mg to 5 mg every 2 to 12 hours	Inexpensive and multiple routes available
Antihistamines Hydroxyzine	25 mg to 50 mg Q4 to 6 hours	Risk of anticholinergic SE and delirium

Nausea (CAPC)

Class	Mechanism	Indications	Drugs	Side Effects
Antidopaminergic Therapies	Block emetic pathways from GI and CTZ Direct pro-kinetic	Opioids, chemo, toxins or drugs known to cause nausea	Prochlorperazine 10 mg po BID to QID or 25 mg IM BID Metoclopramide 10 mg PO QID/MQ Q 4 HR Olanzapine 5 – 10 mg PO	EPS, sedation, hypotension, contraindicated in bowel obstruction
Serotonin receptor antagonists	Block emetic pathways through vagal stimulation, 5-HT3 receptors in GI and CTZ	Chemo, toxins associated with nausea	Ondansetron 4-8 mg po BID to TID Granisetron 1 mg po BID or 2 mg po QD	Constipation, headache
Antihistamines	Uncertain action in the vomiting center	Inner ear pathology, always an adjunct to other agents	Diphenhydramine 12.5 to 50 mg Q 6 hr Hydroxyzine 25 to 50 mg po Q 6 hr Meclizine 25 to 50 mg Q 24 hours	Sedation, constipation, confusion, dry mouth, ortho static

Nausea (CAPC)

Class	Mechanism	Indications	Drugs	Side Effects
Anxiolytics – Benzodiazepines	Work via cerebral cortex pathway	Anxiety, PTSD post-chemotherapy, useful as an adjunct	Lorazepam 0.5 to 1 mg q 6 to 24 hours	Sedation, confusion, falls
Corticosteroids	May relieve cancer associated nausea via reducing inflammatory mediators. Exact MOA is not known	Bone pain, appetite stimulant, brain tumor associated nausea, bowel obstruction	Dexamethasone 2 to 4 mg po or IV Q 6 to 24 hours Others not found to be helpful with nausea	Fluid retention, increased BP, increased BG, mood swings, weight gain, increased risk of infection
Cannabinoids	Receptors are widespread in the CNS, MOA is not known	Refractory nausea, may be useful as adjunct	High CBD, low THC recommended synthetic (dronabinol) reported to be less effective.	Tachycardia, hypotension, decrease GI motility, vertigo, hallucinations

Fatigue

- Multiple etiologies require careful assessment
 - Multiple non-pharmacologic treatments based on etiology have shown to be effective
- Methylphenidate
 - Most commonly used medication for treatment of fatigue in palliative care
 - RCT have shown significant placebo effect
 - Most effective in cancer treatment associated fatigue
 - Limited evidence demonstrates improved mood in significant depression in palliative care
 - 2.5 mg QD starting dose, most patients do well at 5 mg BID (dosing at 0800 and 1300)

Fatigue

- Dexamethasone
 - RCT showed significant improvement in management of fatigue for people receiving 4 mg QD
 - Also showed improvement appetite and overall well-being scores
- SSRIs
 - Multiple studies failed to show improvement in management of fatigue
- Vitamins
 - Not proven to show improvement in management of fatigue
- Ginseng
 - Statistically significant improvement in fatigue scores for people receiving 2,000 mg for 8 weeks (no difference from placebo at 4 weeks)

Constipation – Stimulant Laxatives

Medication	Usual adult dose
Bisacodyl	Enteric coated tabs 10 to 30 mg 1-2 times per day
Senna	Sennoside tablets 8.6 to 15 mg, 2 to 4 tabs as a single daily dose or divided BID

Constipation – Osmotic Laxatives

Medication	Usual adult dose
Polyethylene Glycol	Powder 1-2 scoops (17-34 gms) in 240 ml (8 oz) liquid QD to BID
Lactulose	Liquid, 10 to 20 gms (15 to 30 ml) QD or QOD
Sorbitol	Liquid, 30 gms (120 ml of 25% solution) QD to BID
Glycerin	PR (2 or 3 gms) 1-2 QD
Magnesium Sulfate	Powder, 5-10 gms or 1-2 tsp in 8 oz H2O QD
Magnesium Citrate	Liquid, 11.6 gms or 200 ml QD

Constipation – Emerging Medications for Opioid Induced (OIC)

- Opioid antagonist – majority of symptoms associated with OIC are secondary to stimulation of Mu-opioid receptors in the GI tract, opioid antagonist offer new treatment options
 - Expensive, not generic, rarely covered on hospice formulary (so if started in hospital, would not be covered if patient was discharged to hospice)
- Naloxone, until recently, was the only available agent, patients ingested IV via PO. One non-controlled study found BM in 80% of patients within 1-4 hours. NOTE – 2/3 lost analgesic control. Safe and effective doses should be approximately 10% of the daily MED. MDD is 12 mg QD

Constipation – Emerging Medications for Opioid Induced (OIC)

- Methylnaltrexone bromide: peripherally-acting mu-opioid receptor antagonist. Methylated form of naltrexone, given subcutaneously. Does not cross blood-brain barrier, 6 separate trials found the NNT is 3 for people who have failed to respond to standard laxative therapy.
- Naloxegol: two po peripheral acting mu-opioid receptor antagonist are available in the US
 - Alvimopam: only approved for post-operative ileus
 - Naloxegol: recently approved for OIC in non-cancer patients (current price is \$300 for 30 pills)

Dyspnea

- ▶ Oximetry is not as effective as the subjective report of shortness of breath in managing dyspnea in palliative care.
- ▶ Oxygen therapy: consider for patient with evidence of air hunger. Initial flow rates of 2-6 lpm. An individual response to oxygen cannot be predicted with precision. Often used for family and nurse comfort in EOL situations.
- ▶ For anxiety-based dyspnea see prior anxiety slide

Dyspnea – General

- ▶ Opioid Therapy
 - ▶ Mainstay of therapy for relief of dyspnea in palliative care patients from a variety of causes:
 - ▶ Morphine: 1-2 mg IV every 10 minutes PRN or 5-10 mg po every 30 minutes PRN
 - ▶ Hydromorphone: 0.2 mg IV every 10 minutes PRN or 4-8 mg po every 30 minutes PRN
 - ▶ Fentanyl: 25 – 50 mcg IV every 10 minutes PRN
 - ▶ If PRN fails, consider scheduled intermittent
 - ▶ If scheduled intermittent fails, consider continuous infusion starting at 1 mg / hour (morphine) 0.2 mg / hour (hydromorphone), 25 mcg / hour (Fentanyl)
 - ▶ Multiple RCT do not support the use of nebulized opioids for dyspnea

Dyspnea - Bronchospasm

- ▶ Albuterol 1-2 inhalations Q 4-6 hour PRN (with spacer), if possible use nebulizer as first line
- ▶ Ipratropium bromide: Atrovent 1-2 inhalations TID to QID
- ▶ Beclomethasone: Vancril Inhaler 1-2 inhalations 3-4 times per day (*at times patients may benefit from steroid therapy, po or parental, antibiotics if infection suspected and BiPaP or CPAP depending on goals of care*)
- ▶ Other newer agents available, generally not short-acting and cost prohibitive

Dyspnea – Heart Failure

Furosemide 20-40 mg po X1 dose (know kidney function)

- If effective continue 20-40 mg PO QD or BID
- For longer term, initiate supplemental K+

For patient's refractory to loop diuretics, consider:

- Furosemide infusion with
- metolazone 2.5 to 20 mg PO QD or
- spironolactone 25-50 mg PO QD

Pain - Mild

- ▶ All Pain:
 - ▶ Always consider source, non-pharmacologic interventions and renal function
- ▶ APAP (palliative care first line)
- ▶ NSAID (used sparingly and never in the elderly)
- ▶ Diclofenac (cheaper in Canada)
- ▶ Liquid
 - ▶ APAP 500 mg / ml
 - ▶ Ibuprofen (100 mg / ml)
 - ▶ Indomethacin (25 mg / 5 ml)
- ▶ Topical
 - ▶ NSAIDs, lidocaine, Capsaicin

Pain - Moderate

- ▶ APAP with oxycodone (Percocet)
- ▶ Oxycodone (also available in elixir, check with pharmacy first)
- ▶ Tramadol
- ▶ APAP with tramadol (Ultracet) \$\$\$
- ▶ Tapentadol (Nucynta) and Tapentadol-ER (binds to mu-opioid receptor, inhibits norepinephrine uptake, \$\$\$\$)

Pain - Severe

- ▶ NEVER START OPIOID NAIVE PATIENT WITH LONG-ACTING OPIOID
- ▶ ALWAYS PRESCRIBE SHORT-ACTING FOR BREAK THROUGH
- ▶ Morphine-ER (mainstay)
- ▶ Oxycodone-ER (rarely covered by insurance, no reason to use if patient can take morphine)
- ▶ Oxymorphone-SR (Opana-ER) \$\$\$\$
- ▶ Methadone
 - ▶ Never first line, must be in divided doses, prescriber must be trained, experienced and comfortable using this drug
- ▶ Tapentadol-ER \$\$\$\$

Pain - Severe

- ▶ Topical
 - ▶ Fentanyl transdermal
 - ▶ Not typically first line long acting
 - ▶ Titration is slow, not recommended for uncontrolled pain
 - ▶ Lowest dose 12 ug
 - ▶ Doses above 400 mcg not effective
 - ▶ Buprenorphine transdermal
 - ▶ Dosing Q 7 days
 - ▶ \$\$\$\$

Pain - Severe

- ▶ Short-acting
 - ▶ Morphine (PO, IV, PR, SQ)
 - ▶ Oxycodone (PO and PR only)
 - ▶ Hydromorphone (PO, IV, PR, SQ)
- ▶ Fentanyl
 - ▶ Sublingual tablet (Abstral) \$\$\$\$
 - ▶ Sublingual spray (Subsys) \$\$\$\$
 - ▶ Nasal spray (Lazanda) \$\$\$\$
 - ▶ Lozenge (Actiq) \$\$\$\$
 - ▶ Buccal tablet (Fentora) \$\$\$\$

Ketamine

- ▶ Ketamine (po)
 - ▶ Parental form can be given po
 - ▶ Compounding pharmacy can make oral solution of 50 mg / 5 ml
 - ▶ Dosing 50 mg po tid
- ▶ Ketamine (IV)
 - ▶ Subtherapeutic ketamine with dosing under 0.3 mg/ kg IV have been effectively used to treat pain
- ▶ Ketamine (topical)
 - ▶ Requires compounding pharmacist
 - ▶ Creams can be 5%, 10%, 15% or 20%

References

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