Speed Dating with Pharmacists:
50 Practical Medication Tips at End of Life

Kathryn A. Walker, Pharm.D., BCPS, CPE
Asst Professor, University of Maryland Sch of Pharmacy
kwalker@rx.umaryland.edu
Mary Lynn McPherson, Pharm.D., BCPS, CPE
Professor, University of Maryland Sch of Pharmacy
mmcphers@rx.umaryland.edu

Course Materials & Disclosure

• Course materials including handout(s) and conflict of interest disclosure statement are available to download with this course.
• This presentation is for educational and informational purposes only. It is not intended to provide legal, technical or other professional services or advice.

Nothing to Disclose
Speed Dating with Drugs

- A fast exciting way to meet new people in a relaxed environment

Medication Tip #1
Medication Reconciliation

- Regimented, documented review to avoid drug errors during transitions in care
- Where does hospice stand with this?
  - Survey of two hospice programs
  - An average of 8.7 medication discrepancies per patient
    - 81% omitted medications
  - 55 additional drug interactions rated moderate or severe


Medication Tip #2
Make those dosage increases count!

- DON’T increase by a pre-conceived milligram amount!

<table>
<thead>
<tr>
<th>Increase the total daily dose of opioid by:</th>
<th>For pain levels:</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-50%</td>
<td>Mild-Moderate</td>
</tr>
<tr>
<td>50-100%</td>
<td>Moderate-Severe</td>
</tr>
</tbody>
</table>
Medication Tip #3
Quantifying PRN Opioid use
• Determining the total daily dose of opioids
  – “How many tablets do you take a day at home?”
  – “How many tablets per day do you need to stay comfortable?”
• This conveys that you believe the patient, and realize they need the opioid to achieve comfort.

Medication Tip #4
Pain Management in OAT Patients
• OAT (Opioid Agonist Therapy)
  – chronic buprenorphine or methadone, recovering from heroin abuse
• Buprenorphine patient options:
  – Change buprenorphine dosing to every 4 hours
  – Give a different opioid for pain control and continue buprenorphine
  – DC buprenorphine and begin alternate opioid, titrating to therapeutic response

Medication Tip #5
Pain Management in OAT Patients
• OAT (Opioid Agonist Therapy)
  – chronic buprenorphine or methadone, recovering from heroin abuse
• Methadone patient options:
  – Divide the once a day methadone dose into two or three doses per day and titrate to therapeutic response
  – DC methadone and begin alternate opioid, titrating to therapeutic response
Medication Tip #6
Heroin $/day

- To replace roughly equivalent methadone dose for chronic heroin users:
  - $1 per day of heroin ~ 1 mg/day methadone
  - Example: $60/day heroin use = 60 mg methadone given in divided doses (BID or TID)

Medication Tip #7
Quantifying Heroin Use

- Want to document range of typical use:
  - "how much did you use on an average day if you had money?" $80
  - "how much did you have to use each day to keep from getting ‘sick’ (withdrawing)?" $40

Medication Tip #8
Methods for Methadone Conversion

**Medication Tip #9**

**Naloxone in Opioid-Tolerant Patients**

- Is it opioid intoxication or impending death?
  - Mottling, urine output
  - Pupils, respiratory rate
- Use small doses of naloxone if indicated (don’t totally reverse the opioid – patient will go into screaming withdrawal)
  - Dilute one amp (0.4 mg) in 10 ml normal saline
  - Give 1 ml (0.04 mg) every minute until patient responds.
  - No response after two amps – it’s not the opioid!

**Medication Tip #10**

**Naloxone infusion for LA opioids**

- If opioid reversal is indicated, an infusion may be necessary if secondary to a long acting opioid agent
- Several methods:
  - 4mg in 1 L D5W, and give 100 mL/hr
  - Give 75% of the bolus dose required to reverse
- Monitor for sg/sx of withdrawal

**Medication Tip #11**

**Patient Controlled Methylphenidate (MP)**

- Patient controlled MP 5 mg q2h prn (max dose 20 mg/day) for 7d then 4wk open label
  - Improved fatigue, QOL, appetite, anxiety, insomnia with MP and placebo
  - Most patients took in afternoon/pm

Bruera E et al. JCO 2006;24:2073-2078.
Medication Tip #12
Pain Scales
Anything wrong with this assessment?! Say he says “6/10”

Medication Tip # 12 (cont’d)

Chronic (Background) Pain

Savage Chickens by Doug Savage

Hospice Education Network (c) 2013
Medication Tip #13
Ok, this is actually a PRE-medication tip...

• Pain assessment instruments

**UNIVERSAL PAIN ASSESSMENT TOOL**

[Diagram of pain assessment tool]

**FACES Scale IASP**

[Diagram of FACES Scale]

www.iasp-pain.org/fpsr

**FACES Scale IASP**

- Albanian
- Arabic
- Bulgarian
- Catalan
- Chinese
- Czech
- Dutch
- Estonian
- French
- German
- Greek
- Hebrew
- Hindi
- Hungarian (Magyar)
- Indonesian
- Italian
- Japanese
- Kannada (India)
- Laotian
- Latvian
- Lithuanian
- Malagasy (Malagache)
- Mongolian
- Norwegian
- Persian (Farsi)
- Polish
- Portuguese
- Romanian
- Russian
- Serbian
- Slovakian
- Spanish
- Swahili
- Swedish
- Tamil
- Telugu
- Thai
- Turkish
- Ukrainian
- Wallisian (Uvean)
Medication Tip #14
Proton Pump Inhibitors

• One of the most widely used group of medications in US.
• Recommended first line for serious problems related to gastric acid.
• Given with NSAIDs and CCSs for patients at risk of gastroteoxicity.

Medication Tip #14
Proton Pump Inhibitors

• PPIs are not a free ride!
• Expense!
• Association between long-term use and fracture of hip and vertebrae
  – Due to achlorhydria, leading to malabsorption and deficiencies of calcium and vitamin B12 with subsequent bone loss
  – Risks: > 50 years old, > 1 year therapy, high dose
**Medication Tip #14**
Proton Pump Inhibitors

- “Use of acid-suppressive drugs and risk of fracture: A meta-analysis of observational studies.”
- Pooled odds ratio for fracture:
  - PPIs – 1.29
  - H$_2$RAs – 1.10
- PPI’s are associated with a 29% increased risk fracture:
  - 31% increased risk hip fracture
  - 54% increased risk of vertebral fracture


**Medication Tip #14**
Proton Pump Inhibitors

- More bad news for PPIs:
  - Two fold increase in *Clostridium difficile* colitis
  - Three fold increase in the risk of other enteric infections
  - May be associated with an increased risk of ambulatory pneumonia (controversial)
  - Case reports of PPI-induced acute interstitial nephritis
  - FDA warning about PPI-induced hypomagnesemia (caution with digoxin)


**Medication Tip #15**
Fluconazole – Oropharyngeal Candidiasis

- Single dose fluconazole (Diflucan) in HIV pts
  - 150 mg fluconazole x 1 dose vs. 100 mg itraconazole once daily for a week
  - 75% of fluconazole patients cured on day 8
  - 24% of itraconazole patients cured on day 8
- 220 HIV-infected patients
  - 750 mg oral fluconazole x 1 vs. 150 mg oral fluconazole daily for two weeks
  - Equivalent outcomes

Medication Tip #16
Malodorous Wounds

- Fungating lesions from cancers growing out through the skin can be malodorous
  - Head and neck cancer
  - Breast cancer
  - Renal cancer and others
- Many potential causes, bacterial infections are a significant factor

Baker and Haig Scale of Severity
- Strong
  - Odor is evident upon entering the room (6-10 feet from the patient) with the dressing intact
- Moderate
  - Odor is evident upon entering the room (6-10 feet from the patient with the dressing removed)
- Slight
  - Odor is evident at close proximity to the patient when the dressing is removed
- No odor
  - No odor is evident, even at the patient’s bedside with the dressing removed

Management
- Eliminate bacteria (most anaerobic)
- Disinfectant solution (quarter strength Dakin’s or 1% chlorhexidine gluconate); can be harsh
- Metronidazole gel 0.75% applied to lesion
- Metronidazole 200-400 mg po tid
- Aromatherapy
- Pan of kitty litter under the bed!
Medication Tip #17
Drying Up Secretions

- Tertiary amines
  - Scopolamine, atropine, hyoscyamine
  - Cross BBB and cause sedation, delirium, antimuscarinic
- Quaternary amines
  - Glycopyrrolate – does not cross BBB
- Consider onset of action
  - Scopolamine 12 hours
- Ease of administration – atropine ophthalmic
  - Single dose vs. multi-dose?

---

Medication Tip #17
Ophthalmic atropine for secretions

- Atropine 1%
- One to two drops four times a day sublingual
- DO NOT INSTILL IN EYE
- Adverse effects – dry mouth/throat, blurred vision, palpitations, indigestion/constipation, difficulty urinating

---

Medication Tip #17
Ophthalmic pilocarpine for dry mouth

- Pilocarpine 4%
- One to two drops four times a day on tongue
- DO NOT INSTILL IN EYE
- Adverse effects – sweating, dizziness, diarrhea, nausea/stomach cramps, blurred vision, excessive salivation
Medication Tip #17
Ophthalmic products by mouth

• DOCUMENT intended purpose and route of administration
• Atropine 1% ophthalmic solution, 2 drops to be placed under tongue four times daily to treat excessive salivation.
• Pilocarpine 4% ophthalmic solution, 2 drops on tongue four times daily to treat dry mouth.

Medication Tip #18
Managing Seizures

• How to prevent or manage seizures at EOL when patients are NPO, without using an IV?
• Oral lorazepam concentrated solution
• To prevent seizures:
  – 0.5-1 mg in the buccal cavity every 6 hours
• To treat seizure activity:
  – 1 mg in buccal cavity every 5 minutes, up to 4 doses, or until seizure activity stops

Medication Tip #19
Malignant Bowel Obstruction

• Patients with advanced abdominal or pelvic cancers
• EOL patients are often not surgical candidates
• Patients c/o abdominal pain, intestinal colic, nausea and vomiting, constipation/diarrhea
• Symptom management – stool softener, antiemetics, steroids (reduce edema/inflammation)
• Consider dexamethasone and haloperidol, especially for a partial bowel obstruction
• Avoid motility agents and stimulant laxatives
Medication Tip #19
Malignant Bowel Obstruction

• H2A vs. PPIs to further reduce gastric secretions
  – Ranitidine more effective than PPIs
• Historically, next line is octreotide (Sandostatin)
  – Synthetic somatostatin analog
  – Reduces intraluminal fluid, motility and nausea/vomiting

Support Care Cancer 2009;17:1463-1468

Medication Tip #19
Malignant Bowel Obstruction

• Octreotide 600 mcg over 24 hours as a continuous subcutaneous infusion vs. placebo
  – All patients also received (over 24 hours; bolus or SQ infusion):
    • Ranitidine 200 mg
    • Dexamethasone 8 mg
    • Hydration – (10-20 ml/kg over 24 hours)


Medication Tip #19
Malignant Bowel Obstruction

• Primary outcome – number of days free of vomiting in the initial 72-hour period
  – Octreotide vs. placebo group – no difference (p=0.724)
• Secondary outcomes – Global Impression of Change score, number of vomiting episodes, symptom control, additional medication use, NG tube placement, surgery during study period
  – All nonsignificant but one
    • Octreotide group half as likely to receive hyoscine butylbromide in first 24 hours but 6x more likely by day 3

Medication Tip #20
Management of CCS-Induced HG
• Can cause DM in a previously non-DM patient, or worsen diabetes control
• MOA is multifactorial
  – CCS increase gluconeogenesis
  – Cause insulin resistance (interferes with intracellular glucose metabolism, decreasing glucose transport, and/or effects on insulin receptor binding)

• Resulting blood glucose pattern is primarily post-prandial hyperglycemia
  – Peaks at 2-3 hours, return to baseline ~ 12 hours
• Important not to rely just on fasting BG; check two hour post-steroid administration
• Treatment options
  – Glinides before or after meals
  – RA/SA insulin
  – Intermediate insulin (NPH) prior to steroid administration

Medication Tip #21
Rapid-Acting Insulin Secretagogues
• MOA – stimulates release of insulin
• Examples:
  – Repaglinide (Prandin) 0.5 mg tid (MDD 16 mg)
  – Nateglinide (Starlix) 60 mg tid (MDD 180 mg tid)
• CI/Precautions
  – Hepatic insufficiency, renal insufficiency (adjust repaglinide), hypoglycemic unawareness
  – Give 15 minutes before (or after) meals
  • Use immediately prior to meals containing either ≥250 kcal or ≥30 grams carbohydrate
  – Extra meals, extra dose; skip meal, skip dose
• Adverse effects
  – Hypoglycemia, weight gain, headache, URI
Medication Tip #22
Bladder spasms and urinary discomfort

- Bladder spasms – anticholinergic/antispasmodic agents
  - Atropine, Dicyclomine, Glycopyrrolate, Hyoscyamine, Donnatal, Propantheline
  - Dicyclomine (Bentyl)
    - 10 mg four times daily
    - Increase to 20 qid
    - Max of 40 mg qid

- Colicky bladder complaint
  - Phenazopyridine (Pyridium) - indicated for the symptomatic relief of pain, burning, urgency, frequency and other discomforts arising from irritation of the lower urinary tract
  - 100 mg tid after meals
This just in…

• Swedish researchers report that wild European perch who had measurable oxazepam serum concentrations...
  – Had increased swimming motions
  – Were bolder and more likely to leave school and explore new territories
  – Ate more food

http://www.nytimes.com/2013/02/15

And that’s not all...

• Antidepressants in the water are making shrimp suicidal...??
• Exposure to antidepressants makes shrimp FIVE times more likely to place themselves in life-threatening situation
  – Swim to the light little shrimpie...swim to the light


Medication Tip #23

SSRI and NSAID DI - Case of TY

• TY is a 78 year old man admitted to hospice with a diagnosis of metastatic prostate cancer. On admission he is complaining of the metastatic bone pain, and his prescriber orders naproxen 500 mg po q12h.
• The pharmacist call you later in the day asking what should be done about the drug interaction between the patient’s sertraline, and this new prescription (naproxen).
• What do you say?
Antidepressants

- **High SRI**
  - Fluoxetine, sertraline, paroxetine
- **Intermediate SRI**
  - Venlafaxine, amitriptyline, fluvoxamine, citalopram, imipramine
- **Low SRI**
  - Mirtazapine, bupropion, nortriptyline, desipramine, doxepin, trazodone

Odds Ratio and Antidepressants

- **High SRI group** – OR 2.6 (vs. low-SRI group)
- **Intermediate SRI group** – OR 1.9 (vs. low-SRI group)
- **High-SRI antidepressants** have higher risk of developing upper Gi bleeding vs. low-SRI
  - Even higher with h/o Gi bleed
- **3.7 fold increased risk of blood transfusions** among elderly users of SSRIs who underwent orthopedic surgery

Effect of NSAIDs

- **Concurrent NSAID or aspirin use:**
  - Relative risk 15.6 with NSAIDs
  - Relative risk 7.2 with aspirin
- **Serotonin promotes platelet aggregation; SSRIs limit uptake of blood serotonin by platelets**
- **SSRIs also appear to modify the formation of platelet plugs, as well as the responsiveness of peptide-induced activation of platelets through stimulation of the thrombin receptor**

Mansour A et al. J Fam Prac 2006;55(3).
NSAIDs and Antidepressants

- SSRIs increase risk of bleeds, admission for abnormal bleeding and perioperative transfusion.
  - The higher degree of SRI, the higher the risk of bleeding
- Concomitant use of NSAIDs or aspirin further increases this risk

Medication Tip #24
Citalopram (Celexa) Safety Risk

- August 2011 – FDA issued Drug Safety Communication
  - Citalopram should no longer be used at doses > 40 mg per day due to QT prolongation (previous max was 60 mg per day)
- March 2012 – FDA updated warning

http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm#professionals

Medication Tip #24
Citalopram (Celexa) Safety Risk

- Maximum dose of 20 mg for patients:
  - Hepatic impairment
  - Over 60 years of age
  - CYP2C19 poor metabolizers
  - Taking cimetidine or other CYP2C19 inhibitors
- Not recommended in patients with:
  - Congenital QT prolongation
  - Concomitantly with other QT prolonging drugs
  - Uncompensated HF
  - Bradycardia
  - Predisposition to hypokalemia and hypomagnesemia
  - Recent MI

http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm#professionals
Citalopram and Escitalopram: 
Dose-dependent Change in QTc

<table>
<thead>
<tr>
<th>SSRI</th>
<th>Usual daily dose</th>
<th>Oral solution/suspension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram (Celexa)</td>
<td>20-40 mg per day</td>
<td>Oral solution 20 mg/5 ml (5-20 ml/day)</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>10-20 mg per day</td>
<td>Oral solution 5 mg/5 ml (10-20 ml/day)</td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>20-80 mg/day</td>
<td>Oral solution 20 mg/5 ml (5-20 ml/day)</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>50-200 mg/day</td>
<td>Oral concentrate 20 mg/ml (5-10 ml/day)</td>
</tr>
<tr>
<td>Paroxetine (Paxil)</td>
<td>20-50 mg per day</td>
<td>Oral suspension 10 mg/5 ml (2.5-10 ml/day)</td>
</tr>
</tbody>
</table>

Medication Tip #25
Non-tablet Antidepressants

- Recognition that although citalopram use should be avoided, if possible, in patients with certain conditions because of QT prolongation risk, ECG and/or electrolyte monitoring should be performed if citalopram must be used in such patients.
- Patients with congenital long QT syndrome are at particular risk of Torsade de Pointes, ventricular tachycardia, and sudden death when given drugs that prolong the QT interval. Nevertheless, labeling recommendation for patients with congenital long QT syndrome has been changed from “contraindicated” to “not recommended,” as it is recognized that there may be some patients with this condition who could benefit from a low dose of citalopram and lack viable alternatives.
- The maximum recommended dose of citalopram is 20 mg per day for patients older than 60 years of age.
- Citalopram should be discontinued in patients who are found to have persistent QTc measurements greater than 500 ms.
Approximate Equivalent SSRI Doses

- Fluoxetine 20 mg
- Paroxetine 20 mg
- Sertraline 50-75 mg
- Citalopram 20 mg
- Escitalopram 10 mg
- Fluvoxamine 100 mg

Medication Tip #26
Antidepressants activating vs sedating

<table>
<thead>
<tr>
<th>Sedating</th>
<th>Activating</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Paroxetine</td>
<td>• Fluoxetine</td>
</tr>
<tr>
<td>(Paxil)</td>
<td>(Prozac)</td>
</tr>
<tr>
<td>• Mirtazapine</td>
<td>• Venlafaxine</td>
</tr>
<tr>
<td>(Remeron)</td>
<td>(Effexor)</td>
</tr>
<tr>
<td>• Sertraline (Zoloft)</td>
<td></td>
</tr>
<tr>
<td>• Citalopram (Celexa)</td>
<td></td>
</tr>
</tbody>
</table>
Medication Tip #27
Urine Drug Testing

- Two types of tests: screening and confirmatory
- Limitations:
  - Can NOT tell you timing, route, amount
  - Screening can only detect natural opioids (morphine/codeine) NOT synthetic
  - Metabolites can confuse results
    - Heroin and codeine → morphine
    - Cross-reactivity can lead to false positive results

Medication Tip #28
Topical Salicylates

- Mechanism of action – counterirritant
  - May interfere with transcription factors and kinases involved in inflammatory processes
  - Do not appear to work through COX inhibition
    - 100-fold less potent than COX-2 inhibitors
- Trolamine salicylate – undetectable in serum
- Methyl salicylate applied for four days
  - BenGay, Icy Hot
  - Achieved a low systemic serum concentration
- Efficacy – poor in chronic pain states

Altman R, Barkin RL. Postgraduate Medicine 2009;121:139-147.

Medication Tip #28
Topical Salicylates

- Safety
  - Methyl salicylate has been associated with severe toxicity and deaths after topical application or with accidental or deliberate ingestion
  - Methyl salicylate potentiates effects of warfarin, increasing bleeding risk
  - Adverse side effects more similar to oral NSAIDs compared to other topical products
    - Must consider safety profile when using in patients (decision to avoid ORAL NSAIDs is a reason to avoid using topical salicylates)

Altman R, Barkin RL. Postgraduate Medicine 2009;121:139-147.
Medication Tip #29
Benadryl for sleep

- Very common in OTC sleep products
- Cautions:
  - Sedation
  - Anticholinergic side effects
  - Tolerance

Medication Tip #30
MNTX for OIC

- 1.5 million Americans are treated with an opioid each year
  - Analgesic benefit = central effect
  - ADE (e.g., constipation) = peripheral receptors
- OIC usually prevented/treated with docusate and senna

Peripheral Opioid Antagonists

Block peripheral effects of opioids (mu antagonist) without crossing blood-brain barrier to reverse centrally mediated analgesia

- Alvimopan (Entereg)
- Methylaltrexone (Relistor)
Medication Tip #30
Methylnaltrexone (Relistor)

- Every other day dosing (SQ)
  - 8 mg for patients 84-136 pounds
  - 12 mg for patients 136 to 251 pounds
  - Reduce in patients with severe renal impairment

- Adverse effects
  - Abdominal pain (29%), flatulence (13%)
  - Nausea (12%), dizziness (7%), diarrhea (6%)

- Contraindication: mechanical GI obstruction

Not studied for more than 4 months use

Methylnaltrexone (Relistor)

- Dosage form: Single use vial (12 mg)
- Median times of laxation: 70 min (0.15 mg/kg SQ)
- No change in pain or withdrawal symptoms

$40/vial

Medication Tip #31
Drug-Induced Constipation

<table>
<thead>
<tr>
<th>Therapeutic Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics</td>
<td>Opioids (morphine), NSAIDs (ibuprofen)</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>TCAs, antipsychotics (haloperidol), antiparkinsonian agents (benztropine), antihistamines (H1), antispasmodics (dicyclomine)</td>
</tr>
<tr>
<td>Cation-containing agents</td>
<td>Aluminum (acetate, sucralfate), calcium (acetate, supplements), bismuth, iron supplements, lithium</td>
</tr>
<tr>
<td>Chemotherapies</td>
<td>Vinca alkaloids (vinorelbine), alkylating agents (cyclophosphamide)</td>
</tr>
<tr>
<td>Anthelmintics</td>
<td>Praziquantel, metronidazole, ivermectin (ivermectin)</td>
</tr>
<tr>
<td>Bile acid sequestrants</td>
<td>Cholestyramine, colestipol</td>
</tr>
<tr>
<td>5HT3 receptor antagonists</td>
<td>Ondansetron</td>
</tr>
<tr>
<td>Laxatives</td>
<td>Chronic abuse</td>
</tr>
</tbody>
</table>

Medication Tip #31
Drug-Induced Constipation

<table>
<thead>
<tr>
<th>Therapeutic Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excess fiber</td>
<td>Dietary or prescribed</td>
</tr>
<tr>
<td>Other antidepressants</td>
<td>Monoamine oxidase inhibitors</td>
</tr>
<tr>
<td>Other antiparkinsonian agents</td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Other antispasmodics</td>
<td>Peppermint oil</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Barium sulphate, cholestyramine, polystyrene resin, oral contraceptives, Vitamin C tablets, ¹³¹I thyroid ablation, erythropoietin, backlofen, Pamidronate, alendronic acid, PPI and H₂ antagonists</td>
</tr>
</tbody>
</table>

Rating Scale for Bowel Movements

Type 1: Separate hard lumps, like nuts
Type 6: Fluffy pieces with ragged edges, a mushy stool
Type 7: Watery, no solid pieces

Too Tired to Give A “Poop”
EXHAUSTIPATED!!!

Medication Tip #32
Withdrawing NPPV at EOL

• Reasons to D/C Non-Invasive Positive Pressure Ventilation (NPPV):
  1. Inadequate dyspnea relief >1 hr at max setting
  2. Patient is no longer alert
  3. No longer consistent with goals of care
• If discontinuing... think VENT W/D:
  – SOB: Opioid
  – Agitation/Anxiety: Benzodiazepines
  – Titrate to comfort with mask on
  – Prepare to titrate quickly after removal if needed
Medication Tip #33
Turning up the Heat on Hot Flashes

• Often under-recognized impact on quality of life
• Detailed assessment is key: sx, triggers/patterns, impact on daily life, diary
• Treatment:
  – Independent of tx-related or gender

Medication Tip #33
Turning up the Heat on Hot Flashes

• Hormonal therapy: estrogen and progestins effective in men/women
• Antidepressants (3-41% vs placebo): SSRI or SNRI
  – Venlafaxine, citalopram more effective and low risk of tamoxifen DI (like paroxetine/fluoxetine)
• Gabapentin (35-38% vs placebo): 900-2400 mg/day
• Clonidine: marginal benefit

Medication Tip #34
Daily Lidoderm Patches

• Randomized, prospective, multiple-dose, open-label pharmacokinetic study
• Ten subjects – four lidocaine patches every 24 hours (group 1)
• Ten subjects – four lidocaine patches every 12 hours (group 2)
• Serum samples of blood drawn to assess skin data and overall tolerability and safety were assessed with skin sensory testing
Medication Tip #34
Pharmacokinetics and safety of continuously applied lidocaine patches 5%

- Mean steady-state Cmax values:
  - Group 1 (every 24 hours) = 186 ng/ml
  - Group 2 (every 12 hours) = 225 ng/ml
- 1/7 that of antiarrhythmic effect (~ 1500 ng/ml)
- 1/25 that at which toxicity increases (~ 5000 ng/ml)
- No sensory alterations at patch administration site

Medication Tip #35
Converting to Transdermal Fentanyl
• Use caution relying on the manufacturer’s guidelines for converting to TDF
  – Intentionally conservative
  – CANNOT use in reverse
• Total daily dose of oral morphine ~ transdermal fentanyl patch strength in mcg/ml
  – Oral morphine TDD 100 mg ~ TDF 50 mcg/hour
• Consider body habitus

Medication Tip #36
Speaking of body habitus...
• One study confirms that thin, cachectic cancer patients don’t receive the anticipated benefit from TDF as expected
• When converting OFF TDF, use the last dose where patient responded


Medication Tip #37
Mind the Gap... Of TDF analgesic onset!
• Onset 12-24 hours

[Diagram: MIND THE GAP TDF 0 12 24 Day 1]
Medication Tip #37
Mind the Gap... Of TDF analgesic onset !
• Onset 12-24 hours

![Graph showing onset of TDF analgesic effect](image)

Medication Tip #38
DDIs in Palliative Care
• Retrospective chart review of 200 consecutive PC unit inpatient
• 631 potential DI in 151 patients (75%)
• Median number of meds: 14 (2-25)
• Common DI meds: scopolamine, neuroleptics, metoclopramide, antihistamines, non-steroidal anti-inflammatory drugs, (levo-)methadone, amitriptyline, carbamazepine and diuretics
• No documentation of clinical relevance in high risk for severe DI patients (n=8)

Medication Tip #38
Top Offenders

Red Flag Score: if DDIs class 1-4 per pt. exposed.
Medication Tip #39
Anticoagulation at EOL

- Thromboembolic disease in cancer patients
  - Patients are a higher risk of thromboembolism
  - Patients are at higher risk of bleeding
Medication Tip #39
Anticoagulation at EOL

- Nonvalcular atrial fibrillation
- Anticoagulation does not affect (reduce) symptoms
- AC reduces the absolute risk of stroke by approximately 4% per year
- Median LOS in hospice is < 20 days
- If risk were evenly distributed over time, this would be a 0.22% absolute reduction in stroke risk while enrolled in hospice.

OUCH!


Medication Tip #40
Swearing Shown to Reduce Pain

- Swearing has been shown to allow subjects to withstand discomfort longer, and reduce perception of pain intensity.
- Curse words = coping
- Swearing is cathartic; like a dog or cat yelping in pain if you step on his tail
- This is seen to greater effect in women

Curse Word Formulary

Darn, Nuts, Fudge

Curse Word Formulary

Son of a sea biscuit!
Gosh darn it!
Darn, Nuts, Fudge

Curse Word Formulary

*&^$!, (@))$, *
*
Son of a sea biscuit!
Gosh darn it!
Darn, Nuts, Fudge
Therapeutic Cursing

Medication Tip #41
Drug-Induced ER Admission in Elders

- 2007-2009 data used to estimate:
  - Frequency and rates of hospitalization after ER visits for ADRs in older adults (> 65 years old)
  - Nearly half were in adults > 80 years
  - Nearly 2/3 were due to unintentional OD’s
  - Four medications/medication classes were implicated


Medication Tip #41
Drug-Induced ER Admission in Elders

% Hospital Admissions

- Warfarin
- Insulins
- Oral antiplatelets
- Oral hypoglycemics

Medication Tip #42
All things furosemide...

• What does the name LASIX mean?

**Lasts six hours**

---

**Furosemide Facts**
- Taking with food reduces bioavailability by 30-50%
- *Furosemide vs. torsemide*
  - In systolic HF torsemide significantly reduced total HF readmissions and CV readmissions
  - Torsemide caused a 14% reduction in all-cause mortality
- Torsemide has less inter- and intra-individual variation in bioavailability; longer duration

---

**Equivalencies**
- *Furosemide IV to PO is 1:2*
  - 20 mg IV furosemide = 40 mg PO furosemide
  - Furosemide 40 mg PO ~ Torsemide 20 mg PO
  - Torsemide and Bumetanide IV to PO conversion is 1:1
Medication Tip #43
That dog just WON’T hunt!
• Don’t use topical lorazepam (Ativan),
diphenhydramine (Benadryl), haloperidol
(Haldol) (“ABH”) gel for nausea! Ever!
  – Topical application of medications (NSAIDs)
  – ABH not absorbed systemically at beneficial levels
  – Diphenhydramine is absorbed somewhat
    • Delayed and erratic absorption, contact dermatitis
• Consider targeted drug therapy; intensols

http://www.aahpm.org/advocacy/default/choosing-wisely.html

Medication Tip #44
Maybe you shouldn’t be driving Miss Daisy...
• Hospice/PC patients are complicated
  – Multiple comorbidities, taking many medications
• “Opioid Dose and Risk of Road Trauma in Canada”
  – 5300 cases of road trauma requiring ER services (18-
  64 years old)
  – Matched controls (age, sex, index year, prior road
  trauma, disease risk index)
  – Stratified by opioid dose (very low < 20 OME; very
  high ≥ 200 mg OME)


Medication Tip #44
Maybe you shouldn’t be driving Miss Daisy...
• There was a significant association between
  opioid dose and road trauma
  – Very low dose OME – 21% increased odds of road
    trauma
  – Moderate dose OME – 29% increased odds
  – High dose OME – 42% increased odds
  – Very high dose OME – 23% increased odds
• Concluded opioid therapy increases risk of
  road trauma

Medication Tip #43

Maybe you shouldn’t be driving Miss Daisy...

1. Is your patient driving?
2. Assess overall medical condition (vision, cardiopulmonary/neurologic/psych/MS disease, medication use).
3. Assess for impairment in traffic skills (impaired ADLs, patient/family/caregiver questionnaire, physical examination).
4. If there are concerns, discuss/recommend with patient/family.
5. Educate and counsel patient/family about alternatives.
6. Consider submitting report to DMV if appropriate.


Medication Tip #45

Getting patients to swallow “pills”

- Take several deep breaths to relax neck and throat muscles.
- Hold an ice cube or popsicle in your mouth to numb your throat and calm your gag reflex.
- Take a drink of water before placing pills on your tongue.
- Place the pill on the tip of your tongue. (Others recommend the middle of the tongue. Try both -- see what works for you.)
- Don’t psych yourself out by thinking “I’m taking a PILL”. Think “FOOD.” If you are thinking “PILL”, you will feel your throat tightening.
Medication Tip #46
Maximizing drug delivery from a MDI

- Before actuating the MDI, pick a spot where the wall meets the ceiling and watch it while you inhale the drug
- Elongates throat
- Enhances deposition
- Probably reduces thrush!
Medication Tip #47
Mirabegron (Myrbetriq)

- XR tablets for tx of overactive bladder
- MOA – β3-adrenergic agonist that relaxes a muscle involved with the storage of urine in the bladder
- Dose - 25 mg once qd, with or without food
  - Can increase to 50 mg/day based on response and tolerability of medication
  - Do not exceed 25 mg a day with severe renal impairment or moderate liver impairment

Medication Tip #47
Mirabegron (Myrbetriq)

- Contraindicated – ESRD, severe liver disease, uncontrolled hypertension
- Do not administer with antimuscarinic drugs for overactive bladder symptoms or patients with bladder outlet obstruction
- AE – nasopharyngitis, UTI, constipation, fatigue, hypertension, tachycardia and abdominal pain

Medication Tip #47
Mirabegron (Myrbetriq)

- Drug IA – 2D6
  - Increases metoprolol, desipramine levels
- Effectiveness
  - All are only modestly effective – reduce frequency and incontinence episodes by < 1 episode/day
- Antimuscarinic agents
  - One in seven patients benefit
  - One in five patients experience antimuscarinic adverse effects
Drugs for Overactive Bladder

<table>
<thead>
<tr>
<th>Name</th>
<th>Mechanism</th>
<th>Cost/month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darifenacin (Enablex)</td>
<td>Antimuscarinic</td>
<td>$150</td>
</tr>
<tr>
<td>Fesoterodine (Toviaz)</td>
<td>Antimuscarinic</td>
<td>$150</td>
</tr>
<tr>
<td>Oxybutynin (Ditropan)</td>
<td>Antimuscarinic</td>
<td>$20</td>
</tr>
<tr>
<td>Oxybutynin XL (Ditropan XL)</td>
<td>Antimuscarinic</td>
<td>$75</td>
</tr>
<tr>
<td>Oxybutynin Gel (Gelnique)</td>
<td>Antimuscarinic</td>
<td>$170</td>
</tr>
<tr>
<td>Oxybutynin Patch (Oxytrol)</td>
<td>Antimuscarinic</td>
<td>$225</td>
</tr>
<tr>
<td>Solifenacin (Vesicare)</td>
<td>Antimuscarinic</td>
<td>$190</td>
</tr>
<tr>
<td>Tolterodine (Detrol)</td>
<td>Antimuscarinic</td>
<td>$160</td>
</tr>
<tr>
<td>Tolterodine LA (Detrol LA)</td>
<td>Antimuscarinic</td>
<td>$175</td>
</tr>
<tr>
<td>Trospium (Sanctura)</td>
<td>Antimuscarinic</td>
<td>$170</td>
</tr>
<tr>
<td>Trospium XR (Sanctura XR)</td>
<td>Antimuscarinic</td>
<td>$190</td>
</tr>
<tr>
<td>Mirabegron (Mybetriq)</td>
<td>Beta-3 agonist</td>
<td>$210</td>
</tr>
</tbody>
</table>

Oxytrol approved OTC for Women!

- Indication – overactive bladder
- Women 18 years and older
- Every 4 days transdermal patch
  - Delivers 3.9 milligrams/day
- Adverse effects – skin irritation, constipation, dry mouth (fewer than oral therapy)
- Still Rx for men
- Available Fall 2013

Dude??

- Merck’s studies showed only female consumers appropriately understood info on label, and determine if this product was right for them.
Duh...

• You do NOT need a drug for overactive bladder if the patient is catheterized.

Medication Tip #48
Nonbenzodiazepine Sedative Hypnotics

• FDA news release 1-10-13
  – Requiring manufacturers of zolpidem containing products to lower doses for women; consider lowering for men
  – Serum levels > 50 ng/ml can:
    • Seriously impair driving performance
    • Increase risk of falls in the elderly
    • Cause anterograde amnesia, complex sleep behaviors and hallucinations

http://www.fda.gov/Drugs/DrugSafety/ucm334033.htm

Medication Tip #48
Nonbenzodiazepine Sedative Hypnotics

• Recent case-crossover study found risk of hip fracture was 66% higher during the month after patients were given one of the newer insomnia medications
  – Zolpidem (Ambien), eszopiclone (Lunesta), zaleplon (Sonata)
  – Risk especially high during the two weeks after starting therapy

Medication Tip #49

Codeine and 2D6 Ultrametabolizers

- FDA Drug Safety Communication
  - Codeine use in certain children after tonsillectomy and/or adenoidectomy may lead to rare, but life-threatening adverse events or death
    - Obstructive sleep apnea
  - Children are ultra-metabolizers at 2D6
    - Codeine is metabolized to morphine

Polymorphic distribution for CYP2D6

- Polymorphic = a trait that has differential expression in >1% of the population

Zolpidem Dosing Recommendations for Adults (Non-Elderly)

<table>
<thead>
<tr>
<th>Dosing recommendations in current drug label for zolpidem</th>
<th>FDA's proposed new dosing recommendations for zolpidem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambien, Edluar, Zolpimist</td>
<td>Men: 10 mg once daily, immediately before bedtime; Women: 5 mg once daily, immediately before bedtime</td>
</tr>
<tr>
<td></td>
<td>Men: 5 or 10 mg once daily, immediately before bedtime</td>
</tr>
<tr>
<td>Ambien CR</td>
<td>Men: 12.5 mg once daily, immediately before bedtime; Women: 6.25 mg once daily, immediately before bedtime</td>
</tr>
<tr>
<td></td>
<td>Men: 6.25 mg or 12.5 mg once daily, immediately before bedtime</td>
</tr>
</tbody>
</table>


Polymorphic = a trait that has differential expression in >1% of the population

### Metabolizer status in racial/ethnic groups

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Phenotype</th>
<th>Frequencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP1A2</td>
<td>PM</td>
<td>Caucasians 12%</td>
</tr>
<tr>
<td>CYP2C9</td>
<td>PM</td>
<td>Caucasians 2-6%</td>
</tr>
<tr>
<td>CYP2C19</td>
<td>PM</td>
<td>Caucasians 2-6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chinese 15-17%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Japanese 18-23%</td>
</tr>
<tr>
<td>CYP2D6</td>
<td>PM</td>
<td>Caucasians 3-10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chinese/japanese/ AA &lt; 2%</td>
</tr>
<tr>
<td></td>
<td>UR</td>
<td>Ethiopians 20%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hispanics 7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Scandinavians 1.5%</td>
</tr>
</tbody>
</table>

PM – poor metabolizer  
UR – ultra-rapid metabolizer

Pain Medicine 2004;5(1):81-93

### Examples in palliative care

- **Codeine (CYP2D6)**
  - Poor metabolizers are unable to convert codeine to morphine (no pain relief)
  - Ultra metabolizers at increased risk of toxicity
- **Hydrocodone, oxycodone (CYP2D6)**
  - Structurally similar to codeine and as such their metabolism could be under genetic control leading to variability of clinical response (side effects, efficacy, and dependence)


### Examples in palliative care

- **Phenytoin (CYP1A2, CYP2C9, CYP2C19)**
  - Phenytoin toxicity for poor metabolizers; low levels of drug for ultra-rapid metabolizers at therapeutic doses
- **Diazepam (CYP2C19, CYP3A4)**
  - Unacceptable prolonged sedation in poor metabolizers, unconsciousness noted more in Asian populations

Examples in palliative care

- Venlafaxine (CYP2D6)
  - Metabolism slower in those lacking a functional CYP2D6 gene
- Nortriptyline (CYP2D6, CYP1A2)
  - Ultra-rapid metabolizers require up to 500 mg/day to reach therapeutic dose


Medication Tip #50
Don’t Make Me Sleepy...

<table>
<thead>
<tr>
<th>Medication</th>
<th>Relative potency (mg)</th>
<th>Common dosage (mg/d)</th>
<th>Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Generation Antipsychotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>100.0</td>
<td>300-600</td>
<td>Moderate</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>1-2</td>
<td>4-20</td>
<td>Mild</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>2</td>
<td>5-20</td>
<td>Mild</td>
</tr>
<tr>
<td>Second Generation Antipsychotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>7.5</td>
<td>15-30</td>
<td>Mild</td>
</tr>
<tr>
<td>Clozapine</td>
<td>50</td>
<td>250-500</td>
<td>Marked</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>4</td>
<td>15-30</td>
<td>Moderate</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>80</td>
<td>300-800</td>
<td>Moderate</td>
</tr>
<tr>
<td>Risperidone</td>
<td>1</td>
<td>2-6</td>
<td>Mild</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>20</td>
<td>80-160</td>
<td>Mild</td>
</tr>
</tbody>
</table>

Medication Tip #50
Don’t Make Me Sleepy...

- Quetiapine – antagonizes several receptors:
  - Serotonin 5HT (1A) and 5HT (2)
  - Dopamine D (1) and D (2)
  - Histamine H (1)
  - Adrenergic alpha (1) and alpha (2)
  - No affinity for cholinergic muscarinic or benzodiazepine receptors
One last tip for the road (or, sky, as the case may be...)

A peaceful death is like landing a jet plane - both are best done slowly and gradually, with lots of advance preparation and early/small course corrections.

- You don’t want to pull a sudden sharp bank left while diving steeply.
- Treat symptoms early and consistently
- Adjust medication doses as needed

And Palliative Care!

Course Evaluation & Post-Test

Thank you for viewing this course on the Hospice Education Network.

To conclude this course and to obtain a certificate of completion, you must finish the evaluation and post-test.