Specialized Geriatric Addictions Community of Interest Fact Sheet #4

Opioids, benzodiazepines and the elderly: A pocket guide

OPIOIDS AND CHRONIC PAIN

Chronic pain is a major cause of disability in the elderly. According to the POWER study (a review of the health status of women in Ontario), 31% of women aged 75 and older are limited in their activities of daily living because of arthritis-related pain. Unfortunately, treatment options are limited. NSAIDs must be prescribed with caution, and physicians are reluctant to prescribe opioids because of an increased risk of falls and sedation. But opioids have an important role to play in therapy. Elderly patients with severe biomedical pain conditions often respond very well to low doses of opioids. They are at low risk for opioid addiction, and falls and sedation can be minimized with careful titration.

Opioid Definition: ***Opioids act on the mu endorphin receptors in the central nervous system to relieve pain, decrease bowel motility and (at higher doses) suppress consciousness and respiration.***

Indications for opioid therapy

- Patient has a well-defined pain condition (nociceptive or neuropathic) causing both *pain* and *disability*
- Non-opioid treatments are ineffective, contraindicated, or have intolerable side effects.

Contraindications and precautions

- Currently drinking alcohol heavily
- Cognitively impaired and living alone (unless medication supervision can be arranged)
- Renal impairment
    - Butrans (buprenorphine patch) is preferred in this situation)
- High risk for falls

Prior to prescribing opioids

- Ask about current and past use of alcohol and other drugs
- Ask about mood. Depressed patients tend to have a heightened perception of pain and are less responsive to opioid therapy.
- Check renal and respiratory status, especially risk of sleep apnea.
- Assess risk of falls.
- Consider tapering benzodiazepines (see below)
- Ask about the impact of pain on activities of daily living, eg walking, cooking, visits to family and friends. Have the patient rate the severity of their pain on a 0-10 scale, at rest and with activity.
- Reassess their response to non-opioid treatments, i.e.:
    - **Nociceptive pain – acetaminophen, NSAIDs etc**
    - **Neuropathic pain – anticonvulsants, SNRI's etc**
    - **All types of pain: Mindfulness programs, graded exercise**

Advice and warnings to patient and family

- Advise patients not to drink alcohol at all during the initial titration
- For high risk patients, call the patient or family 1-3 days after initiating opioid therapy to assess for sedation or falls.
- Warn patients and their family members that they may experience some sedation in the first few days after initiation or a dose increase. They should be cautious when getting up, walking, climbing stairs, or driving.
- Warn patients to never take more than prescribed.

- Warn patients to keep their opioid safely stored, and not to give any opioid medications to relatives or friends. Advise patients to contact the physician if a younger family member persistently asks for the opioid,

Office visits

- See the patient frequently during initiation and titration.
- At each office visit, ask about changes in:
  - Social visits and ADL
  - Pain ratings on 0-10 scale, at rest and with activity
  - Mood
- Ask about side effects, especially:
  - Sedation, dizziness and other CNS effects
  - Constipation, nausea
  - Unsteadiness, falls

Oral opioid analgesic conversion table

Opioid	**Equivalence values**
Morphine	30 mg
Codeine	200 mg
Oxycodone	20 mg
Hydromorphone	6 mg
Tapentadol	No equivalence to morphine established but CR has demonstrated comparable pain relief to oxycodone CR (dose ratio 5:1)
Transdermal buprenorphine	No equivalence to morphine established
Transdermal fentanyl	25 μg/hr = 60-134 mg oral morphine per day

Opioid Prescribing protocol

Immediate Release versus Controlled Release

- Initiate opioid trial with Immediate Release (IR) preparations
- Maintain on IR for brief pain (less than 4 hours) or incident pain (triggered by activity)
- For constant pain throughout the day, switch to Controlled Release (CR)
- In long term therapy for constant pain throught the day, IR preparations should not exceed 10-30% of total daily opioid dose

Opioid selection

- Always initiate opioid treatment with the "weak" opioids, ie oral preparations of codeine, tramadol (e.g. Tramacet®, Ultram®, Zytram XL®), or buprenorphine patch (BuTrans®). These medications are effective, and evidence suggests they have a much lower risk of overdose, addiction, sedation and falls than the potent opioids..
- If insufficient analgesia with first-line opioids, prescribe morphine (various generics), oxycodone (various generics, OxyNEO®) and hydromorphone (e.g. Dilaudid®, Hydromorph Contin, Jurnista®)
- Morphine is contraindicated in patients with renal insufficiency. Some evidence suggests that hydromorphone and oxycodone have fewer cognitive effects than morphine in the elderly.
- Prescribe transdermal fentanyl (various generics, Duragesic®) with extreme caution in the elderly. It is very easy to overdose on the patch. Use only if the patient has taken at least 60-100 mg morphine equivalent daily (MED) for at least 2 weeks *(see equivalence table below).*

Initial opioid dose

The elderly are at higher risk for opioid toxicity than younger patients. The initial dose should be no more than half the dose for younger adults, and the interval between dose increases should be at least twice as long.

Opioid titration table for elderly patients

Opioid	Maximum initial dose	Maximum dose increase	Minimum number of days between increases*	Minimum IR dose before conversion to CR
Codeine	100 mg/d	50 mg/d	14 days	150 mg
Transdermal buprenorphine	5 μg/7d	5 μg/7d	7 days	-------
Morphine	20 mg/d	10 mg/d	14 days	30 mg
Oxycodone	15 mg/d	5 mg/d IR, 10 mg/d CR	14 days	20 mg
Hydromorphone	4-5 mg/d	1-2 mg/d IR, 2-4 mg/d CR	14 days	6 mg

***DOSE INCREASES SHOULD NOT BE AUTOMATIC BUT SHOULD BE BASED ON AN INDIVIDUAL ASSESSMENT**

IR = Immediate Release, CR = Controlled Release

Optimal Dose

- Increase dose if insufficient analgesia and no improvement in function. Optimal dose reached if:
- Pain relief at least 2 points on 10 point scale, with no benefit from 1-2 additional increases
- Increased social activity and activities of daily living
- No major side effects

Maximum or "watchful" dose

Opioids have dose-related complications, including overdose, sleep apnea, and falls and fractures. Canadian Guideline's "Watchful dose" is 200 mg Morphine Equivalents per Day (MED, but doses above 120 mg are strongly associated with an increased risk of overdose. We would suggest a watchful dose of 60 mg MED for the elderly, ie one-half the dose associated with overdose in younger patients. (MED 60 mg = 40 mg oxycodone, 240 mg codeine, or 12 mg hydromorphone). At doses above 60 mg MED, the physician should reassess the opioid's analgesic effectiveness and side effects, and decide whether to maintain the dose or taper.

Minimizing adverse effects: Falls, sedation, overdose, constipation

Preventing Falls

- Do not prescribe opioids to cognitively impaired patients unless dispensed and overseen by a caregiver.
- Taper benzodiazepines (see section below)
- Avoid use of opiods at night if possible. If pain wakes the patient up, prescribe the smallest IR opioid dose and warn patients to take extra precautions when getting out of bed.

Preventing sedation and overdose

- Taper benzodiazepines
- Warn patients not to drink alcohol
- Strictly follow guidelines for initial dosing and dose titration
- Warn patients not to take extra doses
- Have an early warning system during initiation or titration of potent opioids: Family members should contact the doctor or call emergency services at the first sign of an overdose. Sedation, slowed speech, 'nodding off' are all early signs of an impending overdose. Patient may appear relatively alert in conversation, yet have respiratory arrest at night while asleep.

Fatigue

Opioids can cause fatigue, either through a direct sedating effect or by contributing to sleep apnea. Patients who report day-time fatigue and/or reduced function should be assessed for sleep apnea. Their opioid dose should be reduced or discontinued, or the opioid should be switched.

Constipation

- Increase fiber, fluid, activity
- If laxatives needed, consider polyethylene glycol (Restorolax), sodium picosulphate (Dulcolax) or lactulose. Polyethylene glycol may be more effective than the others for opioid induced constipation.
- If still troublesome, decrease dose or switch to different opioid
- **Constipation can be the cause of disturbed behaviour**

Opioid tapering

When should the opioid dose be tapered?

- The patient has persistent severe pain and pain related disability despite an adequate dose (eg 60 mg/d morphine equivalent). Evidence suggests that in these circumstances, tapering improves pain, mood and functioning.

- OR-

- The patient has a complication from opioid therapy, e.g. sleep apnea, sedation, and dysphoria.

Outpatient opioid tapering protocol

Formulation	Sustained release preferred (until low dose reached)
Dosing interval	Scheduled doses rather than PRN Keep dosing interval the same for as long as possible (BID or TID) Advise patients not to skip or delay doses
Rate of taper	Taper slowly, no more than 10% of total daily dose EVERY 1-2 WEEKS Let patient choose which dose is decreased (AM, PM or HS) Taper even more slowly when 1/3 of total dose is reached.
Dispensing interval	If patient runs out early, increase frequency to weekly, alternate day or daily
End point of taper	Less than or up to 60 mg of MED ('suggested watchful dose in elderly) This dose should control pain with minimal side effects
Frequency of visits	If possible, see patient prior to each dose decrease
Approach at each visit	Ask not just about withdrawal symptoms but benefits of tapering: more alert, less fatigued, improved mood, improved pain,

Opioid switching: Indications

- Inadequate analgesic response (<2/10 pain relief, no improvement in function)
- Adverse effects e.g. constipation, sedation, falls

Switching Protocol
Because the patient will not be fully tolerant to the new opioid, its MED should be **50%** of the MED of original opioid. *Example*: When switching a patient from 40 mg/d of oxycodone to hydromorphone: a) 40 mg/d oxycodone = 60 mg MED. b) 60 mg MED = 12 mg hydromorphone/d. c) 50% of hydromorphone 12 mg = 6 mg. Therefore start the patient on 6 mg/d in divided doses. Ensure the patient understands that taking extra doses is dangerous. Titrate the dose using the table above.

Opioid Misuse and Addiction

Limiting misuse and diversion
Parents and older relatives are a major source of illicit opioids for adolescents and young adults.

- Warn patients to store their medication in a locked box or other secure location, do not show them to younger relatives, and never share them with others.
- Avoid using the patch in elderly patients with younger adults at home. (Used patches contain a large amount of fentanyl, and young people sometimes simply lift the patch off their elderly relative's skin while they are sleeping.)
- Without anyone else in the office, ask the patient if younger relatives are using their opioid, especially if the patient requires high doses, runs out early, or is accompanied by a younger adult to the office visits.

Prescribing opioids to elderly patients at higher risk for opioid misuse/addiction
Risk factors include co morbid depression and anxiety, or a past history of addiction to alcohol or other drugs. The following precautions are advised for high-risk patients with a chronic pain condition requiring opioid therapy:

- Titrate slowly, keeping the maintenance dose below 60 mg MED
- Dispense small quantities frequently (e.g. 1-3 times per week)
- Watch for aberrant behaviours (running out early, accessing opioids from other sources)
- Use urine drug screens, pill counts and regular office visits to monitor compliance

OPIOID WITHDRAWAL

Time course	Symptoms start six hours after last use of IR opioid, peak at 2-3 days, and begin to resolve by 5-7 days. Psychological symptoms, though, can last for weeks.
Physical symptoms	Flu-like: Myalgias, chills, nausea and vomiting, abdominal cramps, diarrhea
Psychological symptoms	Insomnia, extreme anxiety and irritability, dysphoria and drug craving
Complications	a. Suicide. b. Overdose if opioids taken after a period of abstinence (loss of tolerance). c. Possibly gastric or duodenal ulcer. d. Acute exacerbation of cardiorespiratory illnesses e.g.. Asthma, angina.

Opioid withdrawal: Prevention and management

- ***Do not discontinue opioids abruptly*.** If opioids are to be discontinued, taper the dose slowly.

- ***If patient in acute withdrawal, BuprenorphineL/naloxone (Suboxone®) is the safest and most effective treatment.***
- Initial dose 2 mg sublingual (SL) . Prior to administering buprenorphine,ensure that the patient has not used any opioids for at least 12 hours, and the patient reports symptoms of withdrawal. Buprenorphine can actually precipitate withdrawal if it is given within a few hours of the last opioid dose.The Clinical Opioid Withdrawal Scale (COWS) can be used to monitor withdrawal severity
- Dispense 2-4 mg SL in 2 hours if necessary; maximum 4 mg on 1st day.
- May taper over several days or weeks, or maintain dose
- Ensure clinical observation and recording of vital signs

Opioid addiction – symptoms, signs, behaviours

This is a difficult diagnosis to make, because patients are often reluctant to disclose key symptoms and behaviours, for fear the physician will discontinue the opioid. Diagnosis often requires collateral information from family members, and observation over time of a pattern of behavior.

- Patient's opioid dose high for underlying pain condition
- Aberrant behaviours: Running out early, crushing or biting oral tabs, or accessing opioids from other sources
- The importance the patient attaches to the drug far outweighs its analgesic benefit (e.g. 'pain is 10/10, the hydromorphone only take edge off, but I would die if you stopped it')
- Binge rather than scheduled opioid use
- May be currently addicted to other drugs e.g. alcohol
- Depressed and anxious
- Deteriorating mood and functioning
- Strong resistance to tapering or switching current opioid
- Concerns expressed by family members
- Reports recurrent, frightening withdrawal symptoms
- May acknowledge that they experience immediate improvement in mood after taking the opioid

Management of opioid addiction: Three main treatment approaches can be used:

- ***Abstinence***
  - Less effective than opioid maintenance but often preferred by patients. Should be accompanied by intense inpatient or outpatient psychosocial treatment program. If patient relapses, initiate opioid maintenance.
- ***Structured opioid therapy.***
  - Continued opioid prescribing under conditions that limit misuse. Preliminary evidence suggests it is effective. More convenient for patients and easier to organize. Refer patients for buprenorphine treatment if structured therapy fails. See below for indications and protocol.
- ***Buprenorphine (Suboxone) maintenance***
  - Buprenorphine is a safer maintenance drug than methadone in the elderly. See below for indications and protocol. Buprenorphine may be prescribed by primary care physicians without a methadone license, although training is recommended. Ontario covers Suboxone on its provincial drug plan. Other provincial drug plans only cover Suboxone when it is prescribed by a physician with a methadone license.

Who is a good candidate for structured opioid therapy?

- Only uses opioids supplied by one physician
- Does not alter route of delivery (inject or crush oral tabs)
- Is not currently addicted to alcohol or other drugs

Structured opioid therapy protocol

- Taper dose to below 60 mg MED/d
- Dispense small amounts frequently (e.g. 1-2 times per week)- don't refill if run out early
- Close monitoring with UDS, pill counts, office visits
- Switch to buprenorphine treatment if SOT fails (e.g. patient continues to access opioids from other sources)

Who is a good candidate for buprenorphine-naloxone (Suboxone) treatment?

- Failed at or not a candidate for structured opioid therapy
- Acquires opioids from multiple sources – other doctors, friends and relatives, the street
- Currently misusing alcohol or other drugs
- Injecting or crushing oral tablets

Pharmacology

Buprenorphine is a partial opioid agonist with a ceiling effect, so it is less likely to cause an overdose than potent opioids such as morphine or methadone. It has a long duration of action because it dissociates slowly from the endorphin receptors. It is used in the treatment of opioid addiction because at the optimal dose, it relieves withdrawal symptoms and cravings for 24 hours, and it blocks the action of other opioids because of its tight receptor binding. Its side effects are similar to those of other opioids. See section below for information on training and education on Suboxone prescribing.

Suggested buprenorphine-naloxone protocol for elderly patients

- Taper benzodiazepines.
- Give first dose in office setting if feasible
- Suboxone will displace opioids currently attached to the receptor, precipitating opioid withdrawal. Therefore the physician must ensure the patient has no opioid in their serum before taking the first dose.
    - at least 12 hours since last IR dose, 24 hours since last CR dose
    - patient reports typical withdrawal symptoms e.g. myalgias
- First dose: 2 mg SL. Dose may take several minutes to dissolve.
- Reassess in 2 hours. If patient improved but still in withdrawal, give another 2 mg to take in office or at home. Maximum dose first day should be 4 mg.
- Reassess in day or two. Increase dose by 2 mg at each visit if patient reports withdrawal symptoms, cravings or opioid use. Each dose increase should increase duration of relief from withdrawal/cravings.
- Optimal maintenance dose is 4-16 mg. The optimal dose should relieve withdrawal symptoms and cravings for 24 hours, without causing significant sedation or other side effects.
- If feasible, at the beginning of therapy Suboxone should be dispensed daily under observation by the pharmacist. This is particularly important if the patient has been accessing opioids from other sources. If the patient is unable to attend daily because of limited mobility or other factors, then the physician should arrange supervised dispensing at home by a nurse or reliable relative. Take-home doses may be prescribed once the patient is at an optimal dose and has stopped all unauthorized opioid use.
- The physician should arrange frequent office visits for counseling and urine drug screen monitoring.

Benzodiazepines and the elderly

Rationale for Benzodiazepine Tapering in the elderly

Physicians should attempt to taper benzodiazepines with most of their elderly patients.. Benzodiazepines increase the risk of falls, hip fractures and motor vehicle accidents in the elderly. They can also interfere with cognition and contribute to fatigue and depression. Geriatricians advise that benzodiazepines should be tapered before making a diagnosis of dementia. Even in patients who do not have any apparent adverse effects, a trial of tapering should be considered. Tapering will reduce the risk of future adverse events, and patients and family members often observe an improvement in mood, alertness and function with tapering.

Benzodiazepine withdrawal

Time course	• Onset 2-4 days after abrupt cessation • May take weeks or months to resolve
Symptoms and signs	• Anxiety-related symptoms (panic, irritiability, poor concentration) • Neurological symptoms (dysperceptions, tinnitus, déjà vu) • Sweating, tremor usually not seen except with sudden cessation of high doses
Complications	• Abrupt cessation of high doses (50 mg of diazepam/day or equivalent) can cause acute hypertension, seizures, delirium
Effect on sleep	• Rebound insomnia (vivid dreams, fitful sleep) • Takes several weeks to resolve

******Approach to patient reluctance or resistance to tapering**

Explain that:

- Tapering will improve the patient's mood, and function, and will reduce the risk of adverse effects
- The patient will help the physician decide the rate of the taper,and it will be slowed, halted or reversed if the patient experiences difficulties.

Approach to Tapering

Formulation	• Safest to taper with the patient's current benzodiazepine • Although it is common practice to taper with a long acting benzodiazepine such as diazepam, diazepam can cause prolonged sedation in the elderly and increases the risk of falls.
Adjunctive medication	• Do not use other medications to assist with the taper • Atypical antipsychotics are commonly used off-label for sleep, but they can cause arrhythmias and sudden death in the elderly
Dosing interval	• Scheduled doses rather than PRN • Keep dosing interval the same for as long as possible (BID or TID) • Advise patients not to skip or delay doses
Rate of taper	• Taper slowly, no more than 5 mg diazepam equivalent/day at each office visit • Can taper as slowly as 1-2 mg diazepam equivalent per month • Let patient choose which dose is decreased (AM, PM or HS) Slower tapers are advised for patients who have been on benzodiazepines for a number of years, and patients with an underlying anxiety disorder.
Dispensing interval	If patient runs out early, increase frequency to weekly, alternate day or daily
End point of taper	• Abstinence preferred • Reduced dose if patient experiences significant anxiety or insomnia with abstinence
Frequency of visits	If possible, see patient prior to each dose decrease
Approach at each visit	• Ask not just about withdrawal symptoms but benefits of tapering: more alert, less fatigued, improved mood • Involve family members if possible – they often notice improvements before the patient does

Tapering HS benzodiazepines

- Benzodiazepines taken only night may also be a risk factor for falls
- Taper slowly to minimize rebound insomnia
- Once at the lowest dose, prescribe drug-free nights eg HS bzd 5 nights/week, then 3, then 1

Benzodiazepine Equivalent Table*

Table Appendix F.1 Benzodiazepine Equivalent Table

Benzodiazepine	Equivalent to 5 mg diazepam (mg) **
Alprazolam (Xanax®)***	0.5
Bromazepam (Lectopam®)	3–6
Chlordiazepoxide (Librium®)	10–25
Clonazepam (Rivotril®)	0.5–1
Clorazepate (Tranxene®)	7.5
Flurazepam (Dalmane®)	15
Lorazepam (Ativan®)	0.5–1
Nitrazepam (Mogadon®)	5–10
Oxazepam (Serax®)	15
Temazepam (Restoril®)	10–15
Triazolam (Halcion®)***	0.25

* Adapted from: Kalvik A., Isaac P, Janecek E. “Pharmacy Connection” 1995 20–32; “Compendium of Pharmaceuticals and Specialties,” Canadian Pharmacists Association, 1999.

** Equivalences are approximate. Careful monitoring is required to avoid over-sedation, particularly in older adults and those with impaired hepatic metabolism.

***Equivalency uncertain.

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Resources

National Opioid Use Guideline Group. *Canadian guideline for safe and effective use of opioids for chronic non-cancer pain.* Hamilton, ON: McMaster University; 2010. Available from:http://nationalpaincentre.mcmaster.ca/opioid/cgop_a00_executive_summary.html. Accessed 2011 Sep 20. Includes: a. Canadian Guideline Toolkit (appendix B on website), b. Opioid Manager (website), c. Guideline summarized in: Kahan, M., A. Mailis-Gagnon, L. Wilson and A. Srivastava (2011). Can Fam Physician **57**(11): 1257-66, 1269-76; Ontario Poison Centre (416) 813-5900 (local) or 1-800-268-901; Ministry of Transportation (Ontario) 416-235-1773; DRIC ; Primary care addiction toolkit: www.knowledgex.camh.net. Further references available upon request from authors.