On-Demand Clinical News

Advanced Methadone Concepts for the Hospice and Palliative Care Practitioner

By: Kristin Speer, BCPS, PharmD

Methadone has gained popularity as a generally well-tolerated opioid for end-of-life pain. We know it's especially well-suited for neuropathic pain control, in addition to somatic and visceral pain. We know it's inexpensive, and works well as a long-acting opioid option.

But did you know…

Methadone does not take a while to "kick in?"

Many practitioners are under the impression that methadone takes a long time to start working. However, this is incorrect. Methadone produces analgesia with the very first dose… but it initially behaves as a short-acting opioid. It does take some time to become long acting (usually about a week), until it reaches steady-state. While it can take methadone up to a week or longer to reach steady-state and behave long-acting, it will still provide analgesia—albeit shorter acting—with the very first dose.

When converting to methadone from a high-dose opioid, methadone and the other opioid should be cross-tapered?

When a patient is taking higher doses of opioids, it is important to not abruptly switch them over to methadone ("stop-start" method). This is because, as mentioned above, methadone acts like a short-acting opioid when initiated, and your patient may experience withdrawal symptoms in between methadone doses until it becomes long acting. Using breakthrough opioids to "fill in" may help prevent this, but not as well as cross-tapering PLUS using breakthrough opioids. If you are converting a patient completely over to methadone from a higher dose of another opioid, the cross-taper should occur over 3-5 days, in order to provide a more comfortable, streamlined transition. "Higher dose" is usually considered to be 200-300mg or more of oral morphine equivalents (OME) per day. It is better to lean toward a 3-day cross taper for someone taking about 200-300mg oral morphine equivalents/day, and better to choose a 5-day cross taper when they are receiving very high daily doses. The final dose of methadone calculated/targeted should be reached by the final taper day: so if 30mg/day is your target methadone dose, your taper might look like 5mg BID day 1, 10mg BID day 2, and 10mg TID day 3.

Managing Terminal Secretions at End of Life

By: Kiran Hamid, RPh

Terminal secretions can be defined as the noise created by the flow of air through secretions in the upper respiratory tract. These secretions are also commonly referred to as "death rattle", "terminal congestion", or "noisy secretions". Terminal secretions are a strong predictor of death, with patients often dying within hours of its onset.

Terminal secretions can be divided up into two subgroups. Type I secretions are due to mostly salivary secretions, are more common in the last several hours of life, and usually respond well to anticholinergics. On the other hand, type II secretions are mostly due to accumulated bronchial secretions, can occur over several days, and do not respond well to anticholinergics.

When deciding to treat terminal secretions, non-pharmacological interventions should first be employed. These include re-positioning the patient to a lateral position, providing good mouth care, and decreasing fluids. If these methods do not provide relief, pharmacological interventions should be used. Despite lack of evidence, the most commonly used medications to manage terminal secretions are the anticholinergic drugs: atropine, hyoscyamine, scopolamine, and glycopyrrolate. These medications reduce secretion of saliva and mucus and should be used at the first sign of terminal secretions (they do not dry up secretions that are already present).

Current evidence does not show which anticholinergic agent is superior to another, and does not show that treatment with anticholinergics for terminal secretions is even effective.

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The other opioid should be tapered down as evenly as possible over the same time period. Remember that your ProCare clinical pharmacist is available 24/7 to help you dose methadone safely, and recommend a cross-taper schedule if needed.

Methadone may accumulate significantly in liver impairment?
This is because methadone is inactivated by the liver. If the liver is impaired, methadone can accumulate and cause toxicity. If your patient has liver impairment, start at lower doses, and titrate more slowly.

Methadone might cause hypoglycemia?
In a recent study with cancer patients, oral methadone doses over 40mg/day were associated with hypoglycemia. Many other case reports of methadone-induced hypoglycemia exist. Also, some case reports have associated propoxyphene, which is structurally related to methadone, to hypoglycemia. And methadone has shown to cause hypoglycemia in a dose-dependent manner in mice. For your patients, anticipate possible hypoglycemia and monitor serum glucose more closely when methadone is started/increased.

You don't have to avoid methadone in patients with atrial fibrillation? Having atrial fibrillation or other arrhythmia, while a risk factor for QT prolongation, is not a labeled contraindication to use of methadone. Indeed, many clinicians still use methadone in the setting of arrhythmias. These patients should still be carefully considered before methadone use, however. While methadone should not be written off if the patient simply has an arrhythmia history, it would be prudent to avoid methadone if the patient has *multiple* risk factors for QT prolongation: female gender; dehydration and electrolyte imbalance (including nausea, vomiting, diarrhea); liver impairment; arrhythmia; cardiac disease; and/or other QT-prolonging medications (amiodarone, quetiapine, citalopram, ondansetron, etc). Have a risk-vs-benefit discussion with the patient and caregivers before starting methadone. If started, monitor for new/increased tachycardia, syncope, palpitations and/or diaphoresis, which indicate a new arrhythmia. Remember that clinically significant risk of QT prolongation with methadone has been reported at oral doses of 100-200mg/day or greater, but that this risk is increased, of course, with the presence of additional QT risk factors.

Most patients are good candidates for methadone. Practitioners with a good understanding of methadone know that dosing methadone is a process, not just a calculation, and that monitoring regularly for safety and efficacy is an important feature for success. Most patients are quickly optimized on methadone. Risks can be anticipated and effectively reduced or managed. Methadone often achieves enhanced symptom control while reducing adverse effects from other common opioids, and can be a wonderful tool for pain and symptom control when it is understood well and used appropriately.

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When choosing an anticholinergic to treat these secretions, one must consider various factors, including onset of action of the medication, route and ease of administration to the dying patient, and cost.

When managing terminal secretions in the dying patient, one must consider the impact on the patient's family and caregivers. This is because it has been noted that the sound of terminal secretions can be very distressing to family and caregivers, and that treatment for terminal secretions is very often initiated based on that perceived distress. In contrast to the impact on the family, the effect of terminal secretions on the dying patient is thought to be benign; the patient is not in respiratory distress. Thus, educating and communicating with the family at this difficult time is critical, and may even replace the need for pharmacological interventions.

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Rising Cost Spotlight

Nate Hedrick, PharmD

Medication	Current Cost*	Cost-Effective Alternatives	Clinical Considerations**
Phenobarbital Injection	65mg/mL 15mL: $212 130mg/mL 15mL: $435	(15-day supply of each) Seizures: Lorazepam: $15-$20 Phenobarbital Tabs: $45-$60 *Agitation:* Haloperidol: $18-20 Phenobarbital Tabs: $45-$60	Appropriate alternatives for injectable phenobarbital vary greatly depending on original indication.
Potassium Chloride Oral Suspension	20 mEq/15mL: $240 per 473ml bottle 40mEq /15mL: $450 per 473ml bottle	Potassium Chloride Tablets 10mEq: $8-$15 per 15-day supply 20mEq: $12-18 per 15-day supply	Potassium Chloride Tablets (Klor-Con) can be dissolved by placing the whole tablet in ~4 ounces of water. Allow to dissolve for about 2 minutes, stir well, and drink immediately.

*Please note that drug costs may vary by geographic region and individual pharmacy.
Prices provided above are estimates only and may not reflect the exact cost for a prescription for your hospice.

**Alternatives provided may not be appropriate for all patients and are provided as a general recommendation only.
Please contact a ProCare Clinical Pharmacist for patient-specific recommendations.

Upcoming Lunch and Learn Presentations

March

"Blood Pressure Management at End of Life"

Presenter: Tracey Gordon, PharmD

Tuesday, March 7, 2017 at 3:00pm ET; Wednesday, March 8, 2017 at 12:00pm ET

April

"Cost Effective Medication Use at End of Life"

Presenter: Brett Gillis, PharmD

Tuesday, April 4, 2017 at 3:00pm ET; Wednesday, April 5, 2017 at 12:00pm ET

RSVP by contacting Suzanne Stewart, Lunch and Learn Coordinator, at:
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