ProCare **HospiceCare** *July/August Edition*

On-Demand Clinical News

Prochlorperazine (Compazine) and Promethazine (Phenergan) Tablets; **Pharmacokinetic Properties and Rectal Absorption**

Kristin Braschler, Pharm.D., BCPS

Increasing costs of prochlorperazine (Compazine®) and promethazine (Phenergan®) suppositories are causing hospices to consider, and trial, the administration of the tablet form rectally when the patient is unable to take these medications orally. While there are no clinical studies supporting the safe and effective use of prochlorperazine or promethazine tabs rectally, the drugs' pharmacokinetic (PK) and chemical properties lend support for their rectal absorption and probable efficacy.

REGARDING EFFICACY:
The efficacy of rectally administered prochlorperazine and promethazine tablets is supported by their chemical and PK properties. Both drugs have logP values (4.8) indicating high lipophilicity. This favors mucosal absorption whether in the rectum or stomach. However, for both drug molecules, it appears the time to max serum concentration is delayed when absorbed rectally vs orally, indicating a slower onset. Based on the higher pH (7-8) of the rectum versus the stomach (varies around 3), and the pKa (approximately 8-9) of these drugs, their ionization can be increased and thus absorption can be somewhat less in the rectum. Still, these conditions predict that less than 50% of the drug will be ionized. Therefore the overall effect of the drugs' ionization properties on rectal absorption is difficult to predict and may be of little clinical relevance.

RECOMMENDATIONS for ADMINISTRATION/DOSING:
An appropriate medium can facilitate the administration and release of the drug, its dispersion, and/or rectal retention, but such a medium (such as suppositories) may not be required in all cases for effective rectal absorption. It has been reported that prochlorperazine may be more readily absorbed from the rectum if delivered in PEG (hydrophilic) base, and promethazine may be more readily absorbed from the rectum if delivered in a fatty base such as cocoa butter.

Certain preparation steps prior to administering the tabs rectally may increase their efficacy (however, given the chemical properties of the drugs in tablet form, it appears the whole or crushed tabs would be

Continued on page 4

Highlights from Medication Administration Safety Lunch & Learn May 2014

Cody Midlam, Pharm.D., CGP

An important component of sound medication administration safety practice is to be aware of certain drugs, or situations that are most commonly associated with adverse events or medication errors. There are a number of available resources for health care practitioners through the Institute for Safe Medication Practices (ISMP) at www.ismp.org.

Below is a listing of the Top Ten medications involved in adverse events (many are commonly utilized in the hospice setting):

1. Insulin (8%)
2. Anticoagulants (6.2%)
3. Amoxicillin(s) (4.3%)
4. Aspirin (2.5%)
5. Trimethoprim-sulfamethoxazole (2.2%)
6. Hydrocodone/acetaminophen (2.2%)
7. Ibuprofen (2.1%)
8. Acetaminophen (1.8%)
9. Cephalexin (1.6%)
10. Penicillin (1.3%)

Continued on page 3

Follow us Online & on Twitter! (@PHCpharmacy)

Follow us online and on Twitter to keep up with the latest clinical news and regulatory trends that affect hospice care, or share your own exciting story!

Lunch & Learn Series – June 2014: Neuropathic Pain Summary

Priyanka Narula, PharmD, CGP

Neuropathic pain is pain after an injury or disease of the peripheral or central nervous system. Chronic neuropathic pain is common in clinical practice, and it greatly impairs the quality of life of patients.

Types of Pain	
Nociceptive Pain	**Neuropathic Pain**
• Normal processing of stimuli that damages normal tissue, or has the potential to do so if prolonged • Usually responsive to non-opioids and opioids	• Abnormal processing of sensory input peripheral or central nervous system • Treatment usually includes adjuvant analgesics

Neuropathic pain is characterized by spontaneous and stimulus-evoked types of pain, which are due to various distinct pathophysiological mechanisms in the peripheral and central nervous systems. In some patients, the nerve lesion or injury triggers molecular changes in nociceptive neurons, which become abnormally sensitive and develop pathological spontaneous activity. Inflammatory reactions of the damaged nerve trunk can induce physiologic changes that can cause spontaneous pain. Patients characterize neuropathic pain as numbness, tingling, and burning, throbbing, shooting, sharp or electric-like. It can also present as deep, dull, aching type of pain.

Stepwise pharmacologic management of neuropathic pain (NP)

Step 1

- Assess pain and establish the diagnosis of NP; if uncertain about the diagnosis, refer to a pain specialist or neurologist
- Establish and treat the cause of NP; if uncertain about availability of treatments addressing NP etiology, refer to appropriate specialist
- Identify relevant comorbidities (e.g., cardiac, renal, or hepatic disease, depression, gait instability) that might be relieved or exacerbated by NP treatment, or that might require dosage adjustment or additional monitoring of therapy
- Explain the diagnosis and treatment plan to the patient, and establish realistic expectations

Step 2

- Initiate therapy of the disease causing NP, if applicable
- Initiate symptom treatment with one or more of the following:
  - A secondary amine TCA (nortriptyline, desipramine) or an SSNRI (duloxetine, venlafaxine)
  - A calcium channel a2-d ligand, either gabapentin or pregabalin
  - For patients with localized peripheral NP: topical lidocaine used alone or in combination with one of the other first-line therapies
  - For patients with acute neuropathic pain, neuropathic cancer pain, or episodic exacerbations of severe pain, and when prompt pain relief during titration of a first-line medication to an efficacious dosage is required, opioid analgesics or tramadol may be used alone or in combination with one of the first-line therapies
- Evaluate patient for non-pharmacologic treatments, and initiate if appropriate

Step 3

- Reassess pain and health-related quality of life frequently
- If substantial pain relief (e.g., average pain reduced to 3/10) and tolerable side effects, continue treatment
- If partial pain relief (e.g., average pain remains 4/10) after an adequate trial, add one of the other first-line medications
- If no or inadequate pain relief (e.g., < 30% reduction) at target dosage after an adequate trial, switch to an alternative first-line medication

Step 4

- If trials of first-line medications alone and in combination fail, consider second- and third-line medications or referral to a pain specialist or multidisciplinary pain center. Contact your ProCare HospiceCare clinical pharmacy team for a timely pain assessment and a patient-specific treatment plan.

Continued on page 3

My Patient is Taking High Doses of Methadone, Can I Order the 40mg Tablets from the Pharmacy?

Cody Midlam, PharmD, CGP

As of January 1, 2008, manufacturers of methadone hydrochloride tablets 40 mg (dispersible) have voluntarily agreed to restrict distribution of this formulation to only those facilities authorized for detoxification and maintenance treatment of opioid addiction, and hospitals. Manufacturers will instruct their wholesale distributors to discontinue supplying this formulation to any facility not meeting the above criteria.

Methadone is a long-acting opioid medication used in the treatment of pain and narcotic addiction. The 5mg and 10 mg formulations, indicated for the treatment of pain, will continue to be available to all authorized registrants, including retail pharmacies. The 40 mg methadone formulation is indicated for the detoxification and maintenance treatment of opioid addiction. The 40 mg strength is not FDA approved for use in the management of pain. Thus, the distribution and availability of the 40 mg formulation will be limited to registrants in only those settings using the 40 mg formulation for the appropriate indication.

The DEA and pharmaceutical industry agree that the reported increase in methadone-related adverse events merits action and further agree to a united effort to assure that methadone is properly distributed, consistent with its approved uses. Industry and the federal entities involved commit to monitor the progress of this initiative.

References:

http://www.deadiversion.usdoj.gov/pubs/advisories/methadoneadvisory.htm

Highlights from Medication Administration Safety continued from page 1

Abbreviations and suffixes can be another area with potential for medication errors. A suffix is a letter, number, or combination that is added to the end of a drug name. Below are a few examples of the many ways to indicate a drug is 'extended-release', to illustrate this point. Remember, most products that are extended-release must be taken orally whole, and not crushed, or chewed.

Biaxin **XL** = "extended release"
Coreg **CR** = "controlled release"
Depakote **ER** = "extended release"
Detrol **LA** = "long-acting"
Seroquel **XR** = "extended release"

It's always a good idea to reach out to your ProCare HospiceCare clinical pharmacist team, if you come across a questionable suffix on your patient's medication list. As you can see in the example above, there is no standardization to the process of creating drug names, and there are many ways to signify an extended-release product.

As with any Lunch and Learn, you can find the audio file and a copy of the slides through the ProCare Hospice Care website (www.procarehospicecare.com) under the 'Education' tab.

References:

1. *Institute for Safe Medication Practices. ISMP's List of Products with Drug Name Suffixes. Accessed online 1/30/2013 at: http://www.ismp.org/Tools/drugnamesuffixes.pdf*
2. *Kathryn L. Hahn, PharmD. The "Top 10" Drug Errors and How to Prevent Them. Medscape Pharmacists Education. Accessed online 1/31/2013 at: http://www.medscape.org/viewarticle/556487*

Neuropathic Pain Summary Continued from page 2

TCA= tricyclic antidepressant; SSNRI= selective serotonin and norepinephrine reuptake inhibitor.

References: R.H. Dworkin et al. / Pain 132 (2007) 237–251

Pharmacokinetic Properties and Rectal Absorption, continued from page 1

effectively absorbed, within a reasonable timeframe):

- Crush the tabs before insertion into the rectal vault – create a slurry or paste and place up against the rectal wall
- For Phenergan – mixing the crushed tab in butter/fatty case (but may not be required, may also try water as described above)
- For Compazine – mixing the crushed tab in water/aqueous base (but may not be required)

Educate patients/providers that onset may be delayed. However, if no effect after 1 hour, consideration may be given to repeat dose x 1 after 1-2 hours if the previous dose was not effective.

REGARDING SAFETY:
Concerns do not fall around the safety of the drug molecule itself, since it has been approved for both oral and rectal administration. The two main, clinically relevant, safety concerns are:
1) That the rectal absorption of the tablet may be too fast or too much compared to oral absorption, and/or
2) The tablet form may be irritating to the rectal mucosa.

Care must be taken to consider risks of possible erratic absorption, rectal irritation, or other adverse effects vs benefits of symptom control, and monitor patient closely, adjusting doses accordingly. All things considered, it seems more possible to under-dose a patient by giving the tabs rectally (especially if left whole). However, it still seems reasonable to attempt administration of these tablets rectally when the patient is vomiting or cannot take orally, given the increasing cost of the commercial suppositories. The benefit of symptom control appears to outweigh the potential risks.

References:

1. *DrugBank 4.0 Website. URL: http://www.drugbank.ca. Accessed April 9, 2014.*
2. *Lexicomp Online, Lexi-Drugs Online, Hudson, Ohio: Lexi-Comp, Inc.; 2013; April 15, 2013.*
3. *Davis MP1, Walsh D, LeGrand SB, Naughton M. Symptom control in cancer patients: the clinical pharmacology and therapeutic role of suppositories and rectal suspensions. Support Care Cancer. 2002 Mar; 10(2):117-38. Epub 2001 Nov 9.*

Article Highlights from previous On Demand Clinical Newsletters:

- Medicare Part D Medication Coverage and the Hospice Benefit
- Prolastin®-C Injection and Other Brand Name Alpha-1 Proteinase Inhibitors
- What Makes Some Pollen Cause Allergies, and Not Others?
- Discontinuation of Namenda 5mg and 10mg Immediate Release Tablets

Upcoming ProCare HospiceCare Lunch and Learn Series Topics:

- August 12th and 13th — Delving Deeper into Methadone
- September 9th and 10th — Medication Tapering at End of Life
- October 14th and 15th — Hospice/Palliative Care for the Pediatric Patient

Remember:
You can find a full list of our Lunch and Learn series at the ProCareHospiceCare.com website. Here you can also access past Lunch and Learns (both presentation slides and an audio file to follow along). You can also access all of the past issues of the on Demand Clinical Newsletter via the website, under the 'Education' Tab.

ProCare HospiceCare welcomes all suggestions and comments. If you would like additional information about our services, have ideas for articles, or wish to submit a comment, email us at **resources@procarerx.com**.

ProCare **HospiceCare**
1267 Professional Pkwy., Gainesville, GA 30507
800.377.1037

Editor: Dr. Cody Midlam, PharmD, CGP
Executive Editor: Dr. Meri Madison, PharmD, CGP