



Pharmascript

NEWSLETTER OF THE MARYLAND SOCIETY OF HEALTH SYSTEM PHARMACISTS

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A GLANCE AT POISON PREVENTION

Angel Bivens, R.Ph., MBA, CSPI
Education Coordinator, Maryland Poison Center

Poison Prevention Week, March 16-23, 2003, is upon us again. Although preventing unintentional poisonings should be a year-round activity, Poison Prevention Week has been designated to draw attention to the fact that many childhood poisonings can be prevented. Reaching the poison center is now even easier with the use of the nationwide phone number—**1-800-222-1222!** All callers using this number will reach the local poison center assigned to their calling area. With the exception of residents living in Prince Georges and Montgomery Counties, Maryland callers will reach the Maryland Poison Center located at the University of Maryland School of Pharmacy. Prince Georges and Montgomery County callers will reach the National Capitol Poison Center in Washington D.C.

In 2002, the Maryland Poison Center answered over 59,000 calls. Approximately 35,000 were human exposures, 75 percent of which were handled at home. Over 19,000 of these exposures involved children under the age of 6 years. In addition to the exposure calls, requests for poison information, drug information and animal exposures accounted for 24,000 calls.

The Maryland Poison Center, staffed by pharmacists and nurses, provides telephone consultation for the public as well as for health care professionals 24/7. They can help with unintentional and intentional drug ingestions. Other calls handled by the Maryland Poison Center involve exposures to household chemicals, cleaning products and personal care products, drug information and identification, ingestion of foreign bodies (toys, plants, silica gel), exposures to insecticides and pesticides, and consultation on matters of chemical- and bio-terrorism. Exposures can be dermal, ocular, or by ingestion, inhalation, and/or injection.

The Maryland Poison Center has educational materials available to help everyone be aware of the risks and dangers in their homes. Magnets,

telephone stickers and Mr. Yuk stickers are available to ensure that the telephone number is available in the event of a poison emergency. Other materials are available to teach children about poison prevention. For more information about these educational resources and other educational programs, contact Angel Bivens at 410-706-2151. For educational resources for the Prince Georges and Montgomery County areas, contact Rose Ann Soloway at 202-362-7217.

MSHP OFFERS \$\$ FOR NEW MEMBERS

As part of the 2003 MSHP membership promotion the Membership Committee is offering *20 MSHP dollars* to anyone who sponsors or refers a new member to MSHP.

The dollars are good through December 31, 2004 and can be put toward your 2003 or 2004 Annual Seminar Registration or your own 2004 membership dues.

Membership applications can be requested by phone at MSHP Headquarters at 410/465-9975 or by e-mail at ContactMSHP@aol.com. Applications can also be downloaded from our website at www.msphp.org.

The *MSHP dollars* will be mailed to eligible members beginning in June 2003.

Upcoming Monthly Program Dates

Tuesday March 18th
Tuesday April 29th
Monday May 12th

Details on www.msphp.org when available.

Meperidine (Demerol®):

A drug whose time has come and gone

Ray Weber, PharmD., BCPS, BCOP, Manager, Clinical Pharmacy Services, GBMC

Meperidine is a drug past its prime. The Agency for Health Care Policy and Research Clinical Practice (AHCPR) and American Pain Society (APS) guidelines recommend that meperidine not be used if continued opioid use is anticipated for acute or chronic pain. Instead, meperidine should be used only briefly for the treatment of acute pain in patients who have documented allergic reactions or intolerance to other opioid analgesics or for the management of rigors (shivering) induced by other medications. Meperidine should not be used continuously (i.e., for more than 48 hours) or for any pain conditions that might require more than several days of therapy. The Quality Improvement Effort by the University of Wisconsin to reduce the use of meperidine was celebrated by the JCAHO (Joint Commission on Accreditation of Healthcare Organizations) as a successful model to institutionalize high-quality pain management.

Meperidine is the least potent of the opioid analgesics. When meperidine is used, it is generally under dosed and administered at too infrequent a dosing interval, resulting in inadequate pain treatment. The duration of meperidine's analgesic activity is only 2 to 4 hours, whereas it is generally ordered every 4 to 6 hours leaving the patient in pain at the end of the dosing interval.

The maximum recommended dose of meperidine is 600 mg per 24 hours and therapy should be limited to less than 48 hours. Accumulation of normeperidine, a toxic metabolite of meperidine that is predominately excreted by the kidney, can occur in patients with renal dysfunction or in patients receiving high dose therapy. Levels of normeperidine can also be increased when patients receive Cytochrome P-2D6 inducers (e.g., rifampin, carbamazepine, barbiturates, and phenytoin). The half-life of normeperidine is 15 to 30 hours in patients with normal renal function. As the level of normeperidine increases, so does the risk of seizures, dysphoria, and irritable mood, even in relative healthy younger patients. Meperidine is contraindicated in patients with renal dysfunction. The administration of meperidine in elderly patients is discouraged because of their decreased renal function.

Oral use of meperidine should be avoided as the first pass metabolism converts a higher portion of meperidine to the toxic normeperidine metabolite.

Meperidine was traditionally used over morphine in pancreaticobiliary diseases because it causes less pronounced changes in frequency and amplitude in the sphincter of Oddi. However, there are no reports that meperidine is safer or provides any specific benefit in patients with acute pancreatitis or biliary colic. Hence, the theoretical advantage did not prove to be of clinical benefit.

Meperidine has several unique drug interactions that are not associated with other opioid analgesics. The risk of serotonin syndrome is increased when meperidine is used in combination with serotonin receptor agonists, serotonin reuptake inhibitors (SSRIs), St. John's Wort, lithium, and sibutramine. Serious cardiovascular and neurologic adverse reactions (e.g., hyperexcitability, convulsions, tachycardia, hyperpyrexia, hypertension, coma and death) can occur when meperidine is used with Monoamine Oxidase Inhibitors (MAOIs: e.g., isocarboxazid, phenelzine, tranylcypromine, selegiline). The same risk may occur when the drug is used with agents that have some MAOI activity (e.g., furazolidone, isoniazid, linezolid, and procarbazine).

Meperidine should be restricted to second or third line use when patients are intolerant to the first line opioid analgesics (morphine, hydromorphone, oxycodone, codeine). Meperidine may also be used in the treatment of drug-induced or blood product-induced rigors. The use of meperidine raises the risk of avoidable drug induced injuries. In cases where it is necessary, meperidine should be used with caution. The initial dose should be reduced and the patient closely observed for toxicity when given to any patient with decreased renal function, in the elderly and in those with pre-existing convulsive disorders, or in patients receiving medications known to predispose patients to seizures (e.g. imipenem, phenothiazines, SSRIs, etc.). Given the limitations and risk of meperidine, it is a drug whose time has come and gone.

SEVERE ADR REPORT:

Meperidine Induced Grand Mal Seizure

(Continued on page 3)

WELCOME NEW MEMBERS

Eunah J. Kim
Donald E. Robbins
Brent Sharf
Kathleen Tierno
Marybeth Verbos
Walter Zajac

A 27 year old woman with long standing sickle cell disease presented to the Emergency Department (ED) seeking pain medication for her sickle cell crisis. She had presented several times in the past, but generally leaves "Against Medical Advice" rather than be admitted for pain management. Prior to the ED visit she admitted to taking 100-200mg of oral meperidine at home. In the ED she demanded more meperidine. She was given additional doses of IM meperidine totaling to 300mg. Her pain under control she was preparing to leave the ED when she suffered a tonic-clonic seizure, which progressed to a generalized grand mal seizure and was therefore admitted to the CCU for evaluation. Neurology consultation was obtained. The neurology consultant concurred with the probability that the seizure was due to the large cumulative dose of meperidine and accumulation of the normeperidine metabolite. There was no clear indication for the initiation of anticonvulsants. Meperidine was withheld and oxycodone was used to manage her pain, despite patient requests for meperidine. The patient was discharged two days later without recurrence of seizures. Plans were to follow up with her Primary Care Physician and the neurologist.

The take home points of this case are: 1. Meperidine use should be avoided, as other safer narcotic analgesics are available. 2. Oral use of meperidine should be avoided as the first pass metabolism converts a higher portion to the toxic normeperidine metabolite. 3. When meperidine is used the dose should not exceed 600mg per day. 4. Seizures due to meperidine and its normeperidine metabolite can occur without warning. 5. Other manifestations of meperidine / normeperidine neurotoxicity include: anxiety; fluctuations in level of awareness; hallucinations; agitation; illusions; disorientation; restlessness; bizarre feelings; fear; diaphoresis; shakiness; myoclonic jerks; nervousness; tremors; and confusion. 6. In cases of meperidine / normeperidine neurotoxicity, naloxone (Narcan®) should **NOT** be used. Naloxone does not reverse the effects of normeperidine, and may actually precipitate or worsen seizure activity as the sedative effects of meperidine are reversed allowing the full toxic effects of normeperidine. In such cases discontinue the meperidine completely, add an alternative opiate agonist (morphine, hydromorphone, etc.) and use diazepam, phenytoin or other anticonvulsant as needed for seizure control.

Dear MSHP Members:

The Pharmacists' Education and Assistance Committee is extremely grateful to the MSHP members who have contributed an annual donation to the committee totaling \$240.00. Your generous contribution enables PEAC to continue assisting pharmacists with substance abuse or chemical dependence by providing confidential support and advocacy to impaired pharmacists and their families. Your financial help also enables PEAC to present its 4th Annual CE Seminar to be held Thursday October 16, 2003 at the Beacon Institute in Columbia. This year's seminar topics include pain management, addiction management, buprenorphine and street drugs. Registration brochures will be sent in the mail, so mark your calendars!

For MSHP members that are not familiar with PEAC, we are an independent, not for profit corporation. Donations are tax deductible under Section 501(c) (3). Our mission is to preserve professional health through advocacy and health education. PEAC offers a confidential avenue for addressing a variety of problems that might contribute to impaired practice. Employers can benefit from PEAC services because pharmacists' problems can be addressed and mended. Because of ongoing supervision, employers can be confident in the performance of pharmacists who have completed the PEAC program.

Together, with your financial support and referrals we can continue to help troubled pharmacists facing a difficult dilemma. With direction and guidance they may no longer be a hazard to the public and a liability to employers.

Referrals can be made by contacting (410)452-8683. PEAC confidentiality is assured by state law.

Sincerely thankful,

Patricia Tommasello
Coordinator
Pharmacists' Education and Assistance Committee

ATTENTION POTENTIAL WRITERS

If you have any articles to contribute or have colleagues who would be interested in submitting articles please take advantage of the opportunity to publish in the *MSHP Pharmascript*. Submit articles via e-mail preferably in a Microsoft Word format to the Publications Committee at ContactMSHP@aol.com. The deadlines for submission of copy for the next year are: March 17, April 15, May 15, July 9, August 15, September 15, October 17 and November 21. Short to the point reviews, clinical, distributive or administrative issues are ideal. Thank you.



STIMULANT LAXATIVES REMOVED FROM MARKET

D. Raymond Weber, PharmD, BCPS, BCOP, Manager Clinical Pharmacy Services

The Food and Drug Administration (FDA) issued a final ruling on May 9, 2002 stating that many stimulant laxative ingredients in over-the-counter (OTC) drug products are not generally recognized as safe and effective (GRAS/GRAE) or misbranded. This includes **aloe** (including aloe extract and aloe flower extract) and **cascara sagrada** (including **casanthranol**, cascara fluidextract aromatic, cascara sagrada bark, cascara sagrada extract, and cascara sagrada fluidextract). This ruling was effective on November 5, 2002. **This removal from marketing involves 15 aloe containing products, 160 cascara sagrada products and 125 casanthranol with docusate sodium products** (such as PeriColace®). **The FDA has suggested that the combination products be reformulated to replace the aloe/cascara sagrada containing products with sennosides A and B or sodium carboxymethylcellulose.** For example Shire US Inc., the previous manufacturer of PeriColace® was contacted on November 13, 2002 to discover their plans on reformulating the product to contain a combination of docusate sodium with senna. In the short time since, the brand name PeriColace® was sold to Purdue Pharma who will be marketing PeriColace® as 50mg docusate sodium plus 8.6mg of sennosides with a usual adult dose of two to four PeriColace® per day. If that formulation looks familiar you are right, the active ingredients are the same as Purdue Pharma's Senokot-S®.

The process of reviewing the safety and efficacy of Over-the-Counter products began in the 1970s when the FDA requested that manufacturers submit studies supporting the safety (GRAS) and efficacy (GRAE) of medications that were already on the market for what had been an extended period of time. This was intended to address the older medications, which came to market before the Kefauver Harris Amendment in 1962. Unfortunately the manufacturers did not step up to fill this void with supporting documentation of safety and efficacy. This is at

least partially due to the lack of patent rights on these products, which would ensure a return on the investment to perform the studies. As the FDA now states, "the periods for submission of comments and new data following publication of a notice of proposed rulemaking has closed and no significant comments or new data had been submitted to upgrade the status of these ingredients."

The bottom line is that many products which physicians have prescribed or recommended for years are being removed from the market (i.e. no more cascara to go with the milk-of magensia). Although the deadline was November 5th any product remaining on the market can continue to be used until all supplies are depleted as this is not a true recall but simply removal of the product from further manufacturing and introduction into interstate commerce. Wholesalers are permitted to stock and distribute the laxative products until their inventory is depleted or the product reaches its expiration date. It is estimated that these supply lines should be depleted around February or March 2003. In accord with the FDA ruling cascara sagrada extract and the current PeriColace® formulation of docusate sodium with casanthranol have been removed from the formulary at GBMC. Products such as plain docusate sodium (Colace), plain milk of magnesia, biscodyl (Dulcolax®), sennosides (Senokot®) or the combination product of sennosides and docusate sodium (Senokot-S®) should be considered as the laxatives of choice, while the supplies of the laxatives removed from the market are depleted.

References

1. Food and Drug Administration, HHS, Status of Certain Additional Over-the-Counter Drug Category II and III Active Ingredients, Federal Register, May 9, 2002 (volume 67, number 90).
2. Shire US, Inc. Personal Written Communication 11/13/02.
3. Purdue Pharma, L.P. Medical Information, Personnel Communication 2/3/03

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