// Pain Relief Connection

The Pain Information Newsletter

Provided by MGH Cares About Pain Relief

Archived issues are available at http://www.MassGeneral.org/PainRelief

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In the News

- Merck has announced that it is voluntarily withdrawing Vioxx (rofecoxib) from the market following a series of studies showing an increased risk of cardiac events in patients who have taken the pain-relief medication over a long period of time. Rofecoxib is a non-steroidal anti-inflammatory agent (NSAID) of the cox-2 inhibitor subclass. The FDA web site has additional information.
- The Food and Drug Administration (FDA) has announced the approval of Palladone (hydromorphone hydrochloride) capsules for the management of persistent moderate to severe pain in patients requiring continuous around-the-clock opioid pain relief for an extended period of time. Palladone is an extended-release formulation for once-a-day oral dosing that comes in 12, 16, 24, and 32 milligram (mg.) capsules.
- The FDA has also announced approval of duloxetine (Cymbalta) for diabetic peripheral neuropathy. This is the first drug specifically approved for this indication. The approval was based on the results of two randomized controlled studies involving 1,074 patients showing that 58% of patients treated with duloxetine reported at least a 30% sustained reduction in pain compared with 34% of those who received placebo.
- It has been known for some time that the human body contains receptors for opioids and that the body produces its own opioid-like compounds (endorphins). It has now been demonstrated that humans produce morphine identical to that produced by the opium poppy.
- The International Association for the Study of Pain (IASP) is sponsoring the Global Day Against Pain on Oct 11. The theme is "The Relief of Pain Should be a Human Right."

Patient Resources (journal titles followed by [M] have full text free access on MGH computers)

- The September 15 issue of the *Journal of the American Medical Association* [M] has a Patient Page on "Opioid Addiction." *JAMA* Sep 15, 2004;291(11):1394
- "8 Facts Everyone Should Know About Cancer Pain" is available on line.

Journal Watch (journal titles followed by [M] have full text free access on MGH computers)

- Roykulcharoen V & Good M. Systematic relaxation to relieve postoperative pain. *Journal of Advanced Nursing*[M] Oct 2004;48(2):140-148.
- Schaffer SD & Yucha CB. Relaxation & Pain Management: The relaxation response can play a role in managing chronic and acute pain. *American Journal of Nursing*[M] Aug 2004;104(8):75-82

Pain Education on the Web

- Selected MGH Pain Center clinical conferences are now published in hard copy and online in *Pain Management Rounds*. CME is available for each article.

Pain-Related Education Opportunities

- Oct 14 – 15 (Thu – Fri) **Current Concepts in Cancer Pain Management**. Thursday October 14, 2004 - Friday October 15, 2004. Johns Hopkins University School of Medicine, Turner Bldg. Baltimore, MD **Registration deadline: Oct 11.**

MGH Cares About Pain Relief

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- Oct 16 (Sat) **Across the Life Span...Innovations in Pain Management**. Sponsored by New England Pain Association (NEPA), a regional affiliate of the American Pain Society. Elliot Hospital, Manchester, NH
- Oct 19 (Tues) 5:30pm The first meeting and lecture of the **Boston Pain Forum**, a scholarly collaborative group, will be held at the William Prescott House, 55 Beacon Street. To RSVP: Steven.scrivani@tufts.edu or 617-636-3482
- Nov 5 – 7 (Fri –Sun): **Oncology Nursing Society's 5th Annual Institutes of Learning.** This year's event features a half-day mini-institute on Pain**.** Learn more or register online at http://onsopcontent.ons.org/Meetings/IOL2004/Index.shtml
- Nov 19 – 20 (Fri – Sat): **Pain Management Strategies for the Primary Care Practitioner**. 7th annual CME-accredited meeting. This program will present a primer of the latest developments in the pathophysiology, diagnoses and treatments of pain. Each talk will focus on specific topics directly relevant to the practical problems that a primary care specialist may encounter when confronted with a pain patient. NYU Medical Center, Farkas Auditorium, New York City. For more information contact Leticia Banuchi, tel: 646-459-8516, email: Leticia.Banuchi@nyumc.org.
- **Master of Science in Pain Research, Education, and Policy** (PREP), Tufts University Medical School. An interdisciplinary postgraduate program. For info call 617-636-8541 or e-mail jconnolly@tufts-NEMC.org.

MGH Pain Calendar

- **Oct 14 (Thu) 7 AM –** Special Lecture in Honor of Ether Day: **America's First Gift to Humanity: The Introduction of Anesthetics in 1846.** Julie Fenster, Author of "Ether Day." Clinics 3 amphitheatre.

Chronic Pain Rounds are held Mondays at 12:00N in the Clinics 3 amphitheatre.

Oct 4: "Cranial Neuralgias & Neuropathic Pain" David Keith, DMD
Oct 18: "Pelvic Pain" Edward Michna, M.D.
Oct 25: "Acupuncture & Chronic Pain" Lucy Chen, M.D.

Cancer Pain Rounds are held Wednesdays at 12:00N in the Cox 8 Conference Room.
Palliative Care Grand Rounds are held Wednesdays at 8:00am in the Ether Dome.

MGH Pain Resources:
PainRelief web site: http://www.massgeneral.org/painrelief/
Previous issues of *Pain Relief Connection*: http://www.massgeneral.org/painrelief/Newsletter
Previous Pain Topics articles: http://www.massgeneral.org/painrelief/Pain%20Topics/mghpain_paintopics_index.htm
Patient Care Services Pain Resource Center: http://pcs.mgh.harvard.edu/Secure/Clinical_Resources/Pain_Resources.asp
CCPD educational offerings: http://pcs.mgh.harvard.edu/CCPD/Educational_Offerings/cpd_offerings_calendar.asp
Treadwell Library (Magic): http://magic.mgh.harvard.edu/
MGH Formulary (includes patient teaching handouts in 16 languages): http://www.crlonline.com/crlsql/servlet/crlonline
Partners Handbook: http://is.partners.org/handbook/
Primary Care Office InSite (PCOI) (Clinician and patient information): http://oi.mgh.harvard.edu/pcoi/frontpage_frames.asp

URL notes: **Hold your cursor over the link for a second to see the URL**. If you are reading this in hard copy, this month's links are:
Merck: http://www.merck.com/
Merck announcement on Vioxx: http://www.merck.com/newsroom/press_releases/product/2004_0930.html
FDA Vioxx statement: http://www.fda.gov/bbs/topics/news/2004/NEW01122.html
FDA Palladone announcement: http://www.fda.gov/bbs/topics/ANSWERS/2004/ANS01315.html
Purdue Palladone announcement: http://www.pharma.com/pressroom/news/20040924-01.htm
FDA Cymbalta announcement: http://www.fda.gov/bbs/topics/news/2004/NEW01113.html
Humans produce morphine: http://www.biomedcentral.com/news/20040921/02/
Pain Relief is human Right: http://www.painreliefhumanright.com/
IASP: http://www.iasp-pain.org/
"8 facts . . . about cancer pain" http://wiscinfo.doit.wisc.edu/trc/images/Facts.pdf
MGH Pain Center: http://www.mgh.harvard.edu/paincenter/
Pain Management Rounds: http://www.painmanagementrounds.org/
Johns Hopkins Pain Course: http://www.hopkinscme.net/etrakWebApp/MeetingDetail.aspx?MeetingCode=05-511316
NEPA pain course: http://www.ampainsoc.org/societies/nepa/events.htm
American Pain Society: http://www.ampainsoc.org/
Boston Pain Forum meeting: http://www.massgeneral.org/painrelief/boston_pain_forum1.pdf
Pain Management in Primary Care:
https://tools.med.nyu.edu/CMECourses/index.cfm?fuseaction=courses.DisplayCourse&TheCourseID=1741&SortOrder=byDepartment&TimeFilter=Current&CFID=479872&CFTOKEN=29617506
PREP program: http://www.tufts.edu/med/prep/

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PAIN TOPICS

A Case of Finding the Right Opioid Dose

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Question:
My postoperative patient was a 21-year-old male receiving 2 Percocet every 4 hours but reporting pain every 3 hours. Our service decided to order oxycodone 5mg po q4 hours for breakthrough pain instead of increasing the frequency or the dose. In this situation, should we change the drug, dose, or frequency?

Answering a Question with More Questions:
As with many things, "it all depends." There are several variables to consider.

1. What was the patient actually receiving?
   - Was the patient on the original Percocet dosage strength (5 mg oxycodone + 325 mg acetaminophen)? Percocet now comes in multiple dosage strengths, so calculating the patient's actual use requires knowing the tablet strength he is receiving.
2. Was the dose scheduled around the clock or PRN?
   - In the early post-op period scheduled dosing usually makes more sense than PRN—the patient doesn't have to wait to have pain in order to have an analgesic.
3. How long has he been taking the Percocet?
   - It will take at least several hours to reach a steady state (consistent serum level) of opioid. The combination of around-the-clock dosing and the achievement of a steady state dramatically reduces the peaks and valleys of analgesia that are experienced by patients on PRN-only dosing.
4. How frequently and how close to the scheduled dose does he take the breakthrough dose?
5. Was he asking for it as soon as he needed it?
6. Was there a delay in getting it to him?
7. What is his medication history? Has he used successfully use oxycodone/acetaminophen in the past?

Discussion:
Assuming that other reasons (infection, internal bleeding) for ineffective pain relief have been ruled out, we can look at potential reasons that the patient requests analgesics at 3 hours post-dose. It is conceivable he is that unusual person who metabolizes the opioid a little faster than average and needs it q3 rather than q4 hours. If so, this wasn't really "breakthrough pain," it was "end of dose failure." End of dose failure can occur in either the case of a patient who metabolizes a little faster than most, or in a patient who is right on the edge of needing a higher dose, so that when the peak effect begins to diminish he experiences pain earlier than otherwise expected. Increasing the dose by either giving a higher dose at the same interval or the same dose at a shorter interval should help. It is usually more convenient for both patient and caregiver to increase the dose rather than decrease the interval. Finally, we should recognize that the standard dosing intervals are based on averages and we should tailor our treatments to the patient's needs—except for the burden of frequent dosing, it is not unreasonable to consider changing the dosing interval.

Occasionally there are patients for whom a specific opioid doesn't seem to be effective. However, changing from one opioid analgesic to another because it "isn't working" is usually the wrong strategy. In most cases the dose has not been escalated sufficiently, and thus there has not been an adequate trial of the selected agent. Plain oxycodone (no acetaminophen) is the appropriate drug for breakthrough pain in this case. It can be used to titrate to the appropriate dose (so if he needed it between every scheduled dose, for example, the scheduled dose should be increased). Using it PRN to make up for end of dose failure complicates the regimen and requires the patient to have pain and request analgesia, rather than to maintain the patient at a relative level of comfort, the real goal of pain management. Obviously, it also increases the workload on the nurse without the payoff of improved analgesia for the patient.

Ordering a breakthrough dose at a q4 interval doesn't make much sense when the scheduled dose is also q4. A true breakthrough dose should be more freely available: q1 or q2, reflecting the peak analgesic effect of approximately one hour for oral oxycodone. It should also be given without regard to the scheduled dose. In other words, if the patient requests it, he should receive it even if he is also due for the scheduled dose or had a scheduled dose 30 minutes ago.

Final Thought

Remember that combination analgesics by definition contain more than one drug. The maximum daily dose of the tablet is generally governed by the toxicity of only one of them. In this case, the patient is already taking 2 Percocet every four hours for a total daily dose of 3900 mg of acetaminophen, the recommended daily limit for this drug. The prescriber presumably took this into consideration when ordering oxycodone rather than additional Percocet. The acetaminophen probably plays a significant role in the regimen, so if the decision is made to increase the dose, the new order might logically be 15 mg oxycodone q4 hours plus acetaminophen 650 mg q4 hours.