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Pain ... The 5th Vital Sign

Clinical Focus:

(This series is intended to provide general information and context about medications for the treatment of pain. Clinical experience and judgement, individualization of treatment and consultation with experts and standard referenced\ should guide the treatment of specific patients.)

WORLD HEALTH ORGANIZATION ANALGESIC LADDER: STEP 1—NON-OPIOID ANALGESICS—NSAIDs, PART 1

Pathophysiology of inflammatory pain—A brief look

Step 1 of the Who Analgesic Ladder includes both acetaminophen (see Pain Relief Connection November 2007) and nonsteroidal anti-inflammatory drugs (NSAIDs). Inflammation is a complex process fundamental to immune response and healing, and contributes to many acute and chronic conditions. Tissue injury results in the release of the enzyme Cyclooxygenase-2 (COX 2). COX-2, in turn, “stimulates the production of prostaglandin E2, which promotes a region of localized hypersensitivity surrounding the injury.” (The Scientist) Other types of prostaglandins, stimulated by COX-1, are involved in production of the protective mucosa of the stomach, and the capacity of platelets to clump by becoming sticky. It is unclear what role COX-1 may have in pain and/or inflammation. NSAIDs are thought to provide pain relief primarily by targeting COX-2 at sites of inflammation. Both efficacy and toxicity of most NSAIDs is dose dependent. There has been a dramatic increase in scientific knowledge about NSAIDs in the past 30 years, and especially in the past 10 years. New NSAID classification and drug selection criteria have been proposed based on the relative ability of a drug to inhibit COX-1, COX-2, or both. Some NSAIDs are also antipyretics. Most classes of NSAIDs (nonselective NSAIDs) target both COX-1 and COX-2 to a greater or lesser degree. The newer COX-2 (Celebrex) will be talked about in more detail in the next “Clinical Focus.”

Spectrum of NSAIDs

There are a larger of NSAID (the Micromedex lists 64 drugs) in roughly a half-dozen subclasses. Several are available over the counter, while most are available only by prescription. All NSAIDs are available for oral administration. A few are available in liquid formulation, as chewable tablets, as topical preparations, or a rectal suppositories. One, ketorolac, is available for parenteral administration. Aspirin is found in combination with many over the counter and prescription analgesic products and cold remedies. Ibuprofen is found in certain cold remedies.

Principles of NSAID Therapy

Brandon RHA Cares About Pain Relief
Pain Management Resource Nurse
578-4202
moreb@brandonrha.mb.ca

1. When studied over large populations, no specific NSAID has been found to be more efficacious as an analgesic than the others.
 - Drug and dose should be individualized to patient characteristics, including patient-reported pain relief.
 - If pain is not sufficiently relieved with escalating doses of an NSAID over two weeks, trials with other NSAIDs may be attempted.
2. Assessment should include a history of what has worked in the past and what side effects were experienced.
3. For persistent pain syndromes such as arthritis, dosing should be scheduled rather than PRN.
4. Over the counter NSAIDs or acetaminophen should be considered first line treatment for mild to moderate acute or persistent pain. Note that moderate (WHO Step 2) pain may require addition of an opioid.
5. All NSAIDs have potentially serious and even life-threatening toxicities, especially when used chronically or in high doses. The balance of benefit and risk must be considered in prescribing and managing NSAIDs.
 - Most NSAIDs are excreted by the kidneys: renal function must be considered in prescribing and dosing.
 - History of peptic ulcer, bleeding disorder, cardiac disease, or asthma requires caution and monitoring.
 - Concurrent use of anticoagulants may preclude use of some NSAIDs or require dose adjustment.
 - If a surgical procedure is anticipated, NSAIDs should be stopped or the drug changed to one that does not inhibit platelet aggregation. For disabling pain condition, temporary substitution of an opioid should be considered.
 - The prescriber should know components and doses of all prescription and non-prescription products that the patient is taking.
 - Patient education should include dose and schedule, side effects, and drug-drug interactions.
6. Safety and efficacy for most NSAIDs has not been determined in children; ibuprofen in age-appropriate doses is widely used.
7. Aspirin should not be used in children under 18 years unless specifically prescribed for a non-viral condition.

In The News/Journal Watch

There has been a flurry of media information in recent months about various pain management related issues. Many will be highlighted in this issue of the Pain Relief Connection.

- The FDA warns against codeine use by nursing mothers until genetic tests are refined to identify the 1-28% of infants or mothers who are “ultra-rapid metabolizers”. Codeine had been considered the safest opioid to use during

Brandon RHA Cares About Pain Relief
Pain Management Resource Nurse
578-4202
moreb@brandonrha.mb.ca

breast-feeding, but this metabolic variation can cause respiratory depression in susceptible infants. <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01685.html>

- Berlinger MN, Giesecke T, Bornhovd KD Impact of Transdermal Fentanyl on quality of life in rheumatoid arthritis *Clinical Journal of Pain* 2007; 23:530-4. Patients with rheumatoid arthritis who have severe pain (baseline score 8/10) experienced significant pain reduction with improvements in sleep, functioning, and sense of general well-being when transdermal fentanyl was added to the treatment regiment. (Writer's note: this medication can only be added as per criteria established in the PRISM report 2005 where patient should be taking the equivalent of 100 mg of morphine daily for at least one week before implementation of 25 mcg of transdermal fentanyl)
http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17575494&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
- Vranken JH, Dijkgraaf MG, Kruis MR et al. Pregabalin in patients with central neuropathic pain: A randomized, double-blind, placebo controlled trial of a flexible-dose regimen. *Pain* 2007; Pregabalin relieves pain after brain or spinal cord injuries after one month of treatment.
http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17703885&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
- Moss-Morris R, Humphrey K, Johnson MH, et al. Patient's Perspectives of Their Pain Condition Across a Multidisciplinary Pain Management Program: Do They Change and if So Does It Matter? *Clinical Journal of Pain* 2007;23:558-564. Patients with chronic pain who change their thinking, feel and do better.
http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17710004&ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
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http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17586099&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
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- Ben-Galim P, Ben-Galim T, Rand N et al. Hip-Spine Syndrome: The Effect of Total Hip Replacement Surgery on Low Back Pain in Severe Osteoarthritis of the hip. *Spine*,(2007) 32:2099-2102. Patients having THR surgery have much less hip and back pain with better functioning at 2 year follow-up.
http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17762811&dopt=AbstractPlus
- Davis MP, Lasheen W, & Gamier P. What Oncologists Need to Know About Opioids and Their Complications (2007)*Oncology*, 21 (10): 1229-1238. A good

Brandon RHA Cares About Pain Relief
Pain Management Resource Nurse
578-4202
moreb@brandonrha.mb.ca

- review that vuts through persisting mistaken beliefs about opioid therapy for cancer pain. See companion “clarifying thoughts” by Cherny : 1241-1246, 1249
http://www.cancernetwork.com/showArticle.jhtml;jsessionid=CGDEKAMIFX41AQSNDLPSKHSCJUNN2JVN?articleId=201806617&_requestid=650271
- Gaspardo CM, Miyase CI, Chimello JT, et al. Is pain relief equally efficacious and free of side effects with repeated doses of oral sucrose in pre-term neonates? Pain Oral Sucrose (25% 0.5 mL/kg) was associated with fewer facial and cry indicators of pain compared to those neonates who receive sterile water among those having blood collection procedures. No differences in vital signs or side effects noted between groups. The babies act less distressed, but are still stressed. MAXILENE 4 anyone??????
http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17854995&dopt=AbstractPlus
 - IASP launched the Real Women, Real Pain campaign to draw attention to the significant impact of chronic pain in women and the lack of attention to this global problem. http://www.iasp-pain.org/AM/Template.cfm?Section=Real_Women_Real_Pain&Template=/CM/HTMLDisplay.cfm&ContentID=4629
 - Michael GE, Sporer KA, Youngblood GM Women are less likely than men to receive prehospital analgesia for isolated extremity injuries. (2007) *American Journal of Emergency Medicine*, 25: 901-6
http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=17920974&dopt=AbstractPlus
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http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17766503&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed_Pubmed_ResultsPanel.Pubmed_RVDocSum
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http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17606778&ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed_Pubmed_ResultsPanel.Pubmed_RVDocSum
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http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17606778&ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed_Pubmed_ResultsPanel.Pubmed_RVDocSum

Brandon RHA Cares About Pain Relief
Pain Management Resource Nurse
578-4202
moreb@brandonrha.mb.ca

[TermToSearch=17959348&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17959348&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum)

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- Riest g, Peters J, Weiss M, Dreyer S et al. Preventive effects of Perioperative parecoxib on post-discectomy pain. *British Journal of Anaesthesia*. Administering parecoxib both before and after surgery (peri-operative use) results in less pain and morphine use post-operatively than placebo and either preoperative or postoperative (not both) use of the same medicine. http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=18079431&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
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- Kong VK, Irwin MG Gabapentin: a multimodal Perioperative drug? *British Journal of Anaesthesia*, 99: 775-86. Known to help chronic pain, Gabapentin use in Perioperative pain is reviewed. http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=18006529&ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

CAM

- Acupuncture may be as effective as usual medicines for low back pain according to German researcher Michael Haake and colleagues in September 2007 Archives of Internal Medicine, 167, 1892-1898
- Watching comedy shows helped children tolerate pain for longer periods of time, but did not change the severity of pain. Children aged 7-16 endured experimental pain longer while watching videos they found funny. The study teamed UCLA’s Jonsson Comprehensive Cancer Center with the non-profit organization RX

Brandon RHA Cares About Pain Relief
Pain Management Resource Nurse
578-4202
moreb@brandonrha.mb.ca

laughter™ and is found in *Evidence based Complimentary and Alternative Medicine*.

- Using acupuncture perioperatively significantly reduces pain and analgesic use.
<http://www.medicalnewstoday.com/articles/85803.php>
- Treatment Preferences for CAM in children. When given a choice, children with chronic pain, irrespective of diagnosis, preferred non-invasive approaches that enhanced relaxation and increased somatic control.
<http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=17965769>

Medication Safety

- What's your patient's medication safety plan? PainAction has developed useful information that all patients taking prescription or non-prescription pain relievers should know.

<http://www.painaction.com/painaction/Article.aspx?channelId=2&contentId=124>

Pain Education on the Web (free registration on most sites)

- A revised Pain Management CME program was posted on the AMA website September 2007. CME's are offered through December 2009. There are seven modules ranging from Pathophysiology and assessment to the management of complex neuropathic pain or pain at the end of life.
http://www.ama-cmeonline.com/pain_mgmt/
- Principles of Effective Pain Management at the End of Life (updated and reaccredited) to CME on Medscape
http://www.medscape.com/viewprogram/6079_pnt
- Pain Resource Guide: Getting the Help You Need, is designed to help patients take charge of their pain
<http://www.painfoundation.org/page.asp?file=Publications/Index.htm>

Education:

Managing Pain Before It Manages You. This once-a-week for 9 weeks program is for individuals who are living with persistent (chronic) pain and who are interested in learning how to learn to manage their pain. The classes are one-hour long and are limited to 10 participants. For more information, please contact Bev More, Pain Management Resource Nurse at 578-4202 or to register, contact Pat Shaw, Clinics Clerk 578-4200. The next classes start Thursday April 3 from 1000-1100. *Please do not register if you do not plan to attend.*

Taking The Pain out of Complex Pain Management: Practical Approaches for Improved Services across the Care Continuum

April 11-12, 2008

This conference will be of primary appeal to community based physicians and allied health professionals with an interest in pain management, who work with patients in the community and who refer to specialized pain services in Canada.

Conference Website:

http://capitalhealth.ca/NewsAndEvents/ConferenceAndEvents/Complex_Pain_Mgt.htm

Brandon RHA Cares About Pain Relief
Pain Management Resource Nurse
578-4202
moreb@brandonrha.mb.ca

5th Annual International Symposium of Ultrasound for Regional Anaesthesia
ISURA 2008 April 24-27, 2008
Toronto, Ontario

ISURA 2008 will provide anaesthesiologists a comprehensive overview of ultrasound guided regional anaesthesia for surgery and chronic pain treatment. It also addresses other useful ultrasound applications in anaesthesia.

Conference website: <http://www.usra.ca/ISURA/index.php>

Canadian Pain Society Annual Conference:

May 27-30, 2008
Victoria, BC

CPS website: www.canadianpainsociety.ca

International Association for the Study of Pain 12th World Congress on Pain

August 17-22, 2008
Glasgow, Scotland

IASP website: www.iasp-pain.org/2008Coness.htm

References used for the Pain Relief Connection Newsletter include, among others, the following:

Care Beyond Cure A Pharmacotherapeutic Guide to Palliative Care 2000
McCaffery M., Pasero C., *Pain Clinical Manual* 2nd Edition 1999 Mosby
Professional's Handbook of Drug Therapy for Pain Springhouse 2001
Ballantyne Jane C., *The Massachusetts General Hospital Handbook of Pain Management* 3rd Edition
Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain 5th Edition
American Pain Society 2005
Pereira, J., Bruera e., *Alberta Palliative Care Resource Guide* Alberta Cancer Board 2001
2nd Edition
Roman D. Jovey, MD editor *Managing Pain the Canadian Healthcare Professional's Reference* 2002

End-of-Life Physician Education Resource Center www.eperc.mcw.edu

If you have a question that you would like answered or a case study that you would like to see profiled here, please send the information to Bev More, Pain Management Resource Nurse, CS1-200 BRHC or email to: moreb@brandonrha.mb.ca

Feedback about this newsletter is welcome. Please send comments to moreb@brandonrha.mb.ca

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Pain Management Resource Nurse
578-4202
moreb@brandonrha.mb.ca