Pain: Updates on Diagnostic and Treatment Modalities

ClinicalEdge provides succinct summaries of the latest "must-read" news and research. Here are several recent updates on the management of pain in the primary care setting.

IS ACETAMINOPHEN EFFECTIVE IN EASING BACK AND KNEE PAIN?

Machado GC, Maher CG, Ferreira PH, et al. Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials. *BMJ.* 2015;350:h1225. doi: 10.1136/bmj.h1225.

Acetaminophen is ineffective in treating lower back pain and provides minimal short-term benefit for people with osteoarthritis, a systematic review of 13 randomized, placebo-controlled trials reports.

Two independent reviewers extracted data on pain, disability, and quality of life, as well as adverse effects, patient adherence, and use of rescue medication, and found high-quality evidence that:

- Acetaminophen is ineffective for reducing pain intensity and disability, or improving quality of life in patients with low back pain.
- Acetaminophen provides significant, but not clinically important, benefit for pain and disability in patients with hip or knee osteoarthritis.
- Patients taking acetaminophen are nearly four times more likely to have abnormal results on liver function tests.

COMMENTARY

This study adds to the literature a less potent effect of acetaminophen than we have previously assumed,[1,2] suggesting a significant but not clinically important effect on pain. This result is at odds with the experience of many clinicians, who use acetaminophen regularly as a first-line agent for pain. When there is a dissonance between clinical experience and emerging evidence, one has to ask why. The explanation here may be that acetaminophen, NSAIDs, and opioid analgesics all have their problems and all seem to work better for some patients than others. In clinical practice, we often start with acetaminophen, which works for some patients, and go on to other agents for those in whom acetaminophen does not provide sufficient pain control. Studies that report a small mean effect may not detect the significant effect that can occur for many patients but gets hidden in the mean (which includes patients in whom there is no effect). I am reminded of the statistician who drowned in a river with a mean depth of 3 feet. A common clinical approach, often starting with well-tolerated acetaminophen and then progressing to other agents when needed, still seems sound. **—NS**

1. Bannuru RR, Schmid CH, Kent DM, et al. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. *Ann Intern Med.* 2015;162(1):46-54. doi: 10.7326/M14-1231.
2. Williams CM, Maher CG, Latimer J, et al. Efficacy of paracetamol for acute low-back pain: a double-blind, randomised controlled trial. *Lancet.* 2014; 384(9954):1586-1596. doi: 10.1016/S0140-6736(14)60805-9.

BACK PAIN: DOES EARLY IMAGING IMPROVE OUTCOMES?

Jarvik JG, Gold LS, Comstock BA, et al. Association of early imaging for back pain with clinical outcomes in older adults. *JAMA.* 2015;313(11):1143-1153.

Early imaging for back pain is not associated with better one-year outcomes among patients ages 65 and older, according to a prospective cohort study of 5,239 older patients with a new primary care visit for back pain.

Investigators compared function and pain at the 12-month follow-up visit among 1,174 patients who had early radiographs, 349 patients who had early MRI/CT, and 3,719 controls.

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Commentary provided by **Neil Skolnik, MD,** Associate Director of the Family Medicine Residency Program at Abington Memorial Hospital in Pennsylvania and Professor of Family and Community Medicine at Temple University in Philadelphia. These items were originally published as part of ClinicalEdge (www.clinicianreviews.com/clinicaledge).

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The primary outcome was back or leg pain-related disability, as measured by a back and leg pain disability score. The mean score showed no significant differences between groups.

COMMENTARY

Many guidelines suggest consideration of imaging early on in the diagnosis of low back pain in older adults due to the high prevalence of important underlying causes such as cancer.[1] This study looked at an older population and showed, as has been demonstrated in younger populations, that there is no advantage to early imaging with either x-ray or MRI, though costs were about 25% higher. **—NS**

1. Davis PC, Wippold FJ II, Brunberg JA, et al. ACR Appropriateness Criteria on low back pain. *J Am Coll Radiol.* 2009;6(6):401-407.

ANTI-INFLAMMATORY DRUGS AND ANTITHROMBOTIC THERAPY

Schjerning Olsen AM, Gislason GH, McGettigan P, et al. Association of NSAID use with risk of bleeding and cardiovascular events in patients receiving antithrombotic therapy after myocardial infarction. *JAMA*. 2015;313(8):805-814.

Combining prescription NSAIDs with antithrombotic therapy following myocardial infarction (MI) increases the risk for bleeding and excess thrombotic events, according to a study of 61,971 MI patients with ongoing antithrombotic therapy.

During an average of 3.5 years' follow-up, patients who had taken NSAIDs had increased rates of bleeding and cardiovascular events, with incidence rates per 100-person years as follows:

	With NSAIDs	Without NSAIDs	HR With NSAIDs
Bleeding	4.2	2.2	2.0
Cardiovascular events	11.2	8.3	1.4

HR, hazard ratio

The study authors note that clinicians should use caution when prescribing NSAIDs to patients who have recently experienced MI.

COMMENTARY

The use of NSAIDs in patients who have had coronary disease has been an area of concern for almost a decade. In 2007, the American Heart Association issued a scientific advisory update discouraging use of COX-2 inhibitors in patients with coronary disease and concluding that more data are needed on the cardiovascular safety of conventional NSAIDs.[1] Non-COX-2 selective NSAIDs, such as naproxen, appear to have a better cardiovascular safety profile than those with more COX-2 inhibition. They do carry an increased risk for bleeding. The study reviewed above suggests that patients who have been given NSAIDs, even for a short amount of time, have an increased risk for both bleeding and cardiovascular events, reminding us to carefully weigh the risk and benefit of using these commonly prescribed medications. **—NS**

1. Antman EM, Bennett JS, Daugherty A, Furberg C, Roberts H, Taubert KA; American Heart Association. Use of nonsteroidal anti-inflammatory drugs: an update for clinicians: a scientific statement from the American Heart Association. *Circulation*. 2007;115(12):1634-1642.

CHRONIC FATIGUE SYNDROME GETS A NEW NAME

Institute of Medicine. Beyond myalgic encephalomyelitis/chronic fatigue syndrome: redefining an illness. www.iom.edu/~/media/Files/Report%20Files/2015/MECFS/MECFS_ReportBrief.pdf. Accessed June 4, 2015.

Myalgic encephalomyelitis/chronic fatigue syndrome has a new name and more clearcut diagnostic criteria following a report by the Institute of Medicine. The new name, *systemic exertion intolerance disease* (SEID), better reflects how exertion exacerbates symptoms.

According to the report, the proposed diagnostic criteria for SEID is all three of the following:

- A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities that persists for more than six months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest
- Post-exertional malaise
- Unrefreshing sleep

Plus, at least one of the following:

- Cognitive impairment
- Orthostatic intolerance

The group also recommended that a new code be assigned in the ICD-10 that is not linked to chronic fatigue or neurasthenia.

COMMENTARY

Systemic exertion intolerance disease (SEID) will likely take some time to be integrated into practice as the new name for this condition. This change will also refocus attention on this difficult illness, which has always been challenging because the symptoms

of SEID are nonspecific and overlap with many other illnesses, from hypothyroidism to depression. The guidelines are a welcome addition to the literature, giving us better direction in diagnosing a difficult disease. **—NS**

REVIEW: MOST EFFECTIVE TREATMENTS FOR KNEE OA

Bannuru RR, Schmid CH, Kent DM, Vet al. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. *Ann Intern Med.* 2015;162(1):46-54. doi: 10.7326/M14-1231.

Intra-articular hyaluronic acid offers the best relief for pain in patients with knee osteoarthritis (OA), a meta-analysis of 137 studies with 33,243 subjects reports.

Researchers reviewed randomized trials of adults with knee OA that compared two or more treatments, including acetaminophen, diclofenac, ibuprofen, naproxen, celecoxib, intra-articular (IA) corticosteroids, IA hyaluronic acid, oral placebo, and IA placebo. They found for pain, stiffness, and function all treatments fared better than oral placebo.

- For pain, IA hyaluronic acid was most effective (0.63); acetaminophen was least effective (0.18).
- For function, all of the treatments were superior to oral placebo except IA corticosteroids.
- For stiffness, there was no significant difference among the different treatments.

COMMENTARY

The decision about which medicine to use to treat a patient with osteoarthritis is made on an individual basis, based on effectiveness for pain, as well as safety and cost considerations. Acetaminophen, which is the least effective pain agent studied, probably deserves its place as the most commonly used analgesic for OA based on safety and cost. IA treatments were in general more effective than oral treatments, though it is important to recognize that these studies looked at months, not years, of treatment of OA, and most of our patients are treated over a course of years. **—NS** **CR**

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