

July/August 2017, 7(4)

**In the News**

Yoga vs Physical Therapy for Chronic Low Back Pain

Traditional therapies for chronic low back pain are often ineffective. New research shows that yoga may be a good alternative for treating this condition. According to the National Institutes of Health (NIH), approximately 80 percent of the American adult population will have low back pain at one point or another, with men and women being equally affected. For most of these people, the pain is acute and does not last very long. For others, however, it turns into chronic back pain - meaning that it lasts for at least 12 weeks, even when the cause of the pain has been dealt with. Treatment options for low back pain include muscle strengthening exercises, physical therapy sessions, and analgesic medication. When these therapies fail, surgery is also an option. Unfortunately, none of the above therapies have proven highly successful. Between 25 and 80 percent of people who were treated for chronic low back pain experience a recurrence within a year from the treatment. For this reason, people living with chronic pain often resort to alternative therapies, such as acupuncture or yoga. The NIH report that there is enough evidence to support the "short- and long-term benefits" of yoga for relieving chronic low back pain. Previous studies have indeed suggested that yoga and stretching help ease low back pain. Researchers from the Boston Medical Center set out to examine the effect of yoga sessions on a group of 320 adults with chronic low back pain. The participants were randomly assigned to either attending 12 weekly yoga sessions, 15 physical therapy sessions, or just reading an educational book and newsletters on how to manage chronic low back pain. After these interventions, the researchers continued to follow the participants for 1 year, which included a 40-week maintenance phase. During the maintenance phase, yoga participants either took yoga drop-in classes or practiced yoga at home. Physical therapy participants took part in physical therapy booster sessions or practiced physical therapy at home. These improvements continued to be the same for both yoga and physical therapy after 1 year. As a result, the authors conclude that yoga is a "reasonable alternative" to physical therapy. *Medical News Today. June 2017.*

**Sphenopalantine Blocks for Pediatric Migraine**

The minimally invasive intranasal sphenopalatine ganglion (SPG) block is a safe, effective treatment for children with frequent migraine headaches, according to study results presented at the Society of Interventional Radiology 2017 Annual Scientific Meeting. The technique is performed the same way as in adults. Children and teenagers may be more anxious about this treatment, they may require more emotional support than adult patients. The inspiration for the 200-patient study of children between 7 and 18 years of age at Phoenix Children’s Hospital was two hospital neurologists who treat mainly headache. the investigators limited their criteria to a diagnosis of migraine and status migrainosus. team conducted a total of 310 SPG block treatments on the 200 patients, of whom 149 patients had a single session; 29 patients underwent two sessions; 11 patients had three sessions; and the remaining 11 patients were treated with more than four sessions (between four and 10). The interval between treatment sessions was typically one to two months. Before the intervention, the patient’s pain level was recorded on a scale of 1 to 10. Then, 10 minutes after treatment, patients were asked to compare their pain level, using the same scale. There was an average pain score reduction of slightly more than 2 points, which is a statistically significant difference. “Patients told us they do not care if their headache did not completely go away,” Dr. Kaye said. “The fact that their headache pain decreased from a 7 to a 3 on the pain scale, for instance, is good enough.” It is speculated that headache relief from the SPG block in children lasts weeks to one or two months.

**All NSAIDs Linked to Increased MI Risk**

Use of nonsteroidal anti-inflammatory drugs (NSAIDs), including naproxen, considered by some as one of the safest drugs in this class, is associated with a significantly increased risk for myocardial infarction (MI), results of a new patient-level meta-analysis show.

The analysis showed the heightened MI risk occurred as early as the first week of use and the risk was greater with higher doses. Even though the research suggests the increased MI risk lessened over time, "the findings were not conclusive enough about longer duration," said Dr Bally.

But for most patients, the risk is very small. There was a rapid onset of MI risk in the first week of NSAID use. In this time frame, the probability of increased risk (posterior probability of OR > 1.0) was greater than 90% for all NSAIDs: 92.4% for celecoxib, 97.3% for ibuprofen, 98.6% for diclofenac, and 98.8% for naproxen. Use of higher doses were also associated with increased MI risk. Use for 8 to 30 days at a high dose was particularly harmful for ibuprofen (>1200 mg/day), naproxen (>750 mg/day). But a longer duration of treatment generally did not seem to be associated with greater probability of increased risk for MI. *Medscape Nurses, May, 2017.*

**A Year Later, CDC Opioid Guidelines Still Under Fire**

About a year after the CDC’s controversial opioid guidelines went into effect amid protests from a number of pain specialists, they have come under renewed scrutiny for having an allegedly unscientific basis. A recent study in Pain Medicine (2016;17:2036-2046) found that the federal review process used to justify the recommendations in the CDC guidelines was flawed. Holding studies on opioids to a higher standard of what constitutes a long-term study than that of other pain treatments, including anticonvulsant, antidepressant, nonsteroidal anti-inflammatory drugs (NSAIDs) and behavioral therapies, the study authors wrote, is “responsible for the disqualification of an entire literature” on the efficacy and effectiveness of opioids in managing chronic pain. The authors retrieved reviews of anticonvulsants, antidepressants, NSAIDs, opioids or behavioral interventions for chronic pain from the Cochrane Database of Systematic Reviews, as well as all of the opioid treatment studies that were retrieved for the federal evidence report underpinning the CDC guidelines that were excluded from analysis due to “inadequate duration.” A total of 52 reviews retrieved from the Cochrane database were included in the final analysis. The authors graphed the number of trials included versus duration of treatment for each of the five treatment modalities studied, comparing these with the durations of the opioid trials that were excluded from the federal report. They found that “nearly all” of the trials reviewed had treatment durations of 12 weeks or less, whereas the federal review dropped trials with an observation period of less than a year. The authors concluded that this criterion was “inconsistent with current regulatory standards,” adding that in terms of active treatment in efficacy or effectiveness trials, “published evidence is no stronger for any major drug category or behavioral therapy than for opioids.” Daniel Carr, MD, MA, professor of public health and community medicine and program director of pain, research education and policy at Tufts University School of Medicine, in Boston, and past president of the American Academy of Pain Medicine, who led the study, said he found the exclusion of studies from the federal review process “very unusual,” adding that this led to a biased assessment of opioids compared with other treatment modalities. “The current regulations in the U.S., Europe and Japan are that if you want a drug approved to treat chronic pain, you need to check the efficacy of it—that is, a placebo-controlled trial lasting at least three months—and it has to be replicated, so you need at least two trials,” Dr. Carr said. “And then safety data should go out to a year. Basically, those are the rules. “So when the guidelines said, well, don’t use opioids, use nonsteroidals, the implication would be that if you’re not including the opioid literature, there’s something stronger about the other literature, for all the other treatments,” he continued. “And, in fact, none of the literature contains many trials that runs for more than about a hundred days. And the reason for that is, that’s the usual standard practice and custom. “So there was an implication—and I think it was more than an implication, it was very explicit if you look at some of the CDC press releases—that we’re giving opioids for chronic noncancer pain without any evidence for doing so.

“I felt that was kind of disingenuous, because if you look at the literature on evidence, typically you do a systematic review of evidence at time A and publish it at time B. And then you go back a couple years later, and you update it. You take what you originally published at time B, and you factor in all the interim studies, and update what you published with data from between—let’s say times B and C. And you draw and update your conclusions,” Dr. Carr explained. “Very rarely, you might remove a paper that duplicates data or has something wrong with it, but typically you accumulate the different findings. It’s very, very rare that you would the whole analysis of a literature, and then update it by the same people and find that the earlier literature was not only not updated but entirely excluded,” he said. “So they were very explicit about this, and they said, ‘We had zero papers available to address the question of what is the efficacy and effectiveness of opioids for chronic noncancer pain.’ “That’s almost unheard of,” Dr. Carr said. “So that was the motivation for doing the paper.” Jeffrey Fudin, PharmD, founder and chair of Professionals for Rational Opioid Monitoring & Pharmacotherapy, and co-editor of the Opioids, Substance Abuse and Addictions section of Pain Medicine, agreed with Dr. Carr that the long-term evidence said to be lacking for opioids is also lacking for other treatments for chronic noncancer pain. “There’s not good evidence for any long-term analgesic drugs, really, for extended periods of time. So while one might argue that there’s not good evidence for opioids, we’re seeing all these deaths from opioids,” Dr. Fudin said. “Well, that may be, but in 2015, we saw the same number of deaths from prescription NSAIDs that we saw from prescription opioids, and that’s just from gastrointestinal bleeds without consideration to iatrogenic kidney failure and heart disease. People are just selecting what they want to select and using sensationalizing opioid deaths.” Dr. Fudin added that the fallout from the CDC guidelines has been harmful both to patients and physicians. “I’m often called as an expert witness in court cases, sometimes working on behalf of regulatory agencies, sometimes for the plaintiff. And over the last 12 months, the amount of calls I’m receiving to defend physicians is unbelievable, mostly against state bureaus of narcotics” he said. “More often than not, doctors are being brought up on charges because, somewhere on a spreadsheet, their medical practice popped up as being an outlier in terms of marking daily morphine equivalent doses.” Morphine equivalent daily dose (MEDD), Dr. Fudin noted, is a strategy to limit opioid prescribing across a number of different drugs by calculating their potency in terms of morphine. However, in an editorial in the Journal of Pain Research (2016;9:153-156), Dr. Fudin and his colleagues described MEDD as “grossly flawed,” citing, among other considerations, high variability in the way patients respond to different molecules. Dr. Carr agreed, saying that MEDD “was never intended to be rigid across all people” and calling its inclusion in the CDC guidelines “dangerous,” particularly given that the CDC has an MEDD calculator on its website that can be consulted by primary care physicians without in-depth knowledge of opioids and chronic pain care. In terms of patient harm, Dr. Fudin said he receives “hundreds of emails a month from panicked patients” who have been doing well on opioids for long periods of time—up to 10 to 20 years—whose physicians are now cutting their doses to be consistent with the CDC guidelines. However, not every pain specialist agrees that the CDC guidelines are a step in the wrong direction. Andrew Kolodny, MD, co-director of opioid policy research at the Heller School for Social Policy and Management at Brandeis University, in Waltham, Mass., and executive director of Physicians for Responsible Opioid Prescribing, was critical of Dr. Carr’s study, saying that he sees it as advocacy rather than science. “I’m kind of surprised to see folks still making the ‘the absence of evidence is not evidence of absence’ argument. If they haven’t yet figured out opioids are lousy drugs for most patients with chronic pain, they should try cracking open a medical journal,” Dr. Kolodny said. “I’m just really surprised to see, in the midst of a public health crisis caused by aggressive opioid prescribing, that a paper like this would appear.” While not criticizing the science of the paper as such, Dr. Kolodny likened Dr. Carr’s study to climate change denialism, noting that Tufts University receives funding from the Sackler family, who owns Purdue Pharma LP, the manufacturer of OxyContin (oxycodone). Dr. Carr, however, stated that he received no funding from either the Sackler family or Purdue for the study, and that the study was not politically motivated. Regardless, Dr. Kolodny said the paper was based on a mischaracterization of the AHRQ review. “AHRQ deemed short-term trials to be of ‘inadequate duration’ because its review was trying to find out if long-term use is safe and effective. The feds aren’t unfairly picking on opioids as the authors suggest.” Ultimately, Dr. Fudin said, the larger problem that needs to be addressed is one of education for doctors, particularly primary care physicians who see chronic pain patients. “It’s a problem. We really need to foster safer use of these drugs,” Dr. Fudin said. “Somebody needs to require that physicians become highly educated in pain management. That’s the bottom line. A lot of states require mandatory education, but it’s a joke. Two hours of CME [continuing medical education] is not enough time to really understand how to treat chronic pain, to understand the risks of different drugs.”

**DEA Proposes Change in Production Quota of Controlled Substances**

The Drug Enforcement Administration (DEA) announced a proposed Aggregate Production Quota (APQ) that would reduce the amount of controlled substances being produced in the United States by 20% in 2018, compared with 2017. The APQ is based on the amount of controlled substances needed to meet the legitimate scientific, research, medical, industrial and export needs for 2018, as well as the reserves of these substances. Published in the Federal Register, the proposal aims to reduce the amount of Schedule II opioid painkillers manufactured in the United States, including oxycodone, hydrocodone, oxymorphone, morphine, codeine, fentanyl and others. The CDC released clinical guidelines in 2016 recommending the reduction of opioid prescriptions for chronic pain patients. The DEA and other related federal agencies also have stepped up their efforts in educating clinicians, pharmacists, manufacturers and the public about the potential risks of abusing opioids, stressing the importance of proper prescribing. “Physicians, pharmacists and patients must recognize the inherent risks of these powerful medications, especially for long-term use,” said Acting DEA Administrator Chuck Rosenberg in a press statement. “More states are mandating use of prescription drug monitoring programs, which is good, and that has prompted a decrease in opioid prescriptions.” Since its inception in 1971, the Controlled Substances Act quota system was created to decrease or eradicate diversion from “legitimate channels of trade” by controlling the amounts of materials used to produce controlled substances. Due to the increased risk for abuse, the goal of the quotas is to provide sufficient and constant supply for Schedule I and II drugs intended for legitimate medical use, while limiting the amount available, to reduce the possibility of diversion. In this process, the DEA attempts to balance the production of what is legitimately needed for medical use against the excessive production of these dangerous substances. Annually, the DEA establishes over 250 APQs for Schedule I and II substances. When establishing these APQs, the DEA analyzes data such as estimates of legitimate medical need from the FDA, retail consumption estimates based on prescription dispensing, disposition history and forecasts from manufacturers, DEA internal tracking data and past quotas. After the APQ is established, the DEA provides individual manufacturing and procurement data for those companies who apply for it. The DEA has the ability to revise quotas at any time due to increased sales or exports, new manufacturers, new product developments or recalls.

**Gabapentin Improves Postoperative Pain Control in Regional Anesthesia Setting**

A meta-analysis of randomized controlled trials shows that gabapentin provides additional analgesia benefit in the regional anesthesia setting across a range of surgical procedures. The intervention was preoperative oral gabapentin administration greater than 30 minutes prior to surgical incision, and predefined outcomes were postoperative pain at rest at 12 hours, pain at rest at 24 hours and opioid consumption within the first 24 hours of surgery. Administration of gabapentin resulted in a statistically significant reduction in pain at rest at 12 hours (standardized mean difference [SMD], –48; 95% CI, –0.81 to –0.14; P=0.006), pain at rest at 24 hours (SMD, –31; 95% CI, –0.61 to 0.00; P<0.05) and morphine equivalent requirement at 24 hours (SMD, –44; 95% CI, –0.81 to –0.08; P<0.02) compared with the control in the setting of concomitant regional analgesia. Subgroup studies of neuraxial or peripheral nerve blockade as well as orthopedic or abdominal procedures yielded similar results. Further subgroup analysis of trials involving only one-time preoperative administration of gabapentin showed similar efficacy when compared with patients who received multiple postoperative doses. An examination of side effects found preoperative gabapentin to be associated with higher rates of sedation and lower rates of pruritus than in the control group, and the drug was not associated with dizziness, nausea or vomiting. *Anesthesiology News, AUGUST 7, 2017.* \* Dose of gabapentin used was not provided in this article.

**New NDA for Non-Opioid Pain Medication**

Recro Pharma has submitted a New Drug Application (NDA) for IV meloxicam (30 mg), which contains microcrystal technology, based on positive results from clinical trials showing significant pain reduction and opioid-sparing after surgery, according to a press release from the company. The drug is yet to be named . The studies submitted to the US Food and Drug Administration (FDA) included a Phase III trial in patients following bunionectomy and abdominoplasty surgeries, a large double-blind Phase III safety trial, and 4 Phase II clinical trials for the management of moderate to severe postoperative pain, among others. In the first Phase III efficacy trial, IV meloxicam 30 mg "achieved the primary endpoint of a statistically significant difference in Summed Pain Intensity Difference (SPID) over the first 48 hours (SPID48) compared to placebo in patients following bunionectomy surgery," according to a release from Recro Pharma. In the second Phase III efficacy trial, IV meloxicam 30 mg produced a statistically significant difference in SPID over the first 24 hours (SPID24) compared to placebo in patients following abdominoplasty surgery. Meloxicam is a long-acting, preferential cyclooxygenase-2 (COX-2) inhibitor that has analgesic, anti-inflammatory, and antipyretic activities. Because oral meloxicam has a slow onset of action, largely due to poor solubility, the new agent uses "NanoCrystal” technology, which has been shown to provide a rapid onset of action of meloxicam. The hope is that a more powerful, yet safer, NSAID will help reduce the need for postoperative opioids to manage pain. According to the company, IV meloxicam 30 mg did reduce the overall use of opioids.

**Rexista, Generic Oxycodone, Fails Hurdle Toward Approval**

In a vote of 22 to 1, the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the FDA found that Intellipharmaceutics International Inc's New Drug Application for Rexista (extended-release abuse-deterrent oxycodone hydrochloride) should not be approved at this time. Citing safety concerns about the ability of the product to deter abuse, the committees also voted against abuse-deterrent labeling. However, the committees expressed a desire to review the additional safety and efficacy data for Rexista that may be obtained from human abuse potential studies for the oral and intranasal routes of administration, which the company plans to commence in the next few weeks.

**FDA Clears Noninvasive Device for Intractable Pain**

The US Food and Drug Administration (FDA) has cleared a noninvasive neuromodulation device (Stimpod NMS460, Xavant Technology) for the relief of chronic intractable pain. The device applies a unique, patented pulsed radiofrequency (PRF) waveform to the affected area transcutaneously. This waveform creates electromagnetic effects similar to invasive PRF treatments. Several case studies have shown instant and dramatic relief of chronic intractable pain. The device is focused on the symptomatic relief and management of chronic intractable pain, as well as adjunctive treatment in the management of postsurgical pain and posttraumatic acute pain problems, and as an adjunct for pain control due to rehabilitation.

**Books of Interest**

**Chapter News**

GKCC ASPMN received another 5 years of CNE approval. We even have a nice certificate from the State Board of Education indicating we are approved until 2022! Thank you to everyone who helps in this effort.

**Laughter Does Good Like Medicine**