Are Long-Acting Opioids More Effective Than Short-Acting Opioids for Chronic Pain?

By Steven A. King, MD, MS [2]

The answer to this question has long been considered to be, "yes" and for what seem to be logical reasons related to the nature of chronic pain. But, where's the science to support the belief?

There are many things about pain and its management that were once widely accepted as undisputed fact that subsequent research has found to be of doubtful validity.

A new study calls into question the view that extended-release/long-acting (ER/LA) opioids are more effective than immediate-release/short-acting (IR/SA) formulations for the management of chronic pain.1 The acceptance of the purported benefits of ER/LA opioids is understandable for patients whose pain is continuous and fairly constant over the course of the day. As an accompanying editorial to the article notes, there appear to be many pharmacologic and psychological benefits to their use.2 In contrast to IR/SA opioids, ER/LA opioids avoid the peaks and valleys in pain control that can occur with drugs that provide rapid analgesia but lose their effect over a few hours as the drug and its active metabolites are cleared from the blood. Patients are expected to receive a more steady level of analgesia with ER/LA formulations.

With regard to the psychological benefits, the patients who take ER/LA opioids on a fixed schedule (as typically prescribed) rather than on an as-needed basis (as IR/SA opioids are usually prescribed) needn't "watch the clock" to determine whether they are due for the next dose or decide whether the pain is at a sufficient level to require another dose.

The benefits of ER/LA opioids when compared to IR/SA opioids have seemed to be so obvious that they have generally been accepted with only limited research on whether they are real. In fact, the authors of the current study1 reported that in their review of the literature they found only six previous randomized studies comparing the two formulations, and of these they felt that only three studies provided sufficient information on the study process to be able to determine the validity of their results. Only one of the three reported an advantage from ER/LA opioids and this was for improved quality of sleep.

The current study was performed in Norway on 58 subjects with chronic non–cancer-related pain who were already taking 150 to 300 mg of codeine per day in tablet form, combined with acetaminophen. The participants were randomized to two groups and received either the ER/LA or IR/SA forms of the opioid dihydrocodeine along with separate acetaminophen for an 8-week period. They were given doses equivalent to those of the codeine they had been taking.

Dihydrocodeine was chosen for the study because it is not available in Norway and therefore the patients were unlikely to have any previous experience with it. Dihydrocodeine is available in the United States in combination drugs, but it is rarely prescribed and probably more often as an antitussive than as an analgesic. (I can't recall ever seeing a prescription written for it for pain.) In order to avoid patients being able to determine whether they were taking ER/LA or IR/SA dihydrocodeine from the scheduling of administration, each group received the same number of pills on the same schedule, with placebo pills being used as a fill-in.

The primary outcome measures were pain intensity and its stability, defined as differences between highest and lowest levels as recorded by subjects in a diary during the last week of the study. No differences were found between the two groups. There were also no differences found between them with regard to secondary measures, including quality of life, quality of sleep, and depression. More patients reported adverse events with the ER/LA formulation, although there was no difference in dropout rates between the two groups.

This study has several limitations, most notably the relatively short time span and the small number of subjects. Since many patients with chronic pain take opioids for far longer than 2 months, it is possible that longer durations of use might reveal more differences between the two forms of the drug. Also, since all the subjects were taking the medication on the same schedule, this obviated the
Are Long-Acting Opioids More Effective Than Short-Acting Opioids for Chronic Pain?
Published on Physicians Practice (http://www.physicianspractice.com)

purported benefit of the less frequent dose schedule of ER/LA opioids. However, it does make a very important contribution to the debate over whether ER/LA formulations are more effective for patients with chronic pain, especially in light of the concerns about their misuse. Even though some of these concerns have seemed to be allayed by the reformulation of several of these drugs into tamper-resistant/abuse-deterrent formulations (most notably ER/LA oxycodone [OxyContin]), there is still limited information on how much of an impact these alterations have had on opioid abuse. Furthermore, there are still multiple ER/LA formulations that are not tamper-resistant, including the recently introduced hydrocodone drug Zohydro.

The study also raises the question of whether IR/SA opioids, if they are prescribed on a fixed schedule, provide the same consistent level of analgesia as ER/LA formulations. Since acetaminophen was administered separately from dihydrocodeine in the study, there was no concern about acetaminophen toxicity, which can occur when combination IR/SA opioids are taken too frequently.

If ER/LA opioids do not provide better pain relief or quality of life compared with the IR/SA formulations, we must certainly ask whether their widespread use is warranted in light of the well-recognized problems associated with them. We will need more studies to answer this, but it is clear that the benefits of ER/LA opioids, as well as the long-term use of them for chronic pain, are far from established.

References:


Source URL: http://www.physicianspractice.com/pain/are-long-acting-opioids-more-effective-short-acting-opioids-chronic-pain

Links: