Myth: codeine is a powerful and effective analgesic

Sanjay Arora
Mel E Herbert
Medical Student
Department of Emergency Medicine, Olive View—UCLA Medical Center, 14445 Olive View Drive, Sylmar, CA 91342

Correspondence to:
Dr Herbert
mherbert@ucla.edu

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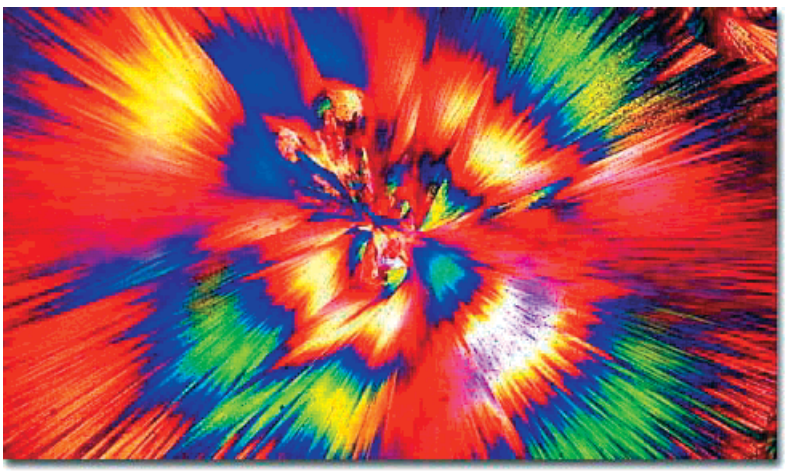
Patients look to physicians not only to prevent and treat disease, but also to alleviate pain and suffering. Pain is the most common complaint among patients seen in the emergency department.[1] A widely held belief is that codeine is a powerful and effective analgesic. The classic therapeutic regimen, endorsed by the American Society of Anesthesiologists Task Force on Pain Management, is to begin with nonopiate analgesia and to add opiate therapy if the level of pain control proves to be inadequate.[2] The most common prepackaged combination therapy is codeine with acetaminophen (Tylenol #3 or #4).[3] The underlying theory of this plan is that using 2 drugs with different mechanisms of action will, in essence, attack the problem from 2 sides. Unfortunately, studies have shown that this combination is at best only slightly more efficacious than nonopiate analgesia alone and results in a greatly increased number of adverse side effects.

In a systematic literature review and meta-analysis of 29 published trials, de Craen and colleagues examined the change in both efficacy and safety when codeine was added to paracetamol (acetaminophen) for the relief of pain.[4] Multiple reviewers were used to assess all studies, and 13 predefined methodologic criteria were applied to assess the quality of each trial. Pain intensity and relief were quantified through visual analog scales. In most studies, 60 mg of codeine was administered; the dosage of paracetamol ranged from 400 to 1,000 mg. Results of the pooled analysis of the 19 single-dose trials showed that adding codeine leads to an increase in analgesic effect of only 5%, as measured by the sum peak intensity difference, and produces similar results in peak pain-intensity difference, total pain relief, and peak pain relief. While the single-dose studies showed a similar incidence of side effects between the 2 groups (pooled rate ratio = 1.1, 95% confidence interval 0.8-1.4), multidose studies showed a significant increase in side effects when codeine was added (pooled rate ratio = 2.5, 95% confidence interval 1.5-3.5).

Boreau et al reported similar findings from a randomized, double-blind, multicenter study in which they compared the use of acetaminophen (400 mg) plus codeine (25 mg) with aspirin (1000 mg) and with placebo in the treatment of acute migraine headache in 198 patients.[5] Response was measured with a visual analog scale in which a patient was asked to mark the intensity of his or her pain on a 100-mm line where 0 is "no pain" and 100 is "worst possible pain." Baseline pain levels ranged from 55.9 to 59.6. Two hours after treatment was administered, the mean pain scores were 36.6 and 39.3 for aspirin and for acetaminophen plus codeine, respectively, with a placebo value of 53.8. Side-effect profiles were similar in the 2 treatment arms of this study.

Analgesic combinations with hydrocodone bitartrate appear to be more effective than those with codeine. Palangio et al performed a randomized, double-blind, multicenter study in which 429 patients were randomly assigned to receive either 1- or 2-tablet doses of a hydrocodone (7.5 mg) plus ibuprofen (200 mg) combination or a 2-tablet dose of a codeine (30 mg) plus acetaminophen (300 mg) combination.[6] Patients who received the 2-tablet hydrocodone plus ibuprofen treatment reported greater daily pain relief than those who received either of the other 2 combinations. In addition, patients receiving codeine were more likely to stop therapy because of side effects.

The myth that codeine is a potent and efficacious analgesic must be exposed so that clinicians can make more rational choices when managing and treating pain.



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Acetominophen with codeine is only slightly more effective in relieving pain than regular Tylenol (acetominophen) alone shown in the photomicrograph

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