Dr Steven King is commended for sharing in his recent article that benzodiazepines are contraindicated in pain management as well as for stating the merit of minimizing opioid risks by initiating opioids at the smallest possible dose with agents of the lowest potency (CONSULTANT, September 2011, page 605).1

However, Dr King mistakenly reported opioid potencies, indicating that oxymorphone, now generically available, was of low potency. The author also inaccurately reported that hydrocodone (Vicodin) and oxycodone (Percocet) were low potency while reporting that methadone and morphine are categorized as more potent opioids. Finally, the author neglected to report that buprenorphine is a high-potency opioid despite being available commercially in multiple FDA-approved formulations.

These are issues of importance as Dr King appropriately advises initiation of opioid treatment with low doses of low-potency agents to minimize iatrogenic sequelae.

Weak opioids include tramadol, tapentadol (Nucynta), and codeine, as Dr King noted. As the author reported that tapentadol characterized by 1/50th the potency of morphine, the 50 mg smallest size offers 1 mg of morphine. Codeine is felt to exert its effects via 10% biometabolism to the active agent of morphine such that 30 mg size tabs offer approximately 3 mg of morphine.

Stronger opioids of intermediately defined potency include morphine, hydrocodone (Vicodin), oxycodone (Percocet), and methadone.2

The strongest opioids include fentanyl at 60 to 80 times morphine potency, buprenorphine at up to 5000% morphine potency, hydromorphone, reportedly up to 11 times the potency of morphine, and oxymorphone at 10 times the potency of morphine.3

Opioid dose reduction via concomitant prescription of nonopioid analgesics may also diminish addiction. Dr King appropriately reported that benzodiazepines diminish opioid potency, but readers should be aware that depositing local anesthetics in proximity to nerves has been reported to potentiate opioid-mediated pain relief by up to 300%,4 thereby diminishing opioid dosing substantially with attendant minimization of risks for overdose death and addiction.

Prescription controlled drug abuse has been reported to be decreased by almost 50%, from 17.8% down to 9%, at abuse-vigilant interventional pain clinics where opioids are supplemental to injection techniques as opposed to clinics where opioids constitute the sole offering by the clinicians.5

Finally, acetaminophen, similar to nerve block injections, adds to opioid potency while also minimizing abuse (addiction and/or diversion). However, Dr King endorsed the use of pure opioid, stating “you can avoid problems with acetaminophen toxicity by giving the opioid alone.” The statement is paradoxical, as Dr King subsequently appropriately advocated “if a patient requires more than 2 doses per day of an immediate-release opioid for an extended period, consider prescribing a long-acting opioid.”1 The incongruity exists as BID dosing of 325 mg of acetaminophen sums 650 mg, considerably lower than the 2009 revised recommendations of 3250 mg maximum daily acetaminophen dosing.

Furthermore, readers should appreciate that acetaminophen-containing products such as Percocet and Vicodin have considerably less abuse potential relative to pure oxycodone or hydromorphone (Dilaudid), the biometabolite of hydrocodone. Opioids are commonly abused via snorting and doing so with acetaminophen induces oronasal fistula,6 palatal perforation,7 soft palate necrosis,8 atypical mycobacterium infection,9 and invasive fungal rhinosinusitis10 as potent disincentives to snort acetaminophen-containing opioids. As such, addicts manipulate the unsuspecting clinician with allergy, intolerance, or end-stage hepatic failure fabrications to avoid acetaminophen-containing opioids. As such, addicts manipulate the unsuspecting clinician with allergy, intolerance, or end-stage hepatic failure fabrications to avoid acetaminophen-containing opioids.

Similarly, criminals intent on diversion will preferentially solicit opioids bereft of acetaminophen as more illicit funds can be obtained from purchasing addicts to achieve euphoria without the tissue destruction risks of insufflating acetaminophen. For this reason, the DEA web site and New Hampshire Board of Pharmacy independently verify the higher street value of pure opioids relative to acetaminophen-containing opioid medications.

The evidence is sufficiently substantial to discourage prescribing pure opioids that the June 2010 issue of Practical Pain Management reported that Tennessee
Board of Medical Examiner guidelines indicate that pure oxycodone is not recommended to be prescribed. Of note, the same published guidelines endorse Dr King’s recommendation to limit short half-life opioids to BID dosing.

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REFERENCES:

Thank Dr Geller for his letter and comments and I am happy to have the opportunity to respond to them. The issue regarding the comparative strengths of many of the opioids is a complex one. What I sought to do was to provide readers the stepladder approach to the prescription of opioids recommended by virtually all the published guidelines on the use of these medications for chronic pain. Thus, it is recommended to begin with drugs such as codeine, hydrocodone, oxycodone, and oxymorphone. However, as I noted in the article, codeine is metabolized to morphine and hydrocodone to hydromorphone, both of which are considered “stronger” opioids and oxycodone is metabolized to oxymorphone. Thus, how valid this stepladder really is remains open to question.

There are a number of medications that have been proven to actually potentiate the analgesic effects of opioids, including the tricyclic antidepressants and the older, nonspecific NSAIDs. However, I must admit I am unaware of evidence demonstrating that acetaminophen does the same.

Dr Geller notes the result of a paper that he interprets as indicating that interventional pain clinics do a better job at controlling abuse of prescription pain medications than do clinics that don’t provide interventions. I disagree with his interpretation of this paper. Not surprisingly, it indicates that the more closely physicians monitor patients’ use of opioids, the less likely abuse will occur. The fact that interventional techniques may also be available appears irrelevant.

I am confused by Dr Geller’s comment that my statement regarding the use of pure opioids is “paradoxical” because if patients only take two doses per day of an opioid-acetaminophen combination they wouldn’t exceed the daily maximum acetaminophen dose. I agree that if everyone followed my recommendation, taking a combination drug would be of little concern. However, as combinations of acetaminophen with codeine, hydrocodone, or oxycodone are recommended to be taken up to four times per day and are often taken even more frequently, it is easy to exceed the maximum acetaminophen dose even if patients are not taking additional acetaminophen separately which, unfortunately, is not an infrequent occurrence. Also, acetaminophen toxicity can occur even if this drug is taken for relatively short periods of time, so this is also an issue in the management of acute pain.

Although theoretically the addition of acetaminophen and the risk of side effects associated with its use should reduce opioid abuse if opioids are prescribed in combination with it rather than the opioids alone, I am unaware of research demonstrating this. The fact that hydrocodone, the most frequently abused prescription opioid in the United States, is only available in combination with other medications and is by far most frequently prescribed in combination with acetaminophen suggests this theory is fallacious. I think it is foolish to prescribe opioids based on their potential street values rather than what is best for the individual patient. If nothing else common sense alone should tell you that if you believe the person to whom you are prescribing a medication is likely to be selling it, you should not be prescribing it.

I should also note that I was unable to find the recommendation of the Tennessee Board of Medical Examiners against the use of pure oxycodone either in the paper Dr Geller cites or in that Board’s own documents. If such a recommendation does exist, I would disagree with it.

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