as slide shows before transmitting them to the students. During testing, students could not use the hyperlinks unless they viewed the case as a slide show.

While our cases focused on cardiovascular topics, these types of cases can be constructed for any therapeutic area and integrate complex patients with multiple problems to be treated for various diseases. PICCs can also extend beyond therapeutics if a patient needs to have a drug extemporaneously compounded or if the pharmacist is consulted for the treatment of adverse drug effects.

We recently began upgrading the cases by integrating tutorials into the cases for students who are interested in advanced concepts or who desire more information than what can be routinely covered during didactic lectures. For example, students can complete the section of questions on warfarin and learn about using pharmacogenetics for warfarin dosing by clicking on a hyperlink to a tutorial where that concept is explained in greater detail and then be hyperlinked back. We also added heart sounds, chest radiographs, and electrocardiograms (ECGs) (with a voluntary tutorial on ECG reading) to make the cases more real and to integrate knowledge from physical assessment. Most of the ECGs, chest radiographs, and heart sounds were accessed freely on the Internet.


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Important lessons in opioid selection

The case report by Kharlamb and Kourlas1 described a 45-year-old woman suffering from what was presumed to be failed back syndrome associated with lower extremity radiculopathy. The patient’s medical history included depression, anxiety, and possible bipolar disorder. The patient was prescribed methadone hydrochloride 5 mg three times daily, in addition to gabapentin and etodolac.

While methadone is a valuable tool used in the treatment of a variety of pain syndromes, its use in this patient posed significant undue risk in many ways. For example, the presence of psychiatric comorbidities has been shown to be associated with increased risk for nonadherence or misuse of opioids in patients treated for pain.2 While noncompliance can be problematic for all opioids, the unique pharmacokinetic profile of methadone necessitates strict compliance with a well-developed and closely monitored regimen to avoid potentially serious adverse events.

The patient’s medication history also indicated risks associated with methadone use. The patient had been taking a low dosage of the weak opioid propoxyphene. Changing therapy from propoxyphene napsylate 200 mg daily to methadone hydrochloride 15 mg daily represents a dramatic increase in total opioid exposure. The effect of this increase is evident in the patient’s report, during a clinic visit one week after this change, of feeling drunk and having difficulty driving. Kharlamb and Kourlas attributed this effect to the initiation of gabapentin, but it was as likely secondary to the use of methadone. Curiously, the dosage of methadone was increased by 50% during this visit despite the patient’s report that her pain was alleviated. Again, the effect of this subsequent increase was “extreme drowsiness,” reported during the follow-up appointment seven days later. While many methods exist for converting treatment to methadone, virtually all are designed to convert another strong opioid to methadone. The American Pain Society states that “a reasonable approach to treating patients with methadone as their first strong opioid is to titrate the patient to adequate analgesia with PRN short-acting opioids, then transition the patient to methadone.”3 Use of these prescribing principles might have prevented the depressant effects of methadone and presented a lower risk of more serious events.

The choice of methadone was also complicated by the use of multiple central nervous system depressants (i.e., alprazolam, gabapentin, fexofenadine), which can synergistically increase the risk of opioid-related adverse effects. During the second clinic visit, the patient was prescribed transdermal fentanyl after the discontinuation of methadone. The use of transdermal fentanyl at this juncture was not ideal, since this formulation’s pharmacokinetic profile makes it an undesirable choice in patients whose opioid requirements have not been established.

Finally, Kharlamb and Kourlas justify the use of methadone (a diphenylheptane) and fentanyl (a phenanthrene) by citing the patient’s stated allergy to codeine. This reasoning may be inappropriate in the presence of true opioid allergy, but true opioid allergy is exceedingly rare. Thus, the assessment of true opioid cross-reactivity is difficult and has led to controversy regarding its clinical significance.4,5 It is likely that the patient’s stated codeine allergy was actually an adverse effect or pseudoallergy, thereby making the use of other opioids reasonable.

The use of methadone in this patient was associated with multiple risks that may have been avoided by designing an analgesic regimen with another opioid. As methadone’s popularity as an analgesic increases, its use must be accompanied by careful patient selection and skillful prescribing in order to preserve its valuable place in the pain management armamentarium.

Letters


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T he original case report was written retrospectively as a result of a reported adverse drug reaction, after which methadone was discontinued. Nevertheless, I disagree with Dr. Cox’s statements that methadone in this patient “posed significant undue risk.” Psychiatric comorbidities may increase the risk for nonadherence or misuse of opioids, but that factor does not account for patient individuality. According to Fine and Portenoy,1 while psychiatric and psychosocial disorders can profoundly affect a patient’s misuse of pain medicines, noncompliance and poor outcomes, even in this population, are rare. Furthermore, as compassionate care dictates in all patients a comprehensive and competent risk assessment was complemented in this patient by stratification and management strategies to lessen the likelihood of adverse events. Wasan et al.2 suggest that psychiatric morbidity is a risk factor for misuse of prescription opioids but also advocate that further investigation of the factors contributing to medication misuse in this patient population is needed. The patient we described had a history of depression, possible bipolar disorder, and anxiety, all of which were deemed stable with current therapy. She had no history of noncompliance or substance abuse, and since she was already taking opioids at the time of referral to the clinic, it was decided to continue opioids.

The terms “weak” and “strong” as applied to opioids can be misleading. Opioids can be described to be more or less potent, or more or less efficacious, or to have more or less affinity for the opiate receptors; as such, “weak” and “strong” are not suitable scientific descriptors for opioids. With that in mind, the switch from propoxyphene napsylate 200 mg daily to methadone hydrochloride 15 mg daily was not necessarily a dramatic increase in total opioid exposure. Several references and conversion tables support the selection of the starting methadone dosage in this patient.3-5 Because methadone has a unique pharmacokinetic profile, its dosage should be based on patient response, clinician experience, knowledge of methadone pharmacokinetics, and published guidelines specific to methadone. Determination of an equianalgesic dosage should not rely solely on published dosage tables, as they often do not differentiate between long- and short-term opioid therapy.

The patient reported that her new analgesic regimen helped to alleviate her pain, but because etodolac and gabapentin had been discontinued, the methadone hydrochloride dosage was increased to 7.5 mg three times daily to ensure pain relief. Dr. Cox, in stating that this increase was unreasonable, forgets the data that suggest that low dosages of methadone may be incrementally increased by a higher percentage than higher dosages of methadone.6,7 This patient was receiving a low dosage of methadone from the start and already had physical tolerance from chronic propoxyphene use. Regardless of propoxyphene’s failure to produce sufficient analgesia, it still had affinity for the opiate receptor and increased physical tolerance.8 Furthermore, the Veterans Affairs–Department of Defense opioid treatment guidelines do not restrict the use of methadone for transition therapy after adjusting short-acting opioid dosages.4 Although methadone is not an extended-release formulation, it is unusual in that it may often be taken three times daily because of its extended half-life.

I believe that transdermal fentanyl was appropriately chosen for this patient because she had a well-established history of tolerability to meperidine. Since long-term meperidine use is not prudent for many reasons, and since meperidine and fentanyl are both phenylpiperidines, fentanyl was clearly the long-term opioid of choice for this patient.8,9 In fact, she responded well to this therapy without any adverse events.

I agree with Dr. Cox that true narcotic allergy is indeed rare. Specific information on this patient’s supposed codeine allergy was not available at the time. She had been taking fexofenadine regularly while using propoxyphene. The methadone-associated reaction happened only after propoxyphene and fexofenadine were discontinued. Perhaps the patient experienced a methadone–induced histamine reaction that may otherwise have been blocked had she continued to take fexofenadine. Because of the sequence of events, this possibility was not realized until after methadone therapy commenced, but the patient was warned of the potential for a similar reaction should she be prescribed propoxyphene in the future in the absence of antihistamines.

I agree with Dr. Cox that methadone warrants skillful prescribing limited to clinicians who have proper training and experience. The initial intent of this case report was to add clarity in aiding clinicians who work with opioids.