On-Demand Clinical News

Clinical Corner: Hydrocodone Drug Reschedule Change Takes Effect October 6, 2014

Nate Hedrick, PharmD

On Friday, August 22, 2014, the Drug Enforcement Administration (DEA) followed the recommendations of the Food and Drug Administration to reschedule hydrocodone combination products (ex: Norco, Hydrocodone/acetaminophen, etc.) from Schedule III to Schedule II of the Controlled Substances Act. The DEA's rationale for the move is to combat prescription drug abuse and to help protect the health and safety of the public. This change is scheduled to go into effect on October 6, 2014, and all prescriptions written on or after that date will need to comply with state and federal laws for Schedule II medications.

In most cases, a maximum of 90 days' supply of hydrocodone combination products may be written for a patient at one time, with no refills allowed. Although the Controlled Substance Act (CSA) prohibits refills of prescriptions for schedule II controlled substances, a practitioner may issue multiple schedule II prescriptions in order to provide up to a 90-day supply of medication.

New prescriptions for these medications may not be phoned in and many states do not have approved systems for electronic transmission of Schedule II medications yet. However, for patients in long term care facilities or hospice care centers, the rules are less strict. Most states allow hospice patients to obtain partial fills of the total amount written, allowing for multiple fills without the need to get a brand new prescription from the physician every time a refill is needed. Furthermore, long-term care and hospice patients may continue to have their prescriptions for Schedule II medications faxed to the pharmacy.

Patients that are currently taking hydrocodone combination products should work with their doctor, nurse, and pharmacist to plan for this change before it becomes an issue. Writing new prescriptions may be necessary, and some patients will benefit from a change to non-scheduled pain medication. Refills on any prescription for hydrocodone combination products written before the October 6th deadline will still be valid until April 8th, 2015 but many pharmacies and insurance companies may update their systems early and refills may not be able to be processed.

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Opioid Use in Renal or Hepatic Dysfunctions

Priya Narula, PharmD, CGP

Renal Insufficiency

Chronic pain is common in patients with chronic kidney disease and may be related to their primary renal disease or other related comorbidities, such as vascular disease or diabetes. It can affect up to 50% of hemodialysis patients, with 82% of them experiencing pain that is moderate to severe.[1] Opioids are often the primary management strategy in these patients. In renal failure, the absorption, metabolism, and renal clearance of opioids are complex. When selecting an appropriate opioid for these patients, the properties of the parent drug and its metabolites must be considered.[2]

There is a lack of pharmacokinetic and pharmacodynamic data of opioids in renal failure, making opioid dosing difficult for clinicians. However, the following adjustments have been proposed for the initial dosing of the safer opioids in renal failure.

- Creatinine Clearance > 50 mL/min: normal dosing
- Creatinine Clearance of 10-50 mL/min: 75% of normal dosing
- Creatinine Clearance < 10 mL/min: 50% of normal dosing

The "normal" opioid dose for any given patient is that which provides adequate pain relief without unacceptable adverse effects. While opioids can be used in renal insufficiency, they require closer monitoring and constant reassessment to ensure that accumulation of active metabolites does not result in toxicity. This should not preclude the effective use of opioids in these patients. With the appropriate selection and titration of opioids, patients with renal failure can achieve analgesia with minimal risk of adverse effects.[3]

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Table 1. General recommendations for opioids in patients with renal insufficiency

Drug	Recommendation	Note
Meperidine	Not Recommended	Accumulation of toxic metabolite, normeperidine, may cause CNS toxicity.
Codeine	Not Recommended	Accumulation of active metabolites in renal failure. Recommended to be avoided in patients with a GFR <30mL/min.
Morphine	Not recommended	Not recommended for chronic use in renal insufficiency (GFR <30mL/min) due to the rapid accumulation of active, nondialyzable metabolites (morphine-6-glucuronide) that are neurotoxic. If morphine must be used, avoid long-acting preparations and monitor closely for toxicity.
Oxycodone	Use cautiously	Metabolized in the liver with 19% excreted unchanged in the urine. There are reports of accumulation of both the parent compound and metabolites in renal failure resulting in CNS toxicity and sedation.
Hydromorphone	Use cautiously	1. Active metabolite, hydromorphone-3-glucuronide (H3G), can accumulate and cause CNS toxicity. 2. Hemodialysis: H3G appears to be effectively removed during HD (can be used safely in HD pts with careful monitoring). 3. It should be used with caution in patients with a GFR < 30mL/min who have yet to start dialysis or who have withdrawn from dialysis.
Fentanyl	Appears safe	Considered relatively safe in renal failure as it has no active metabolites. However, very little pharmacokinetic data exist regarding fentanyl in end stage renal disease. While some studies have shown decreased clearance in renal failure, most studies do not show drug accumulation. Fentanyl is not dialyzable due to high protein binding and a high volume of distribution.
Methadone	Appears safe	No active metabolites and limited plasma accumulation in renal failure due to enhanced elimination in the feces. It does not appear to be removed by dialysis.

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Intercultural Communications in Hospice Care

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Human beings are drawn close to one another by their common nature, but habits and customs keep them apart.
~ Confucius, Chinese Philosopher

Culture, simply defined, is the way of life of a group of people (society) who work together to meet their basic needs. This way of life forms a set of human-made objective and subjective elements that in the past has increased the probability of survival. A dynamic and integrated set of symbols, spirituality (religion), beliefs, values, customs, social organization, and language guide behavior. In her theory and educational model, Nitza Hidalgo defines the three levels of culture as the concrete (dimensions that are visible and tangible such as food and clothing), the behavioral (language, family structure, gender roles, etc.) and the symbolic (values, beliefs, spirituality, etc.). Culture may also be described by the "iceberg theory," where only one-eighth of the iceberg is visible when passing next to it on a boat. The concrete aspect of culture is this tiny fraction that is visible while the majority of the iceberg (the part below the surface of the water and the inner core), which represents the behavioral and symbolic realms, is never visible or tangible.

Intercultural communication occurs between people whose cultural perceptions and symbol systems are distinct enough to alter the event. Each person should respect the others' methods of communicating. In healthcare, numerous cultural queues and indicators play out in the course of a consultation: contextual, time structure, and affect. Language is vital to successful verbal communication. High context communicators indirectly present their message while low context communicators use specific, targeted methods to convey the message in a concrete way.

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Hepatic Insufficiency

The liver is primarily responsible for the metabolism of opioids to their metabolites, thus the pharmacokinetic and pharmacodynamic properties must be carefully reviewed prior to initiating these agents in patients with hepatic insufficiency. Oxidation (involving the CYP450 enzymes) is the major metabolic pathway of most opioids with the exception of morphine and buprenorphine, and oxidation is decreased in patients with hepatic cirrhosis. These changes can be secondary to reduced hepatic blood flow (limiting first-pass metabolism) or decreased CYP450 enzyme levels in these patients. This may result in decreased opioid clearance, increased oral bioavailability, and decreased first-pass metabolism.[4] In patients with liver insufficiency, this can lead to accumulation of the drug in the body with repeated administration and long-term use. Therefore, lower doses and longer administration intervals may be warranted.[5] Morphine is metabolized through glucoronidation, which is less affected in hepatic disease, however morphine has also been shown to have decreased clearance and increased oral bioavailability in patients with liver cirrhosis.[5] Changes such as decreased serum albumin and ascites can also alter opioid volume of distribution which can lead to either increased or decreased drug concentrations, although there is no practical way to predict this apart from close clinical observation.[6]

When making clinical decisions about designing opioid regimens in ESLD patients, it is important to remember that the dose should be based on that which provides adequate pain relief while providing an acceptable side effect profile. In general, lower doses of most opioids should be initiated and caution should be exercised when selecting regular dosing intervals until patients have demonstrated an ability to tolerate more frequent dosing. Doses should not be decreased solely out of concern for hepatic disease, especially if a patient is tolerating a regimen they have been on. Patients with deteriorating liver function should be closely monitored for signs of drug accumulation and need for dose reductions, assuming the level of analgesia remains acceptable. Finally, potential drug interactions involving the CYP450 enzyme system must always be considered as there is potential for non-opioid medications to either induce or inhibit the metabolism of any opioid that is a CYP450 enzyme substrate.

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In terms of time structure, some communicators present their message sequentially (in order from first to last or last to first) while others may do so synchronically (not in order). Communicators may be affective (readily showing emotion) or neutral (stoic) in their conversational style. When communicating, simple present tense should be used when possible. Talk clearly and slowly, repeating key points and giving examples. Avoid medical jargon and slang. Gestures, facial expressions, and nonverbal cues generally improve expression. Be as clear, complete, concise, and cohesive as possible. Encourage admission when there is lack of understanding and address any concerns or questions that arise. The literature supports the use of a professional medical interpreter when communication in the same language is not feasible.

Studies show that beliefs and preferences differ vastly even among members of the same culture, ethnic group, and family. Numerous cultural and individual barriers to patient care exist because of this. Stereotyping, or unfairly accepting that all members of a certain group are the same, and ethnocentrism, or the tendency to believe that one's own culture is centrally important or superior to others, lead to inappropriate assumptions. Objectivity, or overcoming individual biases, and respect for the individual patient and his or her preferences are key. Spirituality (religion) is particularly important in hospice and palliative care because of its role in a patient's perception of life after death. In its broadest sense, spirituality is the meaning patients find in life that impacts coping, decision making, and quality of life that may or may not involve religion. Spiritual or existential distress can in turn exacerbate the presentation of physical symptoms such as pain, anxiety, restlessness, agitation, and depression. Furthermore, for some patients, underlying spiritual suffering may actually be of greater concern than overt physical symptoms such as pain. Spiritual distress, like any other clinical symptom, requires attention and treatment. A myriad of spiritual needs have been defined in the literature and may be grouped into six themes: need for religion, need for companionship, need for involvement and control, need to finish business, need to experience nature, and need for positive outlook. These needs should be addressed as part of each patient's individualized interdisciplinary plan of care to enhance quality of life.

Despite the rapid globalization that has occurred over the past few centuries, intercultural communication still presents today's healthcare professionals with a unique challenge that must be met to be effective clinicians.

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Table 2. General recommendations for opioids in patients with liver insufficiency

Drug Name	Recommendation	Notes
Meperidine	Not Recommended	Accumulation of toxic metabolite, normeperidine (CYP3A4 metabolism), may cause CNS toxicity.
Codeine	Not Recommended	Impaired conversion of codeine (prodrug) to the active compound, morphine by CYP2D6 in the liver to be active.
Morphine	Use cautiously	Recommended to decrease frequency of administration and dosage because of decreased clearance and increased $t_{1/2}$ and oral bioavailability.
Oxycodone	Use cautiously	Risk of accumulation of parent drug due to decreased conversion to metabolites and decreased elimination. Recommended to reduce dose by 1/2 to 1/3 of the usual amount and avoid in severe cirrhosis.
Hydromorphone	Use cautiously	Risk of accumulation of parent drug due to decreased conversion to metabolites and decreased elimination. Recommended to decrease dose by 50% of the usual amount.
Hydrocodone	Use cautiously	Hydrocodone is a prodrug that is metabolized by CYP2D6 to hydromorphone and other metabolites. Hydrocodone dose titrations are limited by the non-opioid component; overconsumption of acetaminophen-containing products is hepatotoxic. In severe liver disease, initial starting doses should be reduced to 50% of usual amount and as the disease progresses, prolonged dosing intervals may also be necessary.
Fentanyl	Appears safe	Pharmacokinetics not altered in patients with cirrhosis.
Methadone	Not Recommended	Risk of accumulation with severe liver disease

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A copy of the final ruling from the DEA can be found here: http://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm

As always, please contact your ProCare HospiceCare clinical pharmacy team if you have any additional questions about how this ruling might affect your hospice or to review patient-specific situations for the most appropriate plan of care.

ProCare HospiceCare welcomes all suggestions and comments. If you would like additional information about our services, have ideas for articles, or wish to submit a comment, email us at **resources@procarerx.com**.

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