University of Illinois Hospital & Health Sciences System
Changing medicine. For good.

Jul/Aug 2016

RxPress

Vol 17 No 4

TABLE OF CONTENTS

CDC Guideline on Prescribing Opioids for Chronic Pain: Focus on Appropriate Opioid Selection

In March 2016, the Centers for Disease Control and Prevention released a guideline on prescribing opioids for chronic pain that is not due to cancer or palliative care. Even though the guideline focuses more on opioid prescribing in a primary care setting, pharmacists practicing within any setting should be familiar with recommendations to successfully manage patients with the diagnosis of chronic pain. This article will describe key recommendations with focus on selection, dosing, and titration of opioids.

Selecting an agent

Preference is given to immediate-release opioids when initiating opioid therapy in patients with chronic pain. Extended-release/long-acting (ER/LA) opioids should be started only in patients who have received immediate-release opioids for at least 1 week. If a patient requires ER/LA agent, methadone should be last line agent due to QT prolongation and long and variable half-life. Fentanyl patches also should be reserved as last line agents because they have complicated dosing and administration that may lead to inappropriate use. Fentanyl patches have a slow absorption over the first 72 hours, and heat can increase patient's exposure to the active ingredient. Detailed education on appropriate medication use is necessary for patients receiving prescriptions for fentanyl patches. Three brand formulations of ER/LA opioids have abuse-deterrent properties approved by the Food and Drug Administration: oxycodone ER (OxyContin), morphine/naltrexone ER (Embeda ER), and hydrocodone ER (Hysingla ER). The role of abuse-deterrent preparations is unclear as of right now due to lack of studies showing significant reduction of abuse with these agents.

Dosing opioids

Providers should start the lowest possible dose of opioids for chronic pain. Evidence shows that the risk of opioid overdose doubles and even quadruples in patients taking 50 morphine mg equivalent (MME) per day or more compared to patients taking less than 20 MME/day. Patients who are 65 years and older or who have renal or hepatic insufficiency are at risk of accumulating opioids due to decreased drug clearance. Therefore, special caution must be exercised when initiating opioids in this patient population.

Opioid titration to higher doses

Some literature supports titrating doses of opioids after 5 half-lives and at least after 1 week for methadone. If a required titration exceeds 50 MME/day threshold, providers should increase frequency of patient monitoring and potentially provide naloxone prescription. Patient who do not achieve pain control with opioids doses at or above 90 MME/day should see a pain specialist and potentially lower doses or discontinue opioids.

Opioid titration to lower doses

Many guidelines recommend decreasing opioid doses by 10% to 50% each week. In cases of overdoses, taper may occur at a much faster rate over 2 to 3 weeks. However, dose reduction by 10% each week may be the best approach especially in patients with long-term use of opioids. Once lowest doses of opioids are reached, providers can extend administration frequency as the next step and discontinue opioids when use falls to one tablet per day. Individual patient factors must be also accounted for when designing a taper schedule. Caution must be exercised in tapering opioids in pregnant women as opioid withdrawal may cause abortion or premature labor.

Management of acute pain

For acute pain not associated with trauma, surgery, malignancies, neurological symptoms, or infections, prescription of immediate-release opioids for 3 days or less should be sufficient. Some cases may require longer duration but it should not exceed 7 days.

Follow up

Providers should schedule follow up in 1 to 4 weeks after prescribing a new opioid or increasing dose of current opioid therapy. Patients with continued opioid therapy should meet with providers every 3 months because patients taking opioid therapy for greater than 3 months are more likely to develop opioid abuse.

Naloxone Rescue Kits

The guideline from the Centers for Disease Control and Prevention recommends offering a prescription of naloxone to patients with high risk for overdose when prescribing opioids for chronic pain. The factors that predispose patients to drug overdose include history of drug overdose or abuse, prescription of opioids with doses at 50 morphine mg equivalent (MME) per day or higher, concurrent benzodiazepine use, and patients who may be increasing their opioid use in the near future.

Literature suggests that availability of naloxone in a community setting may prevent opioid overdoses in patients. Naloxone is a μ-opioid receptor antagonist, which works by displacing opioids from opioid receptors. The medication may be administered through intravenous, intramuscular, subcutaneous, intranasal, nebulization, and intraosseous routes. In the outpatient setting, intramuscular and intranasal are the most common routes of administration for opioid overdose. The onset of action is usually within 2 to 5 minutes after administration, and the effects wear off in 30 to 90 minutes. Such short duration of action may not be sufficient in reversing overdoses from extended-release opioids, methadone, and other opioid agents that have long half-life. The recommended dose of naloxone for overdose reversal is 0.4 to 2 mg, and administration can be repeated every 2 to 3 minutes. Administration of naloxone can cause opioid reversal in some patients, and patients may experience adverse events such as fever, hypertension, tachycardia, agitation, restlessness, diarrhea, delirium, muscle pain, sweating, abdominal cramping, nausea, and vomiting.

Patients who receive naloxone prescription must be counseled on appropriate use and administration of this medication. Naloxone is available as prefilled glass syringes, vials, nasal spray (Narcan), and auto-injectors (Evzio) for use in the community setting. The complete naloxone kit must contain at least 2 doses of naloxone with corresponding administration devices. Naloxone should be carefully stored and used only when necessary to extend its shelf-life. Naloxone can be stored for 12 to 18 months at room temperature. The website *Prescribe to Prevent* (http://prescribetoprevent.org) provides additional information for prescribers and pharmacists on naloxone, patient education, and current state-specific laws.

Prescribers and pharmacists must ensure that patients are able to afford and access naloxone kits. Many insurers cover naloxone kits but some may require prior authorization. Kaleo, manufacturer of Evzio, offers a patient assistance program for naloxone auto-injectors for uninsured patients who do not qualify for Medicaid or Medicare.

Laws regarding access and dispensing of naloxone vary across the country. Illinois laws allow prescribing and dispensing of naloxone to a patient or a person who can administer this medication in the case of overdose. Pharmacists are qualified to dispense naloxone kits without prescription after completion of the approved training by the Department of Human Services. For example, Illinois Pharmacist Association provides the necessary training.

Effectiveness of Prescription Drug Monitoring Programs (PDMP)

Overview

The 2011 White House report, Epidemic: Responding to America's Prescription Drug Abuse Crisis, brought to light the growing prescription drug abuse problem across the United States and made a call for action at the local, state, and national level. One of the goals outlined in the report aimed to establish a prescription drug monitoring program (PDMP) in all 50 states by the year 2014. Thirty five states had operational PDMPs at the time. Forty nine states (excluding Missouri) now have PDMPs. This increase has been accompanied by an expansion of the literature on PDMPs. Historically, the literature has been limited on the topic with the exception of expert testimony and several conflicting observational studies. This article presents recent findings regarding PDMP design, patient and prescriber behavior, and clinical outcomes. A table is also provided with applications to the Illinois PDMP.

Program design

Since every state creates and implements its own PDMP, design and execution varies. Provider use of PDMPs is oftentimes voluntary. Several studies have surveyed providers in search of why health professionals may choose not to participate. Reasons included accessibility issues, time restraints, perceived lack of impact on prescribing habits, ability to navigate, forgotten passwords, and lack of resources (ie, computers). In response to these findings, a 2012 article by Perrone and Nelson suggested a list of "ideal" features PDMPs should possess: ease of access, standardized content, real-time updates, mandatory pharmacy reporting, monitoring of schedule II to V controlled substances and other drugs of concern, interstate accessibility, confidentiality and security, support for public health and research initiatives, and availability of strictly monitored access to non-prescribers. Each of these characteristics can also be found in model PDMP proposals advocated by the National Alliance for Model State Drug Laws and the National Safety Council.

Patient and prescriber behavior

Many studies describe how PDMPs encourage responsible prescribing. Following the Ohio PDMP roll out, the University of Toledo Medical Center Emergency Department tracked changes to written prescriptions once providers reviewed patient PDMP profiles. After consulting the PDMP, providers adjusted 41% of prescriptions; 61% of changes resulted in a de-escalation of opioid therapy (ie, reduced doses or number of opioid prescriptions) while 39% of changes showed greater utilization of opioids. Similar results were observed on a larger scale. A recent article in Health Affairs concluded that PDMP implementation reduced the rate of Schedule II opioid prescribing by 30% or more across 24 states over a 3 year time period. Although PDMP use was voluntary in several states included in the study, there are states that mandate providers to review patient PDMP profiles prior to prescribing opioids. One year after mandating this practice, New York observed a 75% decrease in "doctor shopping" according to the PDMP Program Center of Excellence at Brandeis University. Tennessee adapted similar measures and observed a 36% decrease in the number of patients seeking to fill the same opioid prescription from multiple providers.

Clinical benefits

The clinical benefits demonstrated by PDMPs are unclear. Differences in opioid overdose mortality are typically used to express the clinical utility of PDMPs. An observational study by Paulozzi and colleagues compared drug overdose death and opioid consumption rates in states with PDMPs to those without them between 1999 and 2005. The authors concluded that overdose death rates were unaffected by the presence of a state PDMP and recommended that PDMP managers research ways of improving the clinical impact of such programs. This is the most commonly cited study that questions the clinical benefits provided by PDMPs.

Studies published over the last 5 years are more promising. The number of deaths related to overdose increased by 61.0% (from 1,804 to 2,905) in Florida between 2003 and 2009. Consequently, several statewide initiatives were enacted: expanding pain clinic oversight, law enforcement raids, outlawing the dispensing of schedule II or III drugs from physician offices, mandating PDMP use by 2011, and others. A report from the Centers for Disease Control and Prevention described a 16.7% decrease (535 lives) in the number of overdose related deaths from 2010 to 2012. Largest declines were observed in oxycodone and benzodiazepine associated deaths, 52.1% and 35.6% respectively.

A statistical model credited Florida's PDMP alone for a 25% reduction in oxycodone induced death; every PDMP query resulted in a 0.229 person decrease in oxycodone related death per month. Oregon demonstrated similar results with a 38% decline in opioid overdoses and 58% decrease in death from methadone poisoning between 2006 and 2013. These results followed the establishment of a state PDMP, prior authorization requirement for methadone doses larger than 100 mg, provision of education regarding pain management for health professionals, and expansion of persons able to administer naloxone.

Conclusion

Prescription Drug Monitoring Programs serve as a great opportunity for pharmacists to answer the call from the 2011 White House report for action. As the report and many articles acknowledge, PDMPs are only part of the multifaceted solution needed to reduce prescription drug abuse. Continued research regarding program design, patient and prescriber behavior, and clinical benefits can only lead to further optimization. Although the clinical benefits of such programs are presently unclear, the ability to enhance informed prescribing and encourage responsible prescribing behavior is firmly established. Registering for the Illinois PDMP is simple. Registration is available online (https://www.ilpmp.org) and takes minutes.

Characteristics of an Ideal PDMP (Perrone and Nelson)	Illinois PDMP (IL-PDMP)
Ease of access	Standalone web database (https://www.ilpmp.org) *Pilots taking place across the state (ie, Southern Illinois University, Northwestern Memorial Hospital) to link the IL-PDMP directly with institution EHR/EMR
Real-time updates	Updated weekly (Friday)
Mandatory pharmacy reporting	All outpatient pharmacies. Inpatient pharmacies and drug abuse treatment programs are exempt
Monitoring of prescribing of Schedule II to V drugs and drugs of concern	Already established
Standardized content	Patient name, address, birth, gender, national drug code of controlled substance, date controlled substance dispensed, quantity, prescriber DEA, payment type (ie, Medicaid, cash, third party), patient location code for controlled substances other than those filled at retail (home, nursing, outpatient)
Confidentiality and security	HIPAA and state privacy provisions apply; however, any law enforcement official with an active investigation number may be provided with information
Support for public health initiatives and research	Proactive system that sends prescribers notices once 3 opioids have been filled
Interstate accessibility	Not all 50 states; shares data with several states; lack of PDMP in Missouri impacts accuracy of records in southern Illinois
Availability of strictly monitored access to non-prescribers	Provider designee may use IL-PDMP on practitioner's behalf

EHR/EMR= Electronic Health (or Medical) Record; DEA = Drug Enforcement Agency; HIPAA = Health Insurance Portability and Accountability Act; IL= Illinois; PDMP= Prescription Drug Monitoring Program

Authors: Gennaro Paolella, PharmD candidate
Janna Afanasjeva, PharmD, BCPS
Editor: Janna Afanasjeva, PharmD, BCPS