SAFE AND EFFECTIVE PRESCRIPTION OF CONTROLLED SUBSTANCES

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Topic Overview

Despite regulations and policies that have been implemented to control and manage the use of controlled substances, injury, and death from drug overdose has reached epidemic proportions. Prescribers and pharmacists must continue to educate themselves about the safest methods of writing and dispensing prescriptions in order to reduce misuse while still ensuring appropriate access.

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Target Audience: This educational activity is for pharmacists.

How to Earn Credit: From August 29, 2022, through August 29, 2025, participants must:

1) Read the "learning objectives" and "author and planning team disclosures;"
2) Study the section entitled "educational activity;" and
3) Complete the Post-test and Evaluation form. The Post-test will be graded automatically. Following successful completion of the Post-test with a score of 70% or higher, a statement of participation will be made available immediately. (No partial credit will be given.)

Learning Objectives: Upon completion of this educational activity, participants should be able to:

1. **Identify** the reason for the Controlled Substances Act (CSA) and state-specific regulations for the prescription of controlled substances
2. **Describe** the schedules of controlled substances according to their class or purpose, the relative risk for the misuse of each category of drug, and its potential for the development of substance use disorder
3. **Compare** and contrast the different types of controlled substances based on the accepted medical use and potential for misuse
4. **Identify** how Prescription Drug Monitoring Programs (PDMPs) can be used to help identify inappropriate drug use and prescribing
5. **Identify** best practices for reducing inappropriate controlled substance use while ensuring access in appropriate situations.

Disclosures

The following individuals were involved in the development of this activity: Susan DePasquale, MSN, PMHNP-BC, Amanda Mayer, PharmD, and Jeff Goldberg, PharmD. There are no financial relationships relevant to this activity to report or disclose by any of the individuals involved in the development of this activity.

Introduction

The prevalence of prescription drug use disorder is on the rise, including among patients previously considered low risk. This is especially true of opioid analgesics prescribed for chronic pain, stimulants prescribed for attention-deficit/hyperactivity disorder (ADHD), and benzodiazepines prescribed for anxiety or insomnia. In order to prevent the misuse of controlled substances and reduce the risk of substance use disorders, pharmacists and other healthcare providers should fully understand the different drug Schedules and their risks, carefully follow guidelines related to the prescribing and dispensing of substances within each Schedule, and consistently utilize state monitoring programs.

Controlled Substances Act and Other Regulations

Controlled substances are defined as drugs, medications, or chemicals that are regulated by the Controlled Substances Act (CSA) or state law. A substance's classification as a controlled substance is determined by several factors, including a substance's potential for misuse. Not all drugs listed as controlled substances are narcotics. Often, the lay public may refer to any controlled substance, whether an opioid analgesic, stimulant, muscle relaxant, or illicit drug, under the umbrella term of "narcotic."[1,2]

Controlled substances are primarily governed by the CSA, which was enacted by the U.S. Congress in 1970 as part of the Comprehensive Drug Abuse Prevention and Control Act.[2,3] The CSA is enforced through the Drug Enforcement Administration (DEA).[2] When the CSA was passed, it consolidated several laws that already regulated the manufacture and distribution of certain substances. Additionally, states have passed laws pertaining to controlled substances as well, such as in Florida state. Drugs regulated by the CSA all have a potential for misuse. While opioid analgesics make up a substantial number of controlled substances, there are various other drugs included as well, such as anabolic steroids, stimulants, hallucinogens, and depressants.[3]

Schedules of Controlled Substances

Drugs, substances, and certain chemicals used to make drugs are classified into five distinct categories or schedules. A substance's placement within a schedule depends on several factors, most notably the drug's acceptable medical use (or lack thereof) and potential for misuse.[2,3] Each Schedule has a specific set of parameters for the potential for misuse, currently accepted medical use in the United States (if any), and safety (or lack thereof) when used under medical supervision.

Schedule I Drugs

Schedule I drugs are those that have the highest potential for misuse or the highest potential for leading to substance use disorder. They are drugs that have no recognized medical use within the healthcare community and lack acceptable safety even when used under medical supervision.[3] Schedule I drugs are illicit drugs or "street" drugs in that their manufacture and distribution are usually illegal.

Schedule I substances are not available by prescription since they have no accepted medical use and would not normally be found in healthcare institutions, except in specific research situations.[3] Examples of Schedule I drugs include methylenedioxymethamphetamine (Ecstasy), heroin, lysergic acid diethylamide (LSD), methaqualone (Quaalude), and mescaline (Peyote).

Marijuana, which is legal for use in some states, is classified as a Schedule I drug at the national level.[3] Interestingly, cocaine is not a Schedule I drug, as it has established medical use as a local anesthetic, especially for ophthalmic or nasal procedures.

Schedule II and IIN Drugs ("CIIs")

Schedule II and IIN drugs have less potential for misuse than Schedule I drugs, but they still have a high potential to lead to substance use disorder.[3] Misuse of these drugs can lead to cravings, including a strong physical or

psychological need to use. Unlike Schedule I drugs, Schedule II drugs have accepted uses within healthcare and can be prescribed. They are the most tightly regulated scheduled drugs available by prescription. In practice, Schedule II and IIN drugs are often referred to as "CII" medications, named for the symbol required on manufacturer stock bottles to indicate their schedule.

Schedule II (but not IIN) drugs are sometimes classified as narcotics and are often prescribed for pain control. Examples of Schedule II drugs include hydrocodone combinations, methadone, hydromorphone (Dilaudid®), oxycodone (Oxycontin® and others), morphine, cocaine, meperidine (Demerol®), and fentanyl (Duragesic ®). Notably, single-ingredient codeine products fall under Schedule II.[3]

Schedule IIN drugs have the same potential for misuse as other Schedule II drugs but are not considered narcotics. They are often prescribed as stimulants to promote wakefulness, control symptoms of anxiety, control symptoms of ADHD, or induce sleep. Examples of Schedule IIN drugs include methamphetamine, dextroamphetamine/amphetamine (Adderall®), methylphenidate (Ritalin®), pentobarbital (Nembutal®), and secobarbital (Seconal®).[3] Notice that the naming of Schedule IIN is somewhat counterintuitive, and presumably the "N" stands for non-narcotic.

Prescriptions for CII drugs cannot be phoned or faxed to pharmacies (they must be prescribed via hard copy or electronically), except in a few special cases (namely, for long-term care residents, hospice patients, or emergencies).[4-6] No refills are allowed; each fill requires a new prescription, although prescribers can issue multiple prescriptions at a time (up to a 90-day supply total) within certain guidelines.[7]

Schedule III and IIIN Drugs ("CIIIs")

The drugs that are classified as a Schedule III or IIIN have less potential for misuse than those in Schedules I and II, but they still have an increased

chance of leading to a substance use disorder. Although Schedule III/IIIN drugs can cause physical cravings, they more commonly cause a psychological need when compared to Schedule I or II.[3] Prescriptions may be transmitted by phone, fax, hard copy, or electronic prescribing.[5-6,8] Prescriptions may be written with refills, but are limited to five within a six-month timeframe.[9]

A partial filling of a prescription for a Schedule III or IIIN drug is also allowed in some circumstances.[10] When a partial filling takes place, it is treated in the same manner and with the same rules as a refill of the drug. As with refills, partial prescription filling of Schedule III or IIIN drugs cannot occur more than six months after the date of issue.[10]

Some drugs in Schedule III are opioids used for pain control, such as codeine/acetaminophen combinations (note that codeine-containing medications can fall under other schedules, depending on strength and other active ingredients present). Another example in this drug category is buprenorphine (Suboxone®).[3] Non-narcotic (non-opioid) Schedule III drugs (Schedule IIIN) are prescribed for various other health conditions. Examples of Schedule IIIN drugs include ketamine, anabolic steroids or those products containing testosterone, phendimetrazine (Bontril®), and benzphetamine (Didrex®).[3]

Schedule IV Drugs ("CIVs")

Schedule IV drugs are more commonly prescribed and used within healthcare and have a lower propensity for leading to a substance use disorder when compared to drugs in Schedules I, II, or III.[3] While these drugs may still have a risk of causing physical or psychological cravings, the risks are considered minimal. As with Schedule III drugs, prescriptions may be transmitted by phone, fax, hard copy, or electronic prescribing,[5-6,8] and prescriptions may be written with refills (limited to five within a six-month timeframe).[9]

As with drugs classified in Schedules II through V, Schedule IV drugs have medical purposes. Examples of Schedule IV drugs include alprazolam (Xanax®), diazepam (Valium®), midazolam (Versed®), temazepam (Restoril®), tramadol (Ultram®), carisoprodol (Soma®), triazolam (Halcion®), and clonazepam (Klonopin®).[3]

Schedule V Drugs ("CVs")

Predictably, Schedule V drugs are the least likely of all controlled substances to be misused.[2-3] They are less likely to be prescribed for pain control and instead are often prescribed for conditions such as diarrhea, seizures, or cough.

Prescriptions for Schedule V drugs can be transmitted by phone, fax, hard copy, or electronic prescription.[5-6,8] There are no specific refill limitations. Examples of drugs that are classified as Schedule V medications include Robitussin AC, atropine/diphenoxylate (Lomotil®), pregabalin (Lyrica®), and ezogabine (Potiga®).[3] Notably, there are some Schedule V controlled substances (particularly some codeine-containing cough preparations) that can be sold over-the-counter in some states.

Stock Ordering of Controlled Substances

Schedule CII drugs must be ordered for pharmacy or facility use by using paper triplicate DEA Form 222s or the electronic Controlled Substance Ordering System (CSOS).[11] Only staff with CSOS power of attorney authority (established by a signed power of attorney form that must be kept on premises) are allowed to sign CSOS orders electronically.[11] There are separate intake and recordkeeping requirements for each, depending on whether paper DEA Form 222s or CSOS ordering is used.[11]

Schedule CIII through V drugs can be ordered through normal ordering channels, although wholesalers and distributors will require certain registration documentation (which can be quite extensive) before initially shipping any controlled substance to a pharmacy or facility.

Storage, Recordkeeping, and Disposal of Controlled Substances

Per the CSA, Schedule II through V controlled substances can be stored in one of the two following manners:[12]

1) In a "securely locked, substantially constructed cabinet;"
2) Dispersed in with non-controlled stock in such a way to obstruct theft/diversion (in general, this is interpreted to mean organized in alphabetical order intermixed with non-controls, rather than by schedule or some other grouping).

There are specific recordkeeping and inventory management requirements (at the federal and sometimes state level) that must be followed but that are beyond the scope of this course. For each pharmacy, it is ultimately the responsibility of the pharmacist-in-charge to ensure that all laws (including inventory requirements) are followed.

Pharmacies and facilities are often faced with the dilemma of how to dispose of expired, broken, spilled, or otherwise unusable controlled substances that are still in inventory. Note that this type of disposal is distinct from "wastage" (which is the disposal of an unused portion of a drug that has been removed from inventory for immediate administration to a patient and which has not been entirely administered to the patient, such as with vial overfill). According to the CSA, there are two methods of disposal:[13-15]

1. Destroy on-site using a method that makes the controlled substances completely irretrievable
2. Transfer to a "reverse distributor" for off-site disposal

Both disposal methods are commonly used. Note that methods such as dissolving in water or flushing down the toilet are not considered to fulfill the "irretrievable" requirement. Small and affordable options (such as Rx Destroyer™) are popular methods for irretrievably destroying controlled substances. Additional requirements apply for drugs that are also hazardous substances.

The DEA Form 41 must be witnessed by two employees, and it is kept on-site. The DEA Form 41 is not submitted to the DEA, and it must be available in the case of audit or inspection. DEA Form 41 should not be used to document wastage.[15] Each pharmacy or facility should have established policies for adjusting inventories to account for destruction (and safeguards to prevent inventory adjustments from being used to mask diversion).

State-Level Scheduling and Regulations

States can (and do) schedule drugs in a different manner than the CSA. For instance, gabapentin is not a controlled substance under the CSA but is a controlled substance under some state laws. As is almost always the case, in the event of conflicting state and federal law, the more stringent of the two should be followed.

Additionally, states can (and do) enact additional restrictions regarding other aspects relating to controlled substances, such as prescriptive authority, prescription requirements (especially in the area of limits for prescriptions for opioid-naive patients), patient identification requirements, and registration of prescribers and dispensers at the state level.

Staying Up-to-Date

Federal and state laws regarding controlled substances change from time to time. Additionally, interpretation and guidance can change as well. It is each practitioner's responsibility to be aware of any changes that may affect their practice. This is especially true for areas of practice that have been affected by technological advancements, such as the case for electronic prescribing and ordering of controlled substances.

Drug Enforcement Administration (DEA)

The Drug Enforcement Administration was created in 1973 as the primary organization dedicated to the control of drug use at the federal level.

Prior to its implementation, multiple organizations controlled different aspects of drug enforcement, and the DEA was established to combine their duties.[16]

The DEA operates under the Department of Justice and enforces controlled substances laws and regulations. Among many other tasks, the DEA investigates and prosecutes those who violate the CSA and works to track and take action against those involved with illicit drug trafficking.[16]

Prescribing providers must register with the DEA. This registration also applies to dispensing pharmacies (but not to individual pharmacists).[16] The DEA requires this registration to track and monitor providers who prescribe and dispense controlled substances, thereby limiting access to these drugs to the public and maintaining accountability.

Prevalence of Prescription Drug Misuse

Prescription drug use disorder has become more common in recent years. Individuals with prescription drug use disorders do not necessarily fit into a stereotypical profile.

Prescription drugs are often easier to access (and are often more affordable) than their illicit counterparts. Additionally, their use is typically seen as normal within many groups. Women are more likely to misuse prescription drugs (compared to illicit drugs) than men, especially drugs such as sedatives and tranquilizers, likely due to their perceived safety and social acceptability.[17]

Those who use controlled substances alongside other substances, such as alcohol or tobacco, are at greater risk of using them inappropriately and are more likely to become impaired with their use.[17] Co-ingestion of other substances, such as alcohol with sedatives or tranquilizers, also contributes to overdose deaths.[17]

Mortality rates from the misuse of opioids have risen dramatically over the years, beginning with the first wave of the opioid crisis in the 1990s.[18] The Centers for Disease Control and Prevention (CDC) reports that prescription and illicit opioids led to nearly 450,000 overdose deaths in the U.S, during the period 1999–2018.[18]

Interestingly, from 2017 to 2018, overall opioid-involved death rates declined by 2%. However, during that same time, there was a 10% increase in overdose deaths involving synthetic opioids (excluding methadone). Illicitly manufactured fentanyl is a synthetic opioid that is of particular concern due to its extreme potency. The increase in overdose deaths due to synthetic opioids is reportedly driven by the rise in fentanyl misuse.[19]

Prevention of Prescription Drug Misuse

Prescription drug use has become more prevalent and widespread across age groups and among various social backgrounds. Healthcare providers must take steps to reduce the risk of prescription drug misuse among the patients they serve. Healthcare providers can minimize misuse of controlled substances and reduce the risk of a substance use disorder by following established guidelines and best practices; however, this must be done within the context of ensuring that patients may still access medications being prescribed for appropriate purposes.

Ensuring Appropriate Access

No discussion of the prevention of prescription drug misuse would be complete without addressing the issue of ensuring appropriate medication access. Unless special care is taken, regulations and policies may inadvertently cause real harm to people who genuinely need such medications and obtain and use them safely and legally.[20] Regulations and policies should not discriminate against patients in need of controlled substances, nor should they create unreasonable barriers to access.

Legitimate Concerns or "Red Flags"

If pharmacy staff have a legitimate concern regarding the appropriateness, safety, or legitimacy of a controlled substance prescription, they have an obligation under federal law to seek further information to validate the prescription before dispensing it.[21] Options include contacting the prescriber, discussing the situation with the patient, and checking the state Prescription Drug Registry. States such as California, Florida, and Texas have laws that allow a pharmacist to refuse to fill a prescription if the pharmacist has reasonable concerns regarding the validity of the prescription or the potential for harm to the patient.[22-24] In Florida, there are specific regulations regarding the steps necessary to validate a questionable prescription.[23]

Prescription validation should always be done discreetly with patient privacy in mind. A common practice is to have a staff member phone the prescriber from a back room, which serves the additional purpose of avoiding alerting the patient (which may be wise in egregious cases that will likely be referred to law enforcement).

Basic Prescribing Best Practices

When writing a prescription, the provider should write legibly to reduce the risk of forgery of the document. Illegible writing of a prescription can result in a patient or another person altering the prescription without it being noticed by the pharmacy or the prescriber.[25-27] Protection of the actual prescription pad is essential to prevent theft.[25-27] In general, electronic prescribing is preferred over paper prescriptions as a measure to reduce the risk of forgery and falsification. Prescribers should safeguard their electronic prescribing credentials or digital keys.

Some states require prescribers to check their state PDMP when prescribing controlled substances. Even if this is not required by a practitioner's state, doing so is an advisable best practice.

Basic Dispensing Best Practices

Pharmacists have a "corresponding responsibility" (along with prescribers) to ensure that controlled substances are prescribed and dispensed appropriately.[28] In addition to following all applicable regulations, pharmacists may want to consider the following best practices as time-honored methods to ensure appropriate dispensing of controlled substances:

1. Check the state's PDMP with every controlled substance prescription (this is already required in some states, such as Florida)
2. Enforce a policy that prohibits cash transactions for insured patients (require all controlled substance prescriptions to be processed through insurance, for insured patients).
3. Maintain good working relationships and open lines of communication with other healthcare providers in the community (including prescribers, their staff, and other pharmacies).
4. Take the time to understand the standard pain management contracts commonly used in your area and inform prescribers when their patients are violating contracts.
5. Keep an eye out for conflicting therapies, such as stimulants prescribed together with opioids or benzodiazepines.
6. Investigate any suspicious prescriptions, such as those with inappropriately high dosages or quantities, misspellings, questionable signatures, or any other signals that the prescription may have been forged, altered, or prescribed for an illegitimate purpose.
7. Double-count controlled substances, especially CIIs.
8. Know when to call the doctor, when to have an open and honest (albeit difficult) conversation with the patient, and when to call the police.

Implementation and Use of PDMPs

The majority of states within the U.S., have developed prescription drug monitoring programs to track the prescribing and dispensing of controlled substances through online databases. Although state laws vary, in general,

access is limited to healthcare providers and sometimes to law enforcement under specific circumstances.

There is sustained interest in developing these monitoring programs and incorporating telehealth to reduce substance misuse.[27,29-30] Ultimately, provider participation in these types of programs is a step toward the prevention of the misuse of controlled substances.

Good communication between the patient, prescriber, pharmacist, and other members of the interdisciplinary health team helps ensure that controlled substances are prescribed and used appropriately and safely by the patient.[27,29-30] Communication also helps to ensure that the medications are successful in helping the patient achieve the intended healthcare outcomes, which is an important component of preventing the misuse of these drugs.

When Healthcare Providers Access PDMPs

Some states require providers to check the state PDMP before prescribing or dispensing controlled substances, but many states leave that decision up to provider discretion. Healthcare providers are influenced by a number of factors when it comes to their consideration of utilizing their state PDMP.[31] Witry, *et al.* (2020) reported that a patient's age, diagnosis, and payment method, as well as the type of drug that was prescribed, were important to a healthcare provider's decision whether to consult a state registry or not.[31]

Healthcare providers reported it was more important to check with a PDMP for younger patients than it was for older patients.[31] This appeared to be influenced by the literature showing a higher risk for opioid misuse for patients between ages 18 and 25, as compared to other age groups.[31] This posture may not be appropriate since there are reports that prescription opioid use by older adults is on the rise.[31]

Providers may be more likely to view PDMP use as important for patients requesting opioids for the treatment of headaches, especially since guidelines state that opioids should not be routinely prescribed to patients as a headache treatment.[31] In contrast, healthcare providers view PDMP use for postoperative pain management as less important and were more lenient in this setting when it came to consulting their state PDMP. Witry, *et al.*, points out, however, that this leniency could cause providers to miss potential use problems.[31]

Patients who pay for prescription drugs using cash raised the strongest concerns among healthcare providers. Cash transactions involving controlled substances are reportedly a serious indicator that a patient may be at high risk for opioid misuse.[31] Cash payments are used by patients to evade insurance rejections which may draw a pharmacist's attention to potential misuse.[31]

Case Example: Florida State Prescription Drug Monitoring

Prescription Drug Monitoring Programs in the United States have undergone re-evaluation and some criticism in recent years. Some have suggested that patient privacy and the potential for adverse outcomes for those who live with pain require a more in-depth review of these regulatory programs.[32]

In Florida, epidemic levels of prescription drug misuse led to the enactment of a law in 2009 that created a PDMP under the Florida Department of Health.[32] This online system is known as E-FORCSE (Electronic-Florida Online Reporting of Controlled Substance Evaluation Program).[32] Although the creation of a PDMP was a monumental achievement, a further effort was needed to improve the registry. A number of bills were passed, resulting in various improvements. Significantly, in 2018, a bill was passed to require Florida healthcare providers to check the registry before prescribing or dispensing controlled substances (with certain limited exceptions).[33]
Impact of E-FORCSE

The Florida DPMP annual report (2018-2019) of E-FORCSE included the following statistics:[32]

- Prescriber registrations: 100.1% increase since 2018
- Dispenser registrations: 43.3% increase since 2018
- Prescriber and dispenser queries: 50,688,241 since implementation
- Average morphine milligram equivalents prescribed: 53.3% reduction since 2018
- People who visited 5 or more prescribers and 5 or more pharmacies within a 90-day period (doctor shoppers): 80.7% reduction since implementation

In addition, Florida reported that 455 entities with electronic health record systems from across the state have integrated PDMP information into the clinician's workflow and that they have shared data with 16 other states and with the Military Health System. Additionally, overdoses involving prescription opioids showed a reduced incidence trend.[32]

Drug Diversion and Doctor Shopping

Historically, those who used illicit drugs needed to know a dealer to access or buy these drugs. While this scenario still occurs, people who use controlled substances for non-medical purposes are increasingly interested in obtaining prescription drugs as their choice of drug, often resorting to various methods of obtaining prescription drugs, such as diversion, doctor shopping, and doctor hopping.

Drug diversion describes the process of transferring prescription drugs to a person for whom they were not intended or prescribed, for illicit use.[34] Drug diversion can be seen with established patients who sometimes genuinely need medication for pain control, but who may sell their extra medications as a way of making money. Some people divert drugs because they have a substance use disorder. These individuals who have access to prescription drugs, for one reason or another, may sell a prescription drug and use the money to buy a drug they crave. Also, people may divert drugs from

others, such as friends or partners. Diversion also occurs at the healthcare provider level.[34]

Those who misuse controlled substances that are prescription drugs, may also practice doctor shopping or doctor hopping.[35] Doctor shopping occurs when a patient seeks out multiple prescribers in order to obtain a larger amount of opioids or other controlled substances.[35] Patients who doctor shop often travel great distances to obtain their drugs.[35] They will even cross state lines to obtain the prescription they seek.[35] Some clinicians refer to this behavior as doctor hopping.[35] Doctor hopping is "characterized by above average patient-to-prescriber travel distances and patients bypassing nearby prescribers in favor of more distant ones."[35] Doctor hopping is a clear indication of high-risk opioid use and is distinct from and complementary to doctor shopping. Prescription Drug Monitoring Programs may be used to evaluate a patient's travel patterns as an indicator of potential misuse.[35]

In addition to doctor hopping or doctor shopping, patients often use multiple pharmacies in an attempt to mask their misuse. Additionally, it is common for patients to seek out a new pharmacy if they feel their current pharmacy is suspicious of misuse or is restricting or refusing to fill their prescriptions. When transferring controlled substances prescriptions between pharmacies, it is typical practice for pharmacists to share any drug-seeking concerns about the patient in question. Patients may try to avoid this situation by obtaining a new prescription for use at a new pharmacy (rather than having an old prescription transferred from another pharmacy).

There are many other methods that people use to gain inappropriate access to controlled substances. These techniques not only hurt the people who are diverting and misusing drugs, but they also usually result in additional barriers to care being put into place, even for patients who obtain and take these drugs appropriately.

Safe Prescribing of Opioids

Pain management is a treatment that is intended to reduce pain and improve a patient's ability to function.[33] Medications such as opioids are useful in treating acute or chronic pain. As is the case for patients taking any type of medication, patients taking opioids should be monitored for side effects, drug interactions, and other similar problems; however, they should also be monitored for substance use disorder due to the risk of misuse.[36] A substance use disorder is of particular concern during pain management of chronic pain.[36]

Indications for Opioid Pain Treatment

Importantly, there are many medical scenarios where opioids are considered an appropriate treatment option. Common indications for opioid pain treatment include the following:

- Acute pain management
- Cancer pain or end-of-life care with corresponding pain
- Chronic pain not due to a malignancy

Acute Pain Management

Current guidelines for acute pain management focus on the type of drug used (versus dosage or duration of use).[37] Guidelines typically suggest opioid use only when non-opioid alternatives are considered inappropriate.

A study by del Portal, *et al.* (2016) reported that opioid prescribing has decreased significantly in an acute care setting, from 52.7 percent (before guidelines for the appropriate management of acute pain were issued) to 33.8 percent 12 to 18 months later, based on retrospective chart review.[38] Current postoperative opioid prescribing recommendations (2016) state that drug administration "be based on the specific surgical procedure, type of anesthesia used, patient age, and other variables."[37]

Back pain treatment guidelines released in 2017 by the American College of Physicians indicated the use of nonpharmacologic approaches for acute and subacute back pain should be administered since such pain resolves independently over time. If a pharmacological approach is desired for acute and subacute back pain, nonsteroidal anti-inflammatory drugs (NSAIDs) or skeletal muscle relaxants are recommended.[39]

Cancer Pain and End-of-Life Care

Opioid use for cancer pain and end-of-life care is a widely accepted practice.[36] Monotherapy analgesia, such as opioids (morphine, oxycodone, fentanyl, and others), can often lower the pain felt due to malignancies.[36] The World Health Organization's (WHO's) analgesic ladder outlines an approach for the use of opioids for end-of-life care.[36]

In current pain management medical situations, the WHO analgesic ladder has been described as overly simplistic and inappropriate, especially for people with chronic non-cancer end-of-life pain.[36] Moreover, a greater number of people now survive cancer treatment than was the case during the development of the WHO guidelines. Yang, Bauer, *et al.* (2020) proposed modifications to the analgesic ladder to better align with the current pain management situation.[36]

Chronic Pain (Non-Malignant)

The use of opioids to treat chronic pain has been described as controversial, especially in recent years.[37] Treatment guidelines have been developed by groups such as professional societies, state medical boards, and federal agencies. The U.S. Centers for Disease Control and Prevention (CDC), in particular, has extensively developed prescribing guidelines for chronic pain, emphasizing the use of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology to rate pain quality and the strength of the recommendations.[37] Additionally, SAMHSA, NIDA, FDA, U.S. Department of Veterans Affairs (VA), U.S. Department of Defense (DoD), and others have developed treatment guidelines for chronic pain treatment.[37]

In brief, standard guidelines for safe and appropriate prescribing and dispensing of opioids tend to focus on a few key topic areas, such as 1) provision of educational resources for prescribers and pharmacists, 2) determination of when to initiate or continue opioid treatment for chronic pain, and 3) Opioid selection, dosing, and duration, *i.e.*, "start low and go slow."[37] Caution is typically recommended at any dose based on patient experience and tolerance. Guidelines employing the use of morphine milligram equivalent (MME) are common.[37]

Guidelines also address follow-up, monitoring, and discontinuation of opioid treatment, as well as treatment agreements ("pain contracts") and screening tools for opioid use disorder.[38] Tapering guidelines for opioid treatment are also available, with some suggesting referral to pain specialists.[38] Some state guidelines and regulations may treat chronic versus acute differently. States also have different approaches regarding the degree of autonomy prescribers may have when treating patients with chronic or acute pain.

Special Considerations for Opioid Dispensing

Although pharmacy staff may focus on a few critical opioid dispensing considerations (such as logging prescriptions into perpetual inventories and checking registries), they might not always be similarly aware of a few additional considerations that are of a more clinical nature, especially regarding drug utilization review and patient counseling.

Drug Utilization Review

Due to the potentially dangerous nature of opioids, special attention must be paid during the drug utilization review to recognize and resolve the following potential problems:

- Adverse reactions (often, adverse reactions can be spotted by reviewing the patient's medication list, especially if other medications have been prescribed to address side effects)

- Dosage problems, especially high dosages for opioid-naive patients (although dosages that are too low to be effective should also be addressed)
- Duration problems, especially for opioid-naive patients
- Drug interactions, the most significant of which generally fall into the following categories for opioids:[37,40]
    - Additive central nervous system depression interactions
    - CYP interactions
    - QT-prolongation interactions (for certain opioids)
    - Serotonin syndrome interactions (for certain opioids)
    - Agonist-antagonist interactions

Counseling

A few additional counseling minutes can go a long way to prevent controlled substance disasters. In addition to standard counseling, pharmacists should address safe storage and disposal as well as options for treating opioid overdose (especially in states with naloxone standing orders).

Pharmacists should make sure patients understand the need to keep their medication in a safe place (out of reach of children and in a place not easily subject to theft). This discussion can serve as an excellent segue to help patients understand (in a non-offending way) that these drugs can be misused.

Counseling should include a discussion regarding ways to dispose of any unused or expired medication safely. Take-back programs are a great resource, and personal medication destroyer products are becoming increasingly available.[41] As an option for the last result, patients can mix the drugs with cat litter or coffee grounds and water in a sealable bag and dispose of the bag in the trash.[42] Do not accept any return of a controlled substance into a pharmacy for any reason (except through DEA-approved take-back programs), as this is not legal.[41,42]

Pharmacists may want to consider offering naloxone to patients filling opioid prescriptions (in states with standing orders, as discussed below, or under a collaborative practice agreement). Although this conversation can be awkward, especially if patients feel that they are being judged or viewed as addicts, approaching the subject simply from a safety perspective seems helpful. Remind patients that accidental overdoses happen easily and frequently and that having naloxone available could save the life of anyone in the household (including children) who might somehow end up overdosing.

Naloxone Standing Orders

Most states have naloxone standing orders which allow pharmacists and other providers to dispense naloxone without needing to obtain a patient-specific prescription from a prescriber, as well as laws that provide liability protection for healthcare providers or caregivers involved in the provision of naloxone.[43] Uniquely, these laws generally allow pharmacists to dispense naloxone to a person who may not be the intended ultimate user but instead may be a caregiver or other individual that may come in contact with opioid overdoses. Some states have authorized naloxone prescriptive authority for pharmacists or other similar workarounds, instead of using a statewide standing order.[43]

State laws vary, and some states encourage or require special training (which is usually provided free of charge) for healthcare providers utilizing the naloxone standing order, and some states require specialized counseling (such as providing the patient with certain print materials). States typically restrict which naloxone products are available by standing order (most states allow nasal spray products or automatic injectors.)[43,44]

Opioid Use Disorder and Pain Management

Opioid use disorder (OUD) was previously thought to be rare. However, as opioid prescribing dramatically increased, there was a corresponding increase in OUD treatment and overdose deaths. In recent years, death from opioid overdoses related to pain management and heroin combined have

reached alarming rates. The 2016 National Survey of Drug Use and Health indicated that 1.8 million people had a prescription pain medication use disorder, and 626,000 had a heroin use disorder.[46]

First-line treatment for an OUD involves medication management with methadone, intramuscular naltrexone, or buprenorphine-naloxone (bup-nx). The medication management of OUDs reportedly corresponds with decreased illicit opioid use and relapse, increased treatment engagement, and decreased mortality. A multisite randomized study sponsored by the National Institute of Drug Abuse (NIDA) provided the following statistics related to OUD treatment:[46]

- Illicit opioid relapse rates were over 90% when bup-nx was tapered off after 12 weeks of treatment. Continuing medication treatment is important, and prematurely stopping medication treatment should be avoided.
- Following inpatient detoxification, relapse rates and risk of opioid-related overdose are high unless medication treatment after discharge is continued.
- Many patients who are likely to benefit from medication management of OUDs are not offered such treatment. Identified barriers to treatment include a lack of trained clinicians, poor understanding of the effectiveness of medication treatments, stigma against individuals with substance use disorders (SUDs), and poor insurance coverage.

The authors reported that in 2015, 356,000 individuals were estimated to have received treatment with methadone and 75,000 individuals with bup-nx.[46] Many individuals suffer from homelessness, unemployment, legal problems, lack of social support, isolation, and comorbid psychiatric illness, which are important social factors related to OUDs and medication treatment.

Listening to the patient, providing reassurance, and maintaining transparency are fundamental clinical skills and values that will help to improve patient engagement in treatment outcomes. All interdisciplinary

health team members need to continuously communicate strategies for safe prescribing of opioids for patients known to have an opioid use disorder.[46]

All healthcare providers who prescribe or dispense opioids should be familiar with the particular OUD treatment resources in their communities, which can range from dedicated inpatient treatment ("rehab") facilities to Narcanon groups, licensed addiction counselors and other behavioral treatment providers, and specialized hotlines, such as SAMHSA's confidential free hotline (1-800-662-HELP).[47]

Summary

Controlled substances are defined as drugs, medications, or chemicals that are regulated by the CSA or state law. Not all drugs listed as controlled substances are narcotics.

A substance's placement within a schedule depends on several factors, most notably the drug's acceptable medical use (or lack thereof) and potential for misuse. Each Schedule has a specific set of parameters for the potential for misuse, currently accepted medical use in the United States (if any), and safety (or lack thereof) when used under medical supervision.

There are specific recordkeeping and inventory management requirements (at the federal and sometimes state level) that must be followed but that are beyond the scope of this course. For each pharmacy, it is ultimately the responsibility of the pharmacist-in-charge to ensure that all laws (including inventory requirements) are followed.

Prescription drugs are often easier to access than their illicit counterparts. Their use is typically seen as normal within many groups.

Healthcare providers can minimize misuse of controlled substances and reduce the risk of a substance use disorder by following established guidelines and best practices; however, this must be done within the context of ensuring

that patients may still access medications being prescribed for appropriate purposes.

States have developed prescription drug monitoring programs to track the prescribing and dispensing of controlled substances through online databases. In Florida, epidemic levels of prescription drug misuse led to the enactment of a law in 2009 that created a PDMP under the Florida Department of Health. This online system is known as E-FORCSE (Electronic-Florida Online Reporting of Controlled Substance Evaluation Program).

Historically, those who used illicit drugs needed to know a dealer to access or buy these drugs. While this scenario still occurs, people who use controlled substances for non-medical purposes are increasingly interested in obtaining prescription drugs as their choice of drug, often resorting to various methods of obtaining prescription drugs, such as diversion, doctor shopping, and doctor hopping.

Pain management is a treatment that is intended to reduce pain and improve a patient's ability to function. Medications such as opioids are useful in treating acute or chronic pain. As is the case for patients taking any type of medication, patients taking opioids should be monitored for side effects, drug interactions, and other similar problems; however, they should also be monitored for substance use disorder due to the risk of misuse. Substance use disorder is of particular concern during pain management of chronic pain.

Course Test

1. **A controlled substance is *best* described as a drug that**

    a. falls within the limited category of drugs known as narcotics.
    b. is regulated by the CSA and/or state law.
    c. requires a prescription.
    d. has no accepted medical use.

2. **Controlled substances that are listed as Schedule IIN drugs are often prescribed as**

    a. narcotics.
    b. stimulants.
    c. anxiolytics.
    d. psychotropics.

3. **Drugs, substances, and certain chemicals used to make drugs are classified into five schedules based on**

    a. their accepted medical use if any, and potential for misuse.
    b. whether they are controlled substances or not.
    c. whether they are also restricted under state law.
    d. All of the above

4. **More recently, there has been a significant increase in overdose deaths involving synthetic opioids such as**

    a. thebaine.
    b. methadone.
    c. fentanyl.
    d. morphine.

5. **Among Schedule I drugs, _____ is becoming increasingly popular and is a serious cause of substance use disorders.**

    a. Cocaine
    b. Morphine
    c. Heroin
    d. Cannabis

6. **If a pharmacist has a legitimate concern regarding the appropriateness, safety, or legitimacy of a controlled substance prescription, the pharmacist must**

    a. dispense the prescription regardless of the concern because the patient may suffer more harm if the patient is denied the drug.
    b. dispense the prescription so long as it was signed by a physician.
    c. seek further information to validate the prescription before dispensing it.
    d. report the patient to the appropriate law enforcement agency.

7. **True or False: Policymakers do not need to worry about ensuring appropriate access to controlled substances, since regulations and policies rarely negatively affect patients with legitimate medical concerns.**

    a. True
    b. False

8. **Prescriptions for _____ drugs may not be phoned in or faxed, except in a few special cases.**

    a. Schedule I
    b. Schedule III
    c. Schedule V
    d. Schedule II or IIN

9. **Which of the following statements is true regarding the use of DEA Form 41?**

    a. Completed DEA Form 41s must be sent to the nearest DEA office.
    b. DEA Form 41 can be used to document wastage and on-site destruction of controlled substances.
    c. DEA Form 41 must be completed in triplicate.
    d. DEA Form 41 requires two witnesses.

10. **True or False: All the states that utilize a PDMP tracking system require prescribers in their state to use the system prior to prescribing or dispensing controlled substances.**

    a. True
    b. False

11. States Prescription Drug Monitoring Programs (PDMPs) track prescription drugs using online databases and are available to

a. healthcare providers.
b. patients.
c. the public.
d. All of the above

12. Which of the following statements regarding state-wide naloxone standing orders and laws is false?

a. Most allow providers to dispense naloxone to people who may not be the ultimate users of the products.
b. Most provide some sort of liability protection for providers or caregivers involved in the provision of naloxone.
c. States do not restrict the type of naloxone products that are available by standing order.
d. Some states require special healthcare provider training or special patient counseling instructions.

13. _____ involves a patient traveling great distances or bypassing nearby prescribers in favor of more distant ones in order to obtain opioids or other controlled substances.

a. Doctor hopping
b. Drug trafficking
c. Drug transference
d. Gatekeeping

14. An opioid substance use disorder may be managed using

a. methadone.
b. intramuscular naltrexone.
c. buprenorphine-naloxone.
d. All of the above

15. Transferring prescription drugs to a person for whom they were not intended or prescribed is known as

a. trafficking.
b. transference.
c. redirection.
d. diversion.

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