Chapter 32
Chronic Pain Patients and Substance Abuse

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Key Points

- Silent epidemics: chronic pain and substance abuse
- Terminology
- Managing pain patients within the pain/substance abuse interface
- Screening
- Screening tools
- Abuse-deterrent drug formulations
- Managing patients—specific groups
- Opioid withdrawal and detoxification

Introduction

The physical and mental states of human beings are governed by lifetime experiences and biopsychosocial makeup. They reinforce each other, and sometimes lead to maladaptive states, such as chronic pain, addiction, and so on. Pain and addiction are

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altered biopsychosocial experiences that are both subjective in nature and interact with one another. This interface of pain and addiction has brought about serious public health problems. It also poses ethical and healthcare dilemmas through the conflicting goals of managing pain states: pain relief, i.e. beneficence, and "do no harm", i.e. nonmaleficence [1]. With the rise of medicinal management for chronic pain over the last two decades, addiction has become more prevalent, significantly increasing the risk of morbidity and mortality in this patient population. It is the responsibility of healthcare providers to utilize all the multimodal tools in their armamentarium to provide effective pain relief without unintentionally facilitating substance abuse.

Silent Epidemics: Chronic Pain and Drug Abuse

Pain practitioners simultaneously deal with two significant public health problems, chronic pain and drug abuse. "Chronic pain" is widespread and results in significant bio-socio-economic burden. Almost a third of the US adult population, i.e. over 100 million people suffer from chronic pain [2, 3], costing more than $600 billion annually in healthcare and loss of productivity costs [4]. Chronic pain alone was responsible for 21 % emergency room visits in the United States and almost 25 % of missed workdays [5]. Early and effective pain control is essential to decrease suffering, improve function, and facilitate earlier return to work.

Among other analgesics, opioids are commonly used for managing pain. Their use has substantially grown over the last 10–15 years as a result of guideline changes, newer formulations, and increased awareness to management protocols [6]. Hence, healthcare providers should be able to recognize substance abuse among chronic pain patients due to the inherent abuse potential of opioids. "Drug abuse", i.e. illicit drug use has steadily increased for decades and has now reached a plateau over the last 2–3 years. In 2011, 8.7 % of the total American population aged 12 and over, i.e. 22.5 million Americans, had used an illicit drug in the prior 30 days, which was similar to rate in 2009 [6]. These endemic proportions account for an estimated annual cost of $193 billion in healthcare, criminal justice, and lost productivity [7]. There has been a gradual increase in emergency room (ER) utilization for health issues related to non-medical prescription drug use, as reflected by 1.1 million total ER visits in 2009 alone [8].

Although Marijuana remains the first agent of choice for illicit use [9], there is increasing prescription drug abuse year after year, which ranks second among the most commonly abused agents [6]. Among the US population of 12 years and older, 6.1 million Americans (2.7 % population) used psychotherapeutics for non-medical reasons, while 4.5 million (1.7 % population) Americans were non-medical users of analgesics [9].

"Co-Existence of Chronic pain and Drug Abuse" studies have found relatively lower drug abuse rates in chronic pain patient populations treated with a controlled substance than earlier thought. The prevalence rate of this coexistence varied from 3 to 48 % [10]. Data for chronic pain patients taking a controlled substance suggested

the presence of aberrant drug behavior in 12 % patients, while 3 % were found to develop established drug abuse [11]. On the other hand, studies have shown an increased incidence of chronic pain in substance abusers, i.e. 37 % of patients in a methadone maintenance program reported chronic pain, while 24 % patients in short-term inpatient drug abuse treatment programs reported chronic pain problems [12].

Opioids, being a front-line agent for pain management with a high abuse liability are the most commonly abused prescription agents [8]. Hydrocodone, oxycodone, along with methadone, are the three most common individual opioid agents [6]. With a 400 % increase in prescription opioids, there has been a parallel six fold increase in drug abuse-related health problems. These include a fourfold increase in opioid overdose and a threefold increase in deaths from prescription drug overdoses between 1999 and 2008 [13]. A staggering three-fourth of these deaths were reported as opioid overdoses [13]. To put this in perspective, illicit opioid overdose deaths have surpassed total traffic-related deaths [14]. The risk of drug abuse-related mortality is significantly increased with higher opioid doses and concurrent use of other abused drugs. Polysubstance abuse is a common practice among illicit drug users, with tobacco and alcohol as the commonest agents used in conjunction with another drug. This can be illustrated by the data that showed 34 % of patients in a methadone maintenance program and 51 % in a short-term drug rehabilitation who were admitted for alcohol addiction also abused other agents [11].

Besides the drug abuse-related healthcare issues, there is criminal aspect as well, i.e. drug diversion. Doctor shopping, prescription fraud, and theft are the leading causes of diversion. Almost 70 % of abusers obtain drugs from a friend or relative by borrowing, buying, or stealing [6].

Terminology

There are many terms that are used to describe abnormal drug usage, i.e. dependence, tolerance, misuse, addiction, etc. These terms are often used interchangeably, and sometimes inappropriately.

1. *Physical dependence*: The body's physiologic neuronal response to a specific chemical agent due to prolonged exposure. It is characteristically manifested by "withdrawal symptoms" upon rapid de-escalation or abrupt discontinuation of that specific drug or after administration of drug-specific antagonist.
2. *Tolerance*: The body's physiologic response after repetitive use of drug characterized by the need of increase in dosing of that specific drug to maintain the same effect.
3. *Addiction*: A chronic neurobiological disease state manifested by a pattern of behavior of craving and compulsive use of drug despite resultant self-biopsychosocial harm. This behavior continues to persist even after discontinuation of drug.
4. *Pseudo addiction*: An inappropriate drug-seeking behavior in order to achieve better symptom control reflecting under treatment. This behavior resolves upon symptom relief.

5. *Substance misuse*: Use of prescribed medications for other medical reasons than which it is prescribed for.
6. *Substance abuse*: Use of any drug (prescription or illicit) for non-medical purposes.
7. *Aberrant drug behavior*: Behaviors suggesting drug abuse. These include prescription alteration, borrowing/stealing drugs from others, selling drugs, obtaining prescriptions from multiple providers simultaneously, multiple reports of loss of prescription and drug, using non-prescribed route of drug administration, and obtaining drugs illegally.
8. *Substance use disorder*: A broad umbrella term proposed through psychiatric literature that incorporates the above-mentioned issues.

Managing Pain Patients Within the Pain/Substance Abuse Interface

It is challenging for pain practitioners to achieve a balance between safe and effective pain management, while preventing drug abuse and diversion. This interface creates several patient scenarios and each requires specific attention in management of their pain. These scenarios include:

1. Chronic pain management in patients with
   (a) Low aberrant drug abuse behaviors/risk
      - With no history of drug misuse/abuse
      - With past history of drug misuse/abuse

   (b) Moderate aberrant drug abuse behaviors/risk
      - With no history of drug misuse/abuse
      - With past history of drug misuse/abuse
      - With current drug misuse/abuse

   (c) High aberrant drug abuse behaviors/risk
      - With past history of drug abuse
      - With current drug abuse

2. Acute pain management in patients with
   (a) No history of drug abuse/misuse
   (b) Past history of drug abuse/misuse
      - Remote history
      - Recent, but in recovery
      - Currently in drug maintenance rehabilitation program

   (c) Current drug abuse

Prescription drug abuse is the leading cause of death within substance use disorders. Prescription opioids are the most abused class of medications in the United States [15]. It is vital for healthcare providers to understand the associated risk when an opioid is an option to choose for their pain management. Healthcare providers should utilize all tools to improve identification and/or prevent drug abuse/diversion, while practicing safe and effective medicine. This requires comprehensive initial assessment and drug abuse risk stratification, while maintaining judicial use of resources. The frequency and extent of assessment, monitoring, and resource utilization should be proportional to drug abuse risk stratification, i.e. high-risk patients need more frequent and random urine/blood screening as well as more frequent follow up [16].

Several strategies have been suggested to reach this goal, which help develop individualized management plans for specific patients.

1. Comprehensive clinical history, with emphasis on drug history
2. Psychosocial screening interview
3. Drug risk stratification
   (a) Aberrant behavior screening tools
4. Drug adherence/maintenance
   (a) Screening tools: including screening questionnaires, urinary drug screens
5. Practice support tools—including controlled-substance (i.e. opioid) therapy drug agreement, Risk Evaluation & Mitigation Strategies (REMS), Prescription Drug-Monitoring Programs (PDMPs).

Screening

Every doctor–patient interaction should begin with understanding the patient's problem and background. A detailed clinical history is an essential first step, and should include alcohol, tobacco, prescription, and illicit drug use histories. A psychological screening interview can also be very useful in the evaluation of a patient before introducing any opioids in their treatment regimen (Table 32.1).

When the risk of drug abuse can be stratified, it facilitates developing individualized management plans. Risk stratification divides patients into low, moderate, or high-risk categories. In addition to a detailed history, aberrant behavior screening tools used for risk stratifications include:

1. Urinary Drug Screen—prior to initiating opioid therapies
2. The Screener and Opioid Assessment for Patients with Pain Revised (SOAPP-R)—a validated patient-administered screening tool which contains 24 items designed specifically to stratify the risk of drug abuse in patients with chronic pain. A score of 18 or more reflects risk for opioid abuse. It has sensitivity of 80 % with specificity of 52 % [17].

Table 32.1 Screening of pain patients for drug abuse risk

When considering a controlled-substance in the treatment plan	
Initial risk stratification	Treatment adherence
Comprehensive clinical history	Repeat comprehensive clinical history
Comprehensive medicinal/drug history	Medicinal history
Psychological screening interview	
Aberrant Risk Behavior Assessment Tools	Random urine drug screen (UDS)
Pre-opioid urinary drug screen (UDS)	Aberrant Risk Behavior Assessment Tools
Screener & Opioid Assessment for Patient with Pain (SOAPP-R)	The Current Opioid Misuse Measure (COMM)
Opioid Risk Tool (ORT)	The Pain Medication Questionnaire (PMQ)
Practice support tools	The Pain Assessment and Documentation Tool (PADT)
Prescription Drug-Monitoring Program (PDMP)	Practice support tools
Controlled-Substance Agreement	Prescription Drug-Monitoring Program (PDMP)
Risk Evaluation and Mitigation Strategies (REMS)	Risk Evaluation and Mitigation strategies (REMS)

3. The Opioid Risk Tool (ORT)—another validated 5-item opioid abuse risk tool, administered by the clinician to assess the risk of opioid abuse in pain patients. A score of 4–7 suggests moderate risk, while 8 or more suggests high risk for opioid abuse [17].

These screening tools only reflect the risk of drug abuse, but do not necessitate opioid abstinence. The decision of prescribing opioids depends upon the physician and the patient's individual clinical scenario. Once opioids are initiated and continued in treating a patient's pain, it important to continue appropriate compliance monitoring. Repetitive clinical histories during each visit play a vital role. Several aberrant behavior screening and practice supporting tools have been suggested, including:

1. Random and frequent Urinary Drug Screens
2. Aberrant Behavior Screening tools

   – The Current Opioid Misuse Measure (COMM): a self-administered 17-item validated tool for pain patients with current opioid use to measure ongoing aberrant drug behavior. It should be applied repeatedly during continuation of opioids as a part of an ongoing treatment regimen. Increasing scores correlate with increasing aberrant drug behavior for opioid misuse [17].
   – The Pain Medication Questionnaire (PMQ): a self-administered 26-item questionnaire validated for measuring the progress of chronic pain patients with ongoing opioid usage. Higher scores correlate with increased risk for opioid abuse [17].
   – The Pain Assessment and Documentation Tool (PADT): a clinician administered 41-item questionnaire assessing various pain dimensions and outcomes in long-term opioid usage [17].

3. Practice support tools: Opioid therapy agreements, REMS, PDMPs, abuse-deterrent drug formulations, etc.

There are several screening tools that have been compared. One study showed their efficacies as SOAPP-R>ORT>PMQ>COMM individually, while SOAPP-R with psychological interview had the best sensitivity when utilized in conjunction [18].

Screening Tools

Drug Abuse Risk Factors

There are several parts of a patient's comprehensive history that may suggest drug abuse risk, and identified risk factors require close attention (Table 32.2) [19].

Aberrant Drug Behaviors

During a comprehensive patient evaluation, it is necessary to recognize behaviors, which can reflect the risk of drug abuse or ongoing use. Certain behaviors are more or less predictive of drug misuse (Table 32.3) [20].

Urinary Drug Screens (UDS)

Urine drug screens are used to reveal illicit drugs use, stratify drug-misuse risk, and monitor treatment adherence. They are used randomly and the frequency of use depends on the level of risk and/or changes in patient behavior during treatment.

Table 32.2 Risk factors for drug misuse

Biological	Psychological	Social
Young age	Current/past polysubstance use	Poor social support
Male gender	Illicit drugs	Previous/current history of
Family history of polysubstance abuse	Alcohol	Criminal activity
Exaggeration of pain, beyond extent of injury	Tobacco	DUIs
	Psychological comorbidities	Frequent contact with high risk
	Depression	Situations/places/events
	Severe anxiety	Personnel
	Psychiatric disorders	Decrease functioning at
	History of	Family
	Thrill seeking behaviors	Society
	Preadolescent sexual abuse	Workplace/school

Table 32.3 Aberrant drug behaviors [20]

	Probably less predictive	Probably predictive
Symptoms/signs	Symptom exaggeration	Intoxicated appearance
	Repetitive requests for higher doses	Altered behavior at work, family, or society
Compliance	1–2 occasion of self-dose increase	Several occasions of self-dose increase
		Resisting to get old medical records
		Resisting for urine or blood drug screens
		Noncompliance in appointment for
		Regular, nonprescription-related visits
		Multidisciplinary appointments
Prescription	Drug misuse	Dose prescription forgery
	Trying to get from other practitioners (openly)	Frequent prescription/drug losses
		Trying to get drugs from
		Several providers (doctor shopping)
		Non-medical sources
		Borrowing or stealing drugs from others
		Buying from street (drug dealers, etc.)
Drugs	Requesting specific drug	Selling prescribed drug
	Drug hoarding from periods of lesser pain	Using non-prescribed route of drug administration
		Tampering with drug formulations
		Injection oral formulation
		Snorting oral formulation
Concurrent usage	Tobacco	Alcohol
		Illicit drugs

This information can also be helpful in emergency rooms or within the workplace. However, these tests may not be sufficient for drug-misuse monitoring as they use fixed concentration cut-off levels. Thus can detect recent use or higher drug concentrations, but may miss lower concentrations. Information provided to the clinician may be further limited as most tests only detect a particular class of drugs, and not individual drugs of that class. There is also the possibility of cross-reactivity among different drugs. Furthermore, they do not provide information respective to a patient's variable dosing of medications.

There are two commonly used methods used for Urine Drug Screening: Qualitative Immunoassay and Analytical (Qualitative & Quantitative) Mass Spectrometry [21].

The basis of Qualitative immunoassay UDS is a specific antibody reaction to a particular drug. Rapid "point of care" (POC) evaluations of urine among pain patients monitor treatment adherence, and this is an immunoassay qualitative UDS model. Several POC models such as "UDS cups" or "UDS sticks" are available, and are designed to detect various illicit drugs including some specific drugs, i.e. opioids. By using lower cut-off concentration levels in POC UDS, sensitivity of drug detection is increased and this may be more clinically relevant. Depending on

the situation, these samples can be sent out for further confirmative and even quantitative analysis to designated labs.

Analytical mass spectroscopy utilizes the separation of drug molecules based on their mass and fragmentation pattern through chromatography in order to identify a specific drug molecule, and also isotopic dilution analysis to quantify the drug in urine sample. This method is considered the gold standard for UDS [21]. Not only is drug presence or absence determined through direct drug molecule or metabolite identification, but also the status of the urine sample—adulterated or non-adulterated. There are two chromatographic models available: liquid chromatography–mass spectroscopy or gas chromatography–mass spectroscopy. Liquid chromatography–mass spectroscopy has advantages in that it requires only a very small amount of urine, identifies many more drugs in one test run, and has a faster run time to allow more rapid results to clinicians.

UDS use should be individualized depending on clinical history, comorbid conditions, and drug-misuse risk stratification. The limitations of a particular UDS should be kept in mind while making interpretations from the results. The patient's medicinal history helps in making these inferences (Table 32.4). Various specialty societies recommended the random use of UDS, as studies have shown they can identify high-risk drug abuse, even in the absence of aberrant drug behavior [21].

Controlled-Substance (Opioid) Therapy Agreement

It is common and good clinical practice, to clearly outline the roles and expectations between patients, and healthcare providers in regards to the use and compliance of prescribed controlled substances. One commonly used tool to help establish this understanding is a "Controlled-Substance Agreement" [22]. This is a mutual consent between a patient and healthcare provider/clinic to educate them clearly about

Table 32.4 How to use urinary drug screens

• Should be individualized
• Used randomly
• Should be used as initial evaluation tool for drug-risk stratification
• Should be used on the basis of risk strata:
– *Minimal Risk:* Initial visit, random use, should be used twice a year for treatment adherence monitoring
– *Possible Risk*: Initial visit, random use, more frequent use, i.e. 4–5 times per year or every refill
• Used upon any addition of new drug
• Used upon any new aberrant behavior change
• Confirm test results quantitatively
• Upon positive UDS (i.e. presence of non-prescribed drug, absence of prescribed drug)—Interact with patient for possible discontinuation of opioids, or to establish stricter monitoring including UDS, etc.

their roles, expectations, and possible actions upon noncompliance. These agreements can be quite different among practitioners, but should all incorporate the following statements and conditions [22]:

1. Patients should only:
   (a) use medication(s) as prescribed
   (b) receive scripts for controlled medication(s) only from one physician
   (c) use only one pharmacy to fill those medication(s)
2. Patient should agree to:
   (a) taper off a medication upon no improvement of quality of life or function as directed by the physician
   (b) participate in multidisciplinary aspects of treatment including physical therapy, psycho/behavioral therapies, etc.
   (c) give periodic urine or blood samples for screening
3. Patient is responsible for:
   (a) the safe custody of medication(s)
   (b) maintaining regular appointments
4. Patient fully understands:
   (a) they will not get prescription refills early
   (b) medication(s) will not be replaced if lost/stolen
   (c) upon noncompliance, medication(s) will be discontinued

The purpose of Controlled-Substance Agreement is to promote the patient's education, their compliance, and to ultimately improve outcomes including decreased morbidity and mortality.

Prescription Drug-Monitoring Programs (PDMP)

With the rise in availability and use of more controlled drugs for the management of pain, there has also been a rise in prescription drug abuse and associated mortality. A federal initiative in 2007 suggested that each state should establish and operate a statewide electronic prescription drug-monitoring program (PDMPs) [23]. These programs should monitor drugs prescription in real-time, and should also be accessible to healthcare providers when prescribing controlled substances as part of their treatment plans. PDMPs can not only improve medical care through prescription drug monitoring (i.e. drug interactions, aberrant drug behavior, doctor shopping, etc.), but can also be used as investigative tools to prevent or address drug misuse and diversion.

Except for the state of Missouri, all US states and territories have PDMPs either up and running or in the process of being established. Studies from early PDMP states showed improved medical outcomes and better utilization of opioids.

Table 32.5 Elements of Risk Evaluation and Mitigation Strategy (REMS)

1	A patient package insert – medication guide	Highlighting patient safety information, implemented through the pharmacist with each prescription refill
2	A communication plan for healthcare providers	Tools and materials for healthcare provider education regarding safe prescribing and use of medications i.e. CMEs, letters to practitioners
3	Elements to assure safe use (ETASU)	Dispensing drugs through specific registered pharmacies
		Provider's education and certification for safe prescribing of drugs
		Enrollment of patients, pharmacies, physicians in central registry program
4	An implementation plan for ETASU	An implementation plan for ETASU
		Monitoring of implementation
5	Timetable for submission of assessments	Assess and submit by 18 months, 3 years, and 7 years after or an otherwise specified timetable upon initial approval for REMS by FDA

CME Continuing Medical Education, *ETASU* Elements to assure safe use, *FDA* Federal Drug Administration

Adjustment of opioid treatment regimens resulted in 61 % patients being prescribed less opioid, while 39 % were prescribed higher opioid doses within their treatment regimens [24]. Although different states collect different data points and allow different authorities to get access, PDMPs have significant potential to improve outcomes upon full utilization. Furthermore, PDMPs are becoming increasingly more interactive between states that can further improve their effectiveness.

Risk Evaluation and Mitigation Strategy (REMS)

Various drugs have been approved for clinical use when their benefits outweigh the risks, but still certain medications continue to carry relatively higher risks. The Food and Drug Administration (FDA) recommends/mandates a strategy to ensure the continued benefits outweighing the risks of a specific drug or biological product. This is termed as the "Risk Evaluation and Mitigation Strategy (REMS)" [25]. The FDA requires REMS for several drugs, and various opioids are in this list [26]. REMS has several elements (Table 32.5) all which are not necessarily required for each drug, and the FDA determines these elements for each specific drug.

Upon the finding of new safety information, the FDA reviews drug status for REMS requirements again to ensure that the benefits of the drug outweigh its risks.

Abuse-Deterrent Drug Formulations (ADF)

Pain is an eternal biopsychosocial and socioeconomic problem. It is of prime importance to manage pain early and effectively. Opioids are commonly used to achieve this. With increasing acceptance of opioids for the management of chronic pain, there has

been a significant rise in their availability and utilization in the last decade. Likewise, there has been an increase in drug abuse-related mortality, which has surpassed motor vehicle accidents as the leading cause of death [14]. Opioids are the most common agents used illicitly, with hydrocodone and oxycodone leading the pack [15]. Drug abusers show three patterns of drug use and aberrant drug behaviors:

1. Taking medications faster than prescribed for the prescribed indication, i.e. taking more pills
2. Taking medications illicitly
   (a) using medication faster than prescribed for non-prescribed indications
   (b) mixing controlled medications with other non-prescribed controlled substances, i.e. controlled medications with alcohol or other drugs
3. Illicit use of the drug by manipulative formulations or unapproved alternate routes of administration other than prescribed, i.e. crushing slow release matrix formulations to achieve high concentrations instantly, crushing drug to snort or smoke, crushing, and/or dissolving drugs to inject intravenously

The purpose of these behaviors is to achieve a euphoric state by releasing a high amount of medication at once or delivering a high dose faster. This results in a higher drug concentration (C_{max}) in shorter time (T_{max}). All three aberrant drug behavior patterns are troubling, but the latter two can be life threatening. Drug formulations with the lowest abuse liabilities (C_{max}/T_{max} ratio) should be utilized to prevent or deter drug abuse. Pharmaceutical companies continue developing formulations of opioids with lower abuse liabilities that are difficult and cumbersome to abuse. These formulations are termed as "Abuse-Deterrent Opioids" [27].

Abuse-deterrent formulations are being developed using various pharmacologic engineering processes and they can be categorized broadly into four categories (Table 23.6) [27]:

Table 23.6 Abuse-deterrent technologies [27]

Physical barrier	To avoid destruction or make it difficult to extract an active drug	Oxycontin (new)—resists crushing
		Exalgo (hydromorphone ER)
		Remoxy (oxycodone CR)—resists dissolution/snorting
Aversion	Noxious agents are added to produce an unpleasant sensation upon use through non-prescribed routes of delivery	Acurox (oxycodone + niacin)
Agonist/antagonist combinations	Addition of an antagonist to reduce euphoric effects or cause withdrawal symptoms upon tampering of the drug	Embeda (morphine + naltrexone)
		Suboxone (buprenorphine + naloxone)
Prodrug	Non-active drug that can only be activated in the presence of gastrointestinal enzymatic milieu	KP511 (hydromorphone prodrug)

1. *Physical barriers*: Abuse of a drug can be deterred by:
   (a) physically making the tablet difficult to crush
   (b) a chemical barrier that makes extraction of medication difficult, i.e. upon trying to dissolve with a solvent, it becomes a thick gel, deterring injection
2. *Aversion technology*: Another substance is added with the drug that creates an unpleasant sensation when used in alternate unapproved routes of administration, i.e. snorting. Commonly used aversive agents include niacin, capsaicin, ipecac, etc.
3. *Agonist/antagonist combinations*: Addition of insulated antagonists, i.e. naltrexone, naloxone, with opioids to prevent the euphoric effect of the opioid or to cause an unpleasant withdrawal effect when the otherwise insulated antagonist is released due to manipulation of the drug.
4. *Pro Drug*: A prodrug is an agent that requires enzymatic cleavage or activation in gastrointestinal tract to become an active opioid, thus preventing alternate routes of drug administration.

Some formulations are under development combining two deterrent technologies resulting in even lower abuse liability ADFs. Although ADFs are still in very early stages, there has been no evidence that ADFs will completely stop drug abuse, and ADFs have not yet been shown to decrease the prevalence of drug abuse. Despite this, the use of ADFs can be a good practice to at least attempt to deter drug abuse and promote safer management.

Managing Patients: Specific Groups

Managing Pain in High Abuse Risk Patients

In addition to comprehensive initial assessments, patients with chronic pain and "high drug abuse risk" stratification require more frequent ongoing assessments and increased resource utilization to deliver safe and effective analgesia [28]. Closer monitoring is necessary to prevent abuse and diversion. "Resources" comprise of tools for risk stratification, screening, monitoring, and various aspects of healthcare and judicial systems, including manpower (Table 32.7).

Managing Acute Pain in the Setting of Substance Abuse

Substance abusers also suffer from other health problems requiring certain interventions leading to acute pain that needs to be managed early and effectively. While managing their acute pain needs, practitioners should be aware about their potential risk of reactivation of their addiction issues. For acute pain management these patients fall into three clinical scenarios: Past substance abuser, Patient in Substance abuse maintenance rehab and current active substance abuser (Table 32.8) [29].

Table 32.7 Managing pain in high-abuse risk patients

More assessment	More resources	More monitoring
Detailed initial assessment	Maximize concurrent treatments	More frequent follow-up
Frequent follow-up assessment	Physical rehabilitation	Screening questionnaires for aberrant drug behaviors
More consultation, as needed	Adjuvant analgesics	
Detailed previous history	Psychological therapies	Strict prescribing
Verification of history	Active recovery program	Fewer excuses
Chart reviews	Controlled-Substance Agreement	Supervised dosing
Collateral information	One prescriber	Pill counting on each visit
Supportive networks	One pharmacy	Frequent, but random urine or blood drug screen
Frequent assessment of function	No replacement of	
Detailed medicinal history	"Lost" scripts	Frequent utilization of PDMP
Past medications	"Lost" medications	
Response to medications	No early refills	
Attention to side effects	Prescribing pattern	
Drug-misuse risk stratification	Shorter dispensing intervals	
Initial Urinary Drug Screen	No phone refills	
Risk assessment tools	More education	
	For patients	
	For family members	
	For providers i.e. REMS	

PDMP prescription drug-monitoring programs, *REMS* Risk Evaluation and Mitigation Strategies

Table 32.8 Managing acute pain with history of substance abuse in in-patient setting

Assessment	In-patient management	Discharge
A. Patient recovered from a Substance Abuse Disorder		
Detailed initial assessment	Maximize concurrent treatments	Drug abuse risk stratification
Frequent assessment	Physical rehabilitation	Pre-discharge urine drug screen
More consultation, as needed	Adjuvant analgesics	Education
Pain, addiction, psychiatry	Psychological therapies	Discharge plan
Detailed previous history	Regional anesthetic modalities	Monitoring
Verification of history	More education	Close follow ups
Chart reviews	For patients	Weaning of opioids
Collateral information	For family members	Maximizing adjuvant therapy
Supportive network	Medication choice	Appropriate screening
Frequent assessment of function	Avoid partial-agonist opioid	Aberrant drug behavior

(continued)

Table 32.8 (continued)

Assessment	In-patient management	Discharge
Detailed medicinal history	Choose low abuse-potential drug formulations	Adherence to prescribed drug
Past medications	Develop a plan to avoid relapse or a therapeutic plan upon relapse	
Response to medications		
Attention to side effects		
B. Patient in a Substance Abuse Maintenance Rehabilitation Program		
In addition to "A" above	*In addition to "A" above*	*In addition to "A" above*
Consult—addiction specialists	Continue maintenance drug	Follow up with their maintenance program
Confirm	i.e. Methadone	
Drug	Maximize adjuvants	
Methadone	For buprenorphine/naltrexone	
Buprenorphine	Discontinue 48 h before elective procedure	
Naltrexone	Watch for withdrawal	
Doses from	Upon resumption, titrate up slowly	
Maintenance program		
Prescribing physician		
C. Patient with current substance abuse		
In addition to "A" above	*In addition to "A" above*	*In addition to "A" above*
Confirm drug and frequency of abuse	Emphasis on non-opioid multimodal management	Clear discharge plan
Assess abuse related co-morbidities	Maximize adjuvants	Avoid outpatient opioids
	Use opioids judiciously	May choose abuse-deterrent formulations
Consult—addiction specialist	Use IV opioids i.e. PCA	Short, limited quantity scripts
Consult—psychiatry/ psychologist	May consider abuse-deterrent formulations	Close follow-up, i.e. weekly visits
	Avoid agonist–antagonist formulations	Weaning protocols
		Maximize adjuvant therapy
		Follow-up with addiction specialist
		Clear monitoring
		Compliance with follow-up appointments
		Frequent assessment and abuse risk stratification
Attention for withdrawal		Frequent and random use of screening tools i.e. UDS, PDMP

PCA patient-controlled analgesia, *PDMP* prescription drug-monitoring programs, *UDS* urinary drug screening

Opioid Withdrawal and Detoxification

Physical dependence of opioids could develop as early as within 7 days of exposure to typically several weeks to months of opioid use. This physical dependence predisposes to opioid withdrawal syndrome upon abrupt/rapid discontinuation of opioid, administration of a partial-agonist (i.e. buprenorphine), and/or administering of opioid antagonist (i.e. naloxone, naltrexone). Short-acting substances tend to have a higher potential for a withdrawal compared to long-acting agents, while longer-acting substances tend to have a longer, but less intense withdrawal duration [30].

Acute opioid withdrawal involves multiple systems and often demonstrates predictable patterns. Understanding these clinical manifestations and patterns are essential to make an early diagnosis to prevent any catastrophe. The relevant clinical characteristics of opioid withdrawal symptoms [30] are:

1. Increased pain, irritability, anxiety, restlessness, and myalgias often reported in the back and legs are some of the first subjective complaints.
2. Piloerection and fever are associated with more severe withdrawal, but less commonly seen as patients usually retake the substance before these symptoms appear.
3. Symptoms of anxiety, dysphoria, anhedonia, and insomnia may persist during a less acute phase lasting for weeks to months.
4. Drug craving may be seen throughout, and is likely responsible for relapse during attempted abstinence.

The American Psychiatry Association has defined the DSM V criteria in order to make the diagnosis of opioid withdrawal (Table 32.9) [30].

Table 32.9 Criteria for opioid withdrawal [30]

1. Presence of either of the following:
(a) Cessation of (or reduction in) opioid use that has been heavy and prolonged (i.e. several weeks or longer)
(b) Administration of an opioid antagonist after a period of opioid use
2. Three (or more) of the following, developing within minutes to several days after Criterion A:
(a) Dysphoric mood
(b) Nausea or vomiting
(c) Muscle aches
(d) Lacrimation or rhinorrhea
(e) Pupillary dilation, piloerection, or sweating
(f) Diarrhea
(g) Yawning
(h) Fever
(i) Insomnia
3. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
4. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance

Throughout its course, opioid withdrawal can be both subjectively and objectively measured. The Subjective Opiate Withdrawal Scale (SOWS) and the Objective Opiate Withdrawal Scale (OOWS) are valid and reliable indicators of severity over a wide range of signs and symptoms [31, 32]. The SOWS contains 16 symptoms whose intensity the patient rates on a scale of 0 (not at all) to 4 (extremely). The OOWS contains 13 physically observable signs, rated present or absent, based on a timed period of observation of the patient by a healthcare provider. These scales can be useful for clinicians to not only measure withdrawal severity, but also to monitor patient progress throughout a planned and structured detoxification course.

Detoxification [33]

Detoxification, or monitored withdrawal, usually involves gradual tapering or discontinuing a substance in a dependent individual. The goal is to achieve this safely, while attempting to mitigate the unpleasant effects of the withdrawal syndrome.

Opioid detoxification in an outpatient setting is the preferred method, but patients with polysubstance abuse, complex/unstable medical condition, associated psychiatric disorders, prior failed outpatient detoxification, and noncompliance to treatment will need inpatient detoxifications. Due to their long-acting properties, methadone or Suboxone (buprenorphine–naloxone) are commonly used in outpatient settings. Overall patient treatment retention and total cost [34] is better for methadone, while patient satisfaction [36], convenience [34], and less likelihood of elicit drug [36] usage is better with Suboxone treatment group (Table 32.10). Inpatient anesthesia assistance in rapid opioid withdrawal to minimize undesirable effects of withdrawal i.e. Ultra-Rapid detoxification, is used as a last resort secondary to its increased risk

Table 32.10 Characteristics of methadone and buprenorphine/naloxone

Characteristics	Methadone	Buprenorphine/naloxone (Suboxone)
Receptor affinity	Opioid agonist	Partial opioid receptor agonist
Composition	Racemic mixture of methadone	Abuse-deterrent formulation 4:1 ratio—buprenorphine:naloxone
Half-life	Long 8–59 h	
Initial effect	Takes up to 10 days	May precipitate withdrawal in very early phase
Additional adverse effects	QT_c interval prolongation and torsades de pointes	Less risk of respiratory depression from its "ceiling effect"
Screening needed	ECG screening at regular interval	Regular clinical monitoring
Dose delivery	Supervised	Unsupervised
Treatment retention	Better then Suboxone	Good
Satisfaction and convenience	Good	Better than methadone
Cost	Better than Suboxone, secondary to cost of medication	Comparable, but better than other detoxification strategies

Table 32.11 Opioid detoxification strategies

Setting	Patient with	Method	
Outpatient	Single agent	Long-acting opioid	Step 1: Calculate total daily dose of the long-acting opioid that does not produce withdrawal
		Short-acting opioid	Step 2: Taper the total requirement by 10 % every 3–7 days
			Step 1: Choose a long-acting pure-opioid agonist[a,b]
			Step 2: Calculate total daily dose of short-acting opioid used that does not produce withdrawal
			Step 3: Equi-analgesic conversion to a long-acting opioid of choice[c]
			Step 4: Taper the total requirement by 10 % every 3–7 days
	Multiple agents	Step 1: Choose a long-acting pure-opioid agonist[a,b]	
		Step 2: Calculate total daily dose of opioid used that does not produce withdrawal	
		Step 3: Equi-analgesic conversion to single long-acting opioid of choice[c]	
		Step 4: Taper the total requirement by 10 % every 3–7	
In-patient	Same as outpatient		
	Ultra-rapid	Step 1. Comprehensive medical assessment	
		Step 2. Patient heavily sedated or under general anesthesia with continuous monitoring	
		Step 3. Discontinue opioid and treated with opioid antagonists[d]	
		Step 4. Treat associated adverse symptoms with adjuvants[e]	

[a]Increasing dosing intervals of short-acting opioid may result in repetitive period of withdrawal and thus high risk of relapse
[b]Sustained-Release Oxycodone, Sustained-Release Morphine, methadone, buprenorphine–naloxone (Suboxone)
[c]Upon conversion of opioid reductions for cross-tolerance should be done
[d]Naloxone, naltrexone, etc.
[e]Clonidine for adrenergic overactivity, benzodiazepines for anxiety, muscle relaxants for myalgias

of serious adverse events and lack of additional over all benefit [37]. If inpatient detoxification is required, an addiction specialist/psychologist consultation is needed along with social worker involvement for discharge plan.

Different strategies exist in order to achieve opioid detoxification i.e. increasing dosing interval, tapering down of doses, or both. Patients could be on a single agent or multiple agents, and short-acting and long-acting opioids. A conservative approach to formulate a detoxification plan is shown in Table 32.11.

Conclusion

Opioids are a double-edged sword and chronic pain state is a never-ending war. Healthcare practices across the country are faced with increasing morbidity and mortality related to the use of opioids and substance abuse, which has an overall

negative impact on the socioeconomic burden of this country. Further, diversion, stealing, and illegal acquisition of opioids take a toll on crime and law enforcement. All this is expected to have a staggering growth with changes in healthcare policies that would allow more patients to have access to health care in combination with new government policies such as liberalization of Marijuana Prohibition Laws across the Unites States of America. Hence, it is absolutely essential for healthcare providers to understand the use and abuse potential of opioids, sufficiently equip, and certify themselves in order to perform and conduct opioid detoxification and maintenance programs, and also develop prudent practices to detect, control, and curb the menace of substance abuse in this society.

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