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Review Article

Overview of Prescribed Opioids Misuse and Addiction in Susceptible Individuals

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Abstract

Introduction: Some important drugs in medicine may lead to misuse and addictions in susceptible patients. This usually attributed to their effects is stimulating some pleasure in the brain. Most common examples include opioid. Opioid use disorder (OUD) involves misuse of prescribed opioid, use of diverted opioid, or the use of illegally obtained heroin. It is typically a chronic relapsing illness and is associated with high risk of morbidity and mortality.

Aim of Work: This topic sheds light on the epidemiology, prevention, identification, and management of prescription drug misuse in general with focusing on opioid misuse and addiction.

Methodology: A comprehensive and systematic search was conducted regarding prescription drug misuse and disorders. PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com) were the mainly used database.

Conclusion: Risk factors for misuse of prescribed opioid include a prior history of substance use disorder, younger age among other demographic characteristic, patient with severe pain and concomitant mental disorders. Prevention of prescribed drug misuse is the clinician responsibility in the first place. Principal strategies could be followed including optimizing alternative treatments, patient risk assessment, establishing clear treatment plan; and limiting dose and early refills. Direct and frequent follow-up with patients on opioids is recommended to monitor for and document benefits and harms of treatment. Urine drug testing provides objective about prescribed medication regular take and identify the use of non-prescribed substances. One specific method of management of opioid misuse or use disorder in patient with chronic pain is the use of opioid agonists. The mechanism of these agent is to alleviate withdrawal symptoms and block the acute effects of other opioids.

Keywords: *Opioids; Addiction; Opioid Use Disorder (OUD)*

Introduction

Some important drugs in medicine may lead to misuse and addictions in susceptible patients. This usually attributed to their effects is stimulating some pleasure in the brain. Most common examples include opioid, benzodiazepines, other sedatives, and stimulants. Opioids as an analgesic medication that is known to cause central nervous system depression as well as euphoria. Opioid use disorder (OUD) involves misuse of prescribed opioid, use of diverted opioid, or the use of illegally obtained heroin. It is typically a chronic relapsing illness and is associated with high risk of morbidity and mortality. In the fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-1), the condition named opioid use disorder constitutes opioid abuse and opioid dependence in the previous edition [1].

Despite all efforts and regulation, prescription drug misuse is a continuing issue. An important role to prevent, identify and manage this problem is on physicians who prescribe these medications.

This topic reviews the epidemiology, prevention, identification, and management of prescription drug misuse in general with focusing on opioid misuse and addiction.

Methodology

A comprehensive and systematic search was conducted regarding prescription drug misuse and disorders, management, prevention, opioids misuse with chronic pain. PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com) were the mainly used database. All relevant available and accessible articles of all types were reviewed and included. The terms used in search were: controlled substance, drug misuse, substance use disorder, opioid addiction, management of opioid use disorder.

Terminology and epidemiology

Some drugs carry a high risk for misuse, addiction, and illegal sale. Hence the name "controlled substance" was given in the United State. The aim is to regulate when and how they can be prescribed. Drug misuse means the using of any drugs in any manner and purpose other than that for which it was prescribed. Drugs misuse includes overuse, use it for pleasure, and diversion. Misuse is almost always present in substance use disorder but it is not enough criterion by its own. Non-medical use of drugs was previously used by the National Survey on Drug Use and Health (NSDUH) to imply a similar meaning, however, the term "misuse" was chosen instead since 2015 [2].

Drug use disorder is drug misuse meeting DSM-5 criteria of substance use disorder. This could be mild, moderate, or severe [1].

Misuse of prescription drugs is ongoing and even increasing issue due to greater prescribing of the incriminated medication for therapeutic purposes. This is particularly true of opioid analgesics for patients with chronic pain which was highly prescribed in the last decade [3-5]. In 2016, it is estimated that opioids prescriptions, and misuse by adolescent, have declined [6,7]. However, it was estimated that 3,800,000 adolescents and adults had misused pain medication in one month [8]. Most misusers of opioids obtain it from a relative or friend rather than a prescriber, however, it was suggested that users of prescribed opioid are at highest risk of overdose compared with other resources [9]. Interestingly, about 13 - 25 percent of the controlled prescription medication were prescribed by 1 percent of prescribers [10].

Risk factors, clinical manifestations and complications

Risk factors for misuse of prescribed opioid include a prior history of substance use disorder, younger age among other demographic characteristic, patient with severe pain, and concomitant mental disorders [11]. However, the association is not robust and consistently demonstrated.

Patients with opioid use disorder may appear normal in opioid withdrawal with no indication of opioid misuse. However, acutely intoxicated patients may present by slurred speech, appear sedated with miosis (pinpoint pupil) and a fresh injection sites may be seen by physical examination. The duration of acute intoxication depends upon the half-life of the drug and patient's tolerance to opioids. Patients with chronic use who have developed tolerance may show no acute effects after regular dose used by that patient. These patients are usually seen for other problem and opioid withdrawal symptoms appear with hospitalization. Patients with severe opioid use disorder could appear in a very poor general health. Patients with a mild or moderate disorder may not appear to be in overtly poor health.

Opioid use disorder may appear as a complication or directly related condition as infection. Contaminated drugs and inadequately sterile technique could cause both localized (as cellulitis, abscess) and systemic infections (as endocarditis, osteomyelitis); increasing incidence of hospitalization related to infections was seen since 2000 [12-14]. Patients with opioid use disorder who share needles are at higher risk of blood-borne pathogen as HIV, hepatitis B, and hepatitis C viruses as well as systemic bacterial infections as pneumonia and tuberculosis. Hepatitis C virus infection may also occur with non-injectable use of heroin [15,16].

Opioid affects gastrointestinal function and decrease motility. This usually manifest as constipation, however, other manifestation bloating, early satiety, and pain could be seen. Patients occasionally develop moderate to severe abdominal pain, a syndrome that is occasionally called narcotic bowel syndrome.

Prolonged use of opioid or opioid agonists may result in increased sensitivity to pain (hyperalgesia). The symptoms can be severe and chronic or recurring. Medically supervised withdrawal is proved to markedly alleviate the pain.

Accident is another health consequence of opioid use disorder. Data have shown that heroin user have higher rates of motor vehicle collisions than the general population [17]. Nevertheless, driver under the effect of opioid have significantly increased rates of all-cause mortality [18].

Another rare consequence of opioid use disorder is opioid amnestic syndrome. About 19 cases have been identified in the United States and Canada. The condition characterizes by acute onset amnesia with bilateral hippocampal ischemia by MRI [19]. It is suggested that all these cases were related to fentanyl (synthetic opioid) use [20,21]. Diagnosis of such case could be challenging and require specific testing for fentanyl in patients with evidence of opioid use and use of MRI in the first week of amnesia after overdose.

Prevention

Prevention of prescribed drug misuse is the clinician responsibility in the first place. To achieve this, principal strategies could be followed including optimizing alternative treatments, patient risk assessment, establishing clear treatment plan; and limiting dose and early refills.

The first rule in prevention is using alternative medication whenever they are safe and effective, hence, minimizing controlled substances prescription as possible. Clinical indications for prescribing controlled substances such as pain have evidenced-based management option that can replace or complement the use of opioid. Behavioral management, non-pharmacologic treatment with self-management strategies, physical therapy, as well as non-controlled pharmacotherapy, are effective methods to reduce controlled substance need.

The decision to choose controlled substance as opioid is recommended by guidelines to be initiated strictly when the benefits outweigh the risk [22,23]. Contraindications to treatment with opioid as controlled substance include patients with current untreated substance use disorder, psychiatric illness with poor control, and irregular follow-up [22]. Predicting the likelihood of benefit versus harm of controlled substance prescribing is difficult and scant data are available. Many attempts and tools were developed to predict the risk of misuse without significant impact on practice [24-26]. It is of a great help in assessing the risk of misuse to collect data about the patients

from patients themselves (reported data), providers, and objective sources. Patient-reported data should include substance use history and mental health history as well as family and social history. The clinician should look in physical examination for any signs of substance use as track marks. Additional data could be obtained from medical records, previous or current healthcare providers, state prescription monitoring program if available, and conduct drug testing. The physician judgment, after making the risk profile of patients, directs the decision whether to prescribe opioid and how strict the monitoring should be.

Clinician's role to establish a clear plan requires a thorough discussion of the risks, benefits, and alternative options with the patient before starting a controlled substance [23]. Clinicians should also explain to the patient the importance of follow-up and the strategies to detect any sings of drug misuse; including the definition of misuse and drug use disorder, the time when these drugs should be discontinued, and the possible need for substance use disorder treatment. Written informed consents, agreements on terms of treatment, or treatment plans can be useful tool to document agreement between patients and physicians. Despite the lack of strong evidence on the effectiveness of treatment agreement in reducing the misuse or drug use disorders [27] most experts believe in its importance in in documenting shared decision-making, treatment goal-setting, informed consent, and defining the monitoring plan [22].

One suggested approach to minimize controlled drug misuse include limiting the dose and number of prescriptions. The strongest evidence of this strategies is for opioid prescribing. Studies have consistently shown the association between higher daily opioid doses and greater numbers of prescriptions per month and the higher risk of overdose death [28-30]. Accordingly, it is recommended by the center for disease control and prevention (CDC) that clinicians should avoid increasing the dose of prescribed opioids beyond 90 morphine milligram equivalents per day. The daily dose should be limited to the lowest effective dose with attempt to reduce the dose to lowest level by which the symptoms are tolerable. Other ways to limit the prescribed amount to maintain a calculated schedule with explaining to the patients that early refills will not be provided.

Management

After prescribing the controlled substance, it is physicians responsibility to closely monitor patients for signs of misuse [22,23,31]. Experts recommend a "universal precautions" framework that includes establishing a clear relationship with the patient and thorough documentation of medical and physical history and examination [22,32].

Direct and frequent follow-up with patients on opioids is recommended to monitor for and document benefits and harms of treatment. There is no consensus on how frequent the visit should occur, however, at least one visit every three months or less is recommended in higher risk circumstances [23]. During the follow up of patient with chronic pain on opioid, physician should focus on risks and benefits assessment, the "Five A's" provides a useful framework: Analgesia; Activities of daily living; Addiction; Adverse effects; Adherence to the plan.

During the follow-up, Physical examination plays essential role in providing details about misuse, evidence of intoxication, withdrawal, signs of drug injection or intranasal use. Sometimes family member involvement could aid clear history about a patient's function and use of the medications.

Drug testing is great tools to test for misuse in susceptible individuals. Urine drug testing provides objective about prescribed medication regular take and identify the use of non-prescribed substances [22,33-36]. It is worth to mention that there is no enough evidence to support the role of regular urine test in reducing opioid misuse [27]. However, regular urine testing is better than clinician assessment alone [34]. In one study, 60 percent of patients whose were assessed by their clinician as not at risk of misuse showed positive urine tests of an illicit drug use or the absence of a prescribed medication [37]. Urine is the most commonly used methods due to longer window of detection compared with blood and oral fluid. Oral fluid testing is susceptible to false negatives results especially among smokers. Clinicians should bear in mind the accuracy of different test misinterpretation of results is common and could negatively affect patient care

[38-40]. Random drug testing is also an effective tool to reveal substance use; regular blood testing, on the other hand, could not detect secretive use of substance.

Many initiatives have emerged as a response to epidemic of lethal opioid overdoses in the United States and aimed to educate clinicians about appropriate opioid use and prescribing practices [41-43]. In one case, dissemination of a practice guideline to reduce opioid prescribing by emergency clinicians has resulted in 12 percent reduction in prescriptions per month [44]. The used guideline encouraged emergency clinicians to review patients' recent prescription history; prescribe limited quantity when necessary; refer for further evaluation, treatment, and monitoring; and provide education about opioid risks and limited benefits.

Physician should plan in advance the way to deal with drug misuse if developed. In this approach, full and clear discussion and agreement with the patients should take place. Prescription drug misuse may range from mild single episode to severe form of illegal drug source. The clinician's response should be proportional to the severity and the pattern of the behaviors. As an example, a response to a single minor deviation from the patient's treatment agreement may be to provide counseling and intensify monitoring; a response to more severe or persistent misuse may be to discontinue controlled substances.

One specific method of management of opioid misuse or use disorder in patient with chronic pain is the use of opioid agonists. The mechanism of these agent is to alleviate withdrawal symptoms and block the acute effects of other opioids. Adequate dose of opioid agonist help patient with use disorder to return to a productive lifestyle and engage in pro-social behaviors. As the patient is stabilized on an appropriate dose, machines and car operation is possible without significant impairment [45].

Methadone and buprenorphine are well-studied type of opioids agonist. Patients on these drugs are physically dependent, however, the pattern of behaviors associated with addiction to heroin, illicit fentanyl, or pharmaceutical opioids are not present [1,46]. Successful management with opioid agonist may entail prolonged period of use up to many years, fewer percent of patients could be tapered off successfully in a shorter period. Candidates for tapering attempt include patients with interest in tapering without illicit drug use and have good psychosocial stability and supports. After a thorough discussion, patient may elect to discontinue agonist medication by very slow tapering over several months to years.

Conclusion

Some important drugs in medicine may lead to misuse and addictions in susceptible patients. This usually attributed to their effects is stimulating some pleasure in the brain. Most common examples include opioid. Opioid use disorder (OUD) involves misuse of prescribed opioid, use of diverted opioid, or the use of illegally obtained heroin. It is typically a chronic relapsing illness and is associated with high risk of morbidity and mortality. Risk factors for misuse of prescribed opioid include a prior history of substance use disorder, younger age among other demographic characteristic, patient with severe pain, and concomitant mental disorders. Prevention of prescribed drug misuse is the clinician responsibility in the first place. Principal strategies could be followed including optimizing alternative treatments, patient risk assessment, establishing clear treatment plan; and limiting dose and early refills. Direct and frequent follow-up with patients on opioids is recommended to monitor for and document benefits and harms of treatment. Urine drug testing provides objective about prescribed medication regular take and identify the use of non-prescribed substances. One specific method of management of opioid misuse or use disorder in patient with chronic pain is the use of opioid agonists. The mechanism of these agent is to alleviate withdrawal symptoms and block the acute effects of other opioids.

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