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Review Article

Opioid Crisis

Abstract

Deaths from opioid overdose in the United States doubled between 2000-2014. An increase in prescription opioid drug-induced fatalities parallels a rise in the frequency of these medications being prescribed. Although the number of legal narcotics sold in this country has nearly quadrupled, there is no change reported in the degree of pain Americans experience. Deaths are most common among those opioid users who are drug dependent, even though overdoses occur in medical and non-medical narcotic users who are not addicted.

Public health efforts have focused on providing patients with chronic pain appropriate access to opioid pain relievers, while reducing non-medical usage. However, that alone has been insufficient to curb opioid overdoses. There remains a high opioid-related morbidity and mortality among people with pain, even for those receiving these analgesics for legitimate clinical reasons. Research results demonstrating the safety and efficacy of narcotics for chronic, non-cancer pain are not evident. Surveys of patients prescribed opioids over the long-term indicate that most of them continued to experience significant distress; yet, some of them, also experience greater comfort and were without abuse of medication.

Physicians should avoid unnecessary opioid prescribing for some people with chronic conditions, although it is difficult to predict which patients might be vulnerable to addiction versus who might benefit from these pharmaceuticals. Because of such uncertainty, it is helpful when doctors screen personal and family histories for substance abuse and provide careful, regular monitoring. Strategies for reducing abuse of prescription analgesic drugs focus on physician prescribing regulations that are thus far not consistently effective.

Introduction

Over the past 25 years, doctors have been increasingly prescribing opioid drugs to people for chronic pain [1]. Fatalities due to unintentional opioid poisoning in the United States (US) are second in death only to automobile collisions [2]. In the last decade, a public health concern focused on a substantial increase in accidental prescription opioid drug-induced deaths, which parallels a rise in the frequency of these medications being prescribed [2].

Over 30 million people abuse opioids worldwide; about two million in the US evidenced substance use disorders related to prescription opioid pain relievers (OPR) during 2012 [3]. Over nine million Americans consume opioids for long-term pain control [4]. Approximately 467,000 are addicted to heroin [5]. During 2012, there were about 259 million prescriptions filled for opioid medications, a quadrupling since 1999 [6].

About 100 million Americans suffer from chronic pain and many ingest opioids for relief. OPRs are helpful in the short-term; however, their effectiveness often diminishes over time and physical dependence emerges [7]. The per-capita ingestion

of oxycodone in the United States is the highest in the world, almost twice as much as in Canada and between 5-10 times the rates of some similar other countries [8]. Although the number of prescription opioids recently sold has nearly quadrupled, there is no change reported in the degree of pain Americans experience [9-12].

Between 2000-2014, deaths from opioid overdose reportedly doubled, from six to about 15 per 100,000 persons [13]. Approximately 61% of the 47,055 fatalities from all drugs specifically involved an opioid. The age-adjusted rate increased significantly from 2000-2014, up 14% during 2013-2014 [13]. The economic costs were over \$55 billion [14]. More people than ever died from overdoses in 2014; the majority of these deaths involved an opioid, nearly half a million between 2000-2014 [9,13]. These overdoses kill about 78 Americans daily [9]. Approximately 82% of these fatalities are induced by prescription opioids, of which 92% are unintentional heroin overdoses; the remainder are attributed predominantly to suicide or "undetermined intent" [15]. Overdose prevention is a major public health concern [16].

While fentanyl and tramadol accounted for the largest rise in drug overdose death rates, for methadone such frequencies

doubled to nearly two per 100,000 [13]. Death by heroin overdose rose by 26% and tripled since 2010 to over three per 100,000 in 2014.¹³ Natural or semisynthetic opioids like morphine, oxycodone, and hydrocodone were involved in fatalities at almost four per 100,000, the highest among all opioids, with a 9% increase during 2013 [17,18].

Data comparing buprenorphine versus methadone in tapered doses for managing opioid withdrawal remains limited, but data suggests that buprenorphine and methadone have similar capacity to ameliorate opioid withdrawal, without significant adverse effects [19]. Opioid dependence is a chronic disorder requiring long-term treatment. Effective options for management include pharmaceutical agents (e.g., methadone, buprenorphine and/or naltrexone) and psychosocial interventions. However, relapse rates following cessation of treatment are high, with only an estimated 25% of heroin-dependent individuals remaining abstinent after receiving methadone treatment [19]. Relapse following non-compliance with oral naltrexone is a particular concern. Episodes of opioid abuse during non-compliance have been associated with relapse to opioid dependence [20].

Emergency department contacts and substance-abuse treatment admissions related to prescription opioids have increased significantly, along with a substantial rise in healthcare costs [15]. Besides overdose mortality, other adverse outcomes include emergencies due to non-medical opioid pain reliever use and neonatal abstinence syndromes. From 1997-2011, there was a nine fold increase in the number of individuals seeking treatment for addiction to these pain relievers [16].

Orthopedists were more likely than primary care physicians to write prescriptions for patients with Medicaid for chronic non-cancer pain. Prescribing such medication is an individualized transaction involving many different clinical parameters for each patient and/or doctor [21]. Emergency physicians provide narcotic analgesics three times more than their colleagues and are documented to have more opioid dependent patients. This suggests that receiving an opioid for even one encounter could increase future long-term opioid abuse and potentially increase adverse outcomes among elderly people. It is not known whether over-prescribing by some practitioners is amenable to intervention [22].

Emergency room contacts are frequent among opioid users, but only a minority of the visits were associated with back pain [23]. Nonetheless, more than half of these patients received a prescription for an opioid. They were also high utilizers of all clinic services, and co-morbidity with mental health concerns was also noted. As with clinic visits, the probability of hospitalization was associated with opioid abuse, with a nearly four-fold greater chance of being hospitalized, even after adjusting for age, gender, co-morbidity, and sedative-hypnotic use. A minority of these patients are monitored in a pain clinic; most of them are managed in primary care or emergency departments. This was true even though access to pain clinic services were easily available [23].

Use

Although opioid overdoses occur in medical and non-medical opioid users who are not addicted, deaths are most common among those who are drug dependent. Recognizing non-medical abuse, enhances efforts to address this crisis by preventing or treating addiction. Although increased opioid consumption over the past two decades is largely ambulatory, prescribing for chronic, non-cancer pain and acute pain among hospitalized patients has also risen. In 2009-2010, physicians prescribed opioids to over 50% of non-surgical hospitalized patients [16,24].

Twenty-five million people in the US initiated non-medical pain reliever usage between 2002-2011 [25]. Over 5% of the population 12 years or older utilized opioid pain medication non-medically [26]. The incidence of non-medical use increased in the 1990s and peaked in 2002, with nearly three million new non-medical applications. Since 2002, non-medical utilization has declined; yet, overdose deaths, admissions for addiction treatment, and other similar events have risen dramatically [25]. Prescription pain drugs are taken by about 14% of pregnant women and resulted in a 300% rise in neonatal abstinence syndrome occurrence [27,28].

Public health efforts have focused on preserving access to OPRs for chronic pain patients, while reducing non-medical usage, but that alone was not sufficient to curb overdose frequencies. Non-medical usage includes that without a prescription and applications other than as prescribed or for an induced emotional experience. There remains a high opioid-related morbidity and mortality among people with pain, even when receiving these medications for legitimate purposes [16].

Age

Overdose deaths occur most often among adults aged 45-54. Those 55-64, evidence the greatest increase in overdose mortality, despite opioid abuse being most common among people between the ages of 15-24 [16].

Middle-aged women and elderly adults are more likely than others to experience pain complaints. Iatrogenic opioid addiction may explain why they have the largest increase in drug-induced hospitalizations. Over the past decade, Caucasian women, ages 55-64, have the biggest escalation in fatalities [16]. The National Institute on Drug Abuse has documented a decline of illegal street drug use by youths and recognized an alarming rise in their abuse of prescription opioids. In 2005, a survey of 12th graders, revealed non-medical usage of hydrocodone at over 9% and about 5% taking oxycodone [29].

Heroin

Most lethal overdoses involve prescription opioids, and heroin is related to these medicines since many users become addicted to OPRs before switching to other drugs. The National Survey on Drug Use and Health reports that 80% of heroin users say that their opioid utilization began with prescription pharmaceuticals, but then switched to heroin since it is cheaper [5]. Thus, opioid addiction is associated with rises in heroin-

related morbidity and mortality. Heroin addiction treatment admissions for Caucasians aged 20–34 years have risen since 2001, and overdose deaths among those at ages 18–44 rose 171% [5,16,17]. Surprisingly, the fatality rate associated with heroin is inversely related to opioid drug prescribing; these deaths increased between 2002–2006, plateaued in 2006–2008, and decreased during 2009–2013 [30]. There is a positive relationship between non-medical opioid use and the people choosing to use heroin [31].

Suicide

The prevalence of suicide attempts among opioid addicts is between 8%–17% [27,32]. Suicide is often underestimated; yet, 23% of opioid addicts in a detoxification unit and 28% of those maintained on codeine have attempted suicide.

Veterans

About 60% of veterans deployed in the Middle East and 50% of the older ones complain of chronic pain [33]. Veterans are twice as likely to die from accidental opioid overdoses as civilians. Untreated pain escalates the risk of suicide and poorly managed OPR regimens can also be dangerous. During 2010–2015, the number of veterans with opioid-use disorders grew, spiking to 55%. Approximately 13% of veterans, or 68,000, utilize opioids [17,33,34].

Causes

The National Survey on Drug Use and Health, reports abuse of prescription pain medicine is widespread and not concentrated in urban areas. The cause of this distribution is unclear, but prescription drug monitoring programs are not influencing these trends. Most subjects surveyed denied obtaining prescriptions from physicians; roughly 60% said they got their medications from friends or family [29].

Theft from pharmaceutical distribution chains such as hospitals or pharmacies are a source of drug diversion. In 2003, millions of doses of the opioid analgesics like fentanyl, hydromorphone, meperidine, methadone, morphine, and oxycodone were reported stolen, including several million of hydrocodone [29]. Stealing and/or sharing the prescription medicines of friends and relatives or obtaining multiple prescriptions from different doctors is a large source of prescription abuse; however, the relative contributions from these sources is not clear [29].

An often unreported aspect of the opioid crisis is the involvement of the pharmaceutical companies. The manufacturers have a substantial role in augmenting opioid prescribing; this might occur by influencing medical education through encouraging physicians to prescribe these drugs for patients in pain, while downplaying the dangers. Even people who have overdosed on opioids have an easy time obtaining new prescriptions, even sometimes from the same doctor. Most persons who regularly take these analgesics are physically dependent. Efforts to stop the drugs or reduce the dosage precipitates opioid withdrawal. The patients may not recognize the withdrawal, but they know these symptoms are

alleviated by resumption of opioids. Consequently, they believe they need these medications to function and that facilitates even minimally effective drugs to become self-perpetuating. For many chronic pain patients, opioids do not relieve pain, but they are required to avoid narcotic withdrawal [35–37].

Although analgesic abuse is a public health crisis, the news media often frame the problem as a criminal justice issue. Between 1998–2012, some reports about opioids cite illicit drug dealing by physicians, patients, and others. Most opioid abusers were involved in criminal activity [38]. Frequently reported causes of this were illegal drug dealing and the most common solutions were law enforcement actions. Prevention-oriented approaches, such as prescription drug-monitoring programs, are suggested, but less than 5% noted expanding substance abuse treatment. Even fewer recommended medication-assisted treatments, such as buprenorphine [38,39].

Adversity

When sold illegally, the cost of opioids escalates multiple times over that at a pharmacy. Opioid abuse negatively affects patients and their family. Many addicts are not able to function well in society and may neglect important aspects of their lives, like child care. While the most severe adverse effects of opioids such as addiction, overdose, and death are stressed, some lesser consequences like constipation may not be [38].

Conclusion

While opioids are studied in short-term research, few chronic pain subjects are enrolled in longer-term trials because it is not practical to require prolonged placebo trials. Although there are a range of other drugs for pain control, such as non-steroidal anti-inflammatory agents, few investigations reveal comparative effectiveness nor evidence benefits of long-term opioid use [4].

Long-term research demonstrating the safety and efficacy of opioid pain relievers for chronic, non-cancer pain have not been documented. Surveys of patients with such issues receiving long-term opioid pain relievers indicate that most of them continued to experience significant discomfort and dysfunction. Clinicians should use caution and avoid unnecessary prescribing of OPRs for patients with various chronic conditions [16].

Many individuals on high-dose opioids, incur an increased risk for death. No investigation has evidenced high-dosages to be beneficial over the long-term. Approximately 4% of men and 2% of women on high-dose opioids (defined as >200 mg of morphine or equivalent per day) have died of opioid-related causes [38].

Nearly 10% of the general population will develop an addictive disorder in their lifetime, most often to alcohol. It is difficult for physicians to predict which patients might be vulnerable. Because of this uncertainty, doctors ought to screen for personal or family histories of substance abuse and provide monitoring on a regular basis. It is important to intervene if there are concerns and to minimize abuse or diversion [29].

Everyone should know about the abuse potential of these medications, and about how to avoid such problems. Tactics for reducing abuse of prescription analgesics focus on physician regulations and prescription monitoring; however, such practices are not always effective [29]. It remains unclear as to which patients would benefit from opioid prescribing. Further research about indications for developing dependence or addiction are needed [33,38]. The medical profession, society, and governmental agencies are concerned about opioid abuse. Treatment options are expanding and include pharmaceutical and non-pharmaceutical therapies. Regulations about prescribing and distributing such medications are tightening and remain an area of continued concern.

It is important to ensure that people who need pain relief continue to have access; doctors should be sure that patients receive these drugs when indicated. They also must be vigilant about abuse potential [29]. The American Pain Society and the American Academy of Pain Medicine have convened a panel to create a pain-control protocol to improve the safe management of chronic, non-cancer pain [29,40].

Physicians should monitor for signs of drug abuse or aberrant behavior and for evidence about the quality of patient lifestyle. Assess the level of function at the start of treatment, establish goals for the activities that pain alleviation will allow, and closely schedule regular follow-up appointments [29].

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