Journal of Addiction Research & Therapy

Miller and Oberbarnscheidt, J Addict Res Ther
2017, 8:2
DOI: 10.4172/2155-6105.1000311

Short Communication OMICS International

Prescription Opioid Medications: Efficacy in Chronic Pain

Miller NS MD JD[1] **and Oberbarnscheidt T MD PhD**[2*]

[1]*CEO of Health Advocates PLLC, East Lansing, MI, Clinical Professor of Psychiatry, Department of Psychiatry, Medical College of George, Augusta University, Augusta, Georgia, USA*

[2]*Central Michigan University, Department of Psychiatry, Saginaw, MI, USA*

[*]**Corresponding author:** Thersilla Oberbarnscheidt, Resident, Central Michigan University College of Medicine, Saginaw, Michigan, USA; E-mail: Thersilla.oberbarnscheidt@cmich.edu

Received date: February 22, 2017; **Accepted date:** March 17, 2017; **Published date:** March 21, 2017

Background and Policy

The current problems and costs, in terms of economic, medical, legal and personal, surrounding opioid pain medications and treatment of chronic pain are alarming and unrelenting. Are the policies for prescribing opioid medications currently in place working to treat chronic pain? This paper will review and assess the current liberal policies governing opioid medications and chronic pain and answer the following questions: What is the evidence for the efficacy of long term prescribing of opioid medications for pain? How does the use of opioids compare to other medications in the treatment of pain? What are the adverse consequences of chronic prescribing of opioid medications? Why are opioids prescribed widely and commonly? Do the benefits outweigh the risks from long term prescribing of opioid medications? [1-5].

Drugs classified as opioids, such as Oxycontin, Oxycodone, Chydrocodone and Vicodin, are ostensibly used to treat mild, moderate and severe pain despite, after the review of the current literature, that there is no medical support for the efficacy of long term prescribing of opioid medications. Although the use of opioids to treat pain has skyrocketed, complaints of pain problems have actually correspondingly increased [6].

Additionally, economic, medical and personal adverse consequences have soared including but not limited to pain and suffering, death, disability, and criminal activity driven by opioid addiction and dependence [6]. Whereas there is evidence for prescribing opioids for short-term pain relief, there is not significant evidence for maintenance of pain relief or improved function over longer periods of time [1,7,8].

Efficacy Hypothesis

For the past 30 years, opioids have been a growing player in treating chronic nonmalignant pain. A systematic review performed by Kissin et al. [1] tested the following hypotheses: A) that there is not strong evidence that long-term opioid treatment of chronic nonmalignant pain is effective and B) that the assessment of the risk of addiction has been neglected and is a main problem.

Kissin et al. [1] performed an initial literature search resulting in 2,356 articles from the 30 year period between 1983-2012. The literature search was reduced to 250 articles relevant to chronic non-malignant pain, then to 53 original clinical research studies. Analysis showed that only 25 of these studies were randomized control studies. Only one of these studies lasted three months or longer. None of the studies had both high quality evidence and long-term opioid treatment. Thus, assessment of articles on chronic opioid therapy for non-malignant pain indicates there is insufficient high-quality evidence of its efficacy [1].

The problem of opioid addiction in chronic pain was discussed only in six articles and the problem of death associated with opioid treatment of chronic pain was discussed in only three articles. The issue of safety of opioid treatment revealed itself most dramatically in rising numbers of opioid overdose deaths. In 2007, 11,499 deaths were caused by overdoses of opioids, roughly a four-fold increase compared with 1999 [1]. Even an increase of that size somehow did not trigger a timely response by medical journals [9].

Still, opioids use, misuse and addiction are the main contributors to opioid overdose deaths. Yet when opioid treatment for chronic non-malignant pain was being introduced, addiction was not presented or discussed and even downplayed in early articles and editorials. Could the acceptance of this new indication for opioid treatment be responsible? The extreme neglect of these vital issues causes and contributes to the dangerous and vast opioid consumption by the United States.

In 2006, Eriksen et al. [10] performed an epidemiological study about critical issues with opioids in chronic non-malignant pain. Ten thousand sixty-six Danish individuals from a representative national random sample were interviewed and took part in a self-administered questionnaire and participants reporting pain were divided into opioid and non-opioid users. Opioid usage, compared to non-opioid use, was significantly associated with reporting of moderate/severe or very severe pain, poor self-rated health, not being engaged in employment, higher use of the health care system, living alone (being separated/divorced or widowed) and a negative influence of quality of life [10].

In the group of those experiencing pain, approximately 90% of opioid users reported moderate severe or very severe pain compared with 46% in the non-opioid group. Regarding the key outcome goals of opioid treatment: pain relief, improved quality of life, and improved functional capacity, Erikson found that treatment with opioids failed to fulfil any of these goals.

Teater reports that although there may be some benefit over placebo when opioids are used short term, there is no benefit over non-opioid medications when used for longer than four months [11]. Several other reviews have concluded that no evidence exists to support long-term use of opioids to treat chronic pain [7,12].

Comparison of Opioids to Other Non-Opioid Analgesics

In assessing the effectiveness and strength of comparative pain medications, multiple clinical studies use the statistical measure:

number needed to treat (NNT.) The NNT value represents the number of patients who must be administered a specific intervention for one person to experience 50% pain relief. 50% pain relief is considered effective treatment because it increases functionality and quality of life. When considering treatment options for pain relief, we ask how many people must be treated with a specific intervention for one person to achieve effective treatment. A lower NNT means a more effective intervention. An intervention with an NNT of 1 means that everyone who takes the medicine has a 50% reduction in pain, the medicine is 100 percent effective. An intervention with an NNT of 2 means that two people must take the medication for 1 to have a 50% reduction in pain. If an intervention had an NNT of 8, 8 people would have to be treated for 1 person to have 50% pain relief [6].

It was found that NSAIDs have much lower NNT values than opioids. Oxycodone 15 mg has an NNT of 4.6; 46 people would have to be treated for 10 to get 50% pain relief. Tramadol 50mg has an NNT of 8.3; 83 people would have to be treated for 10 to achieve 50% pain relief. When clinically assessed, these interventions are not as powerful as the frequency and duration of their prescribing and as pharmaceutical companies claim and advertise. On the other hand, Ibuprofen 200 mg+acetaminophen 500 mg have an NNT of 1.6; if 16 people are treated, 10 will receive 50% pain relief. Diclofenac 100mg has an NNT of 1.8; if 18 people are treated 10 will receive relief. Thus, NSAIDs produce 50% pain relief more often than opioids and many that are treated with opioids do not achieve the desired outcome. Importantly, patients are left without pain relief and suffering from the negative side effects of opioids [6].

In a study in the Journal of the American Dental Association, after quantitative systematic reviews, Moore concluded that 325 mg of acetaminophen+200 mg Ibuprofen provides better pain relief after dental surgery than opioids while also having fewer adverse effects [13,14]. In another study, assessing patients who were treated for herniated discs, Radcliffe found that those who were initially treated with opioids rather than NSAIDs had an increased incidence of surgery and a greater chance of being on opioids 4 years later, yet no significant changes in overall outcome [15]. The lack of efficacy of long-term opioid treatment has also been proven by epidemiological studies [10].

Currently, it is estimated that more than 9 million Americans use chronic opioid therapy to treat non-malignant pain [5,16] The standard of care in the practice of medicine today is supposed to provide the best treatment with the least harm. Health care providers prescribe opioids as powerful painkillers but evidence proves they are less effective than over the counter Ibuprofen. When the proven benefits of chronic opioid therapy are considered in conjunction with the risks, we must ask ourselves how we can ethically continue this treatment with opioid medications.

Common Clinical Issues

Patients are often admitted to health facilities due to suicidal ideation or attempts and associated psychiatric symptoms. They complain of depression, anxiety, low daily functioning, increased pain, and often are comorbid with other drug use such as marijuana, Adderall, and various benzodiazepines. These patients often seek anti-depressants or increased doses of their current medications but they fail to recognize the encompassing root of their emotional, behavioral and physical ailments: prescription opioids, benzodiazepines, marijuana and Adderall [17,18].

Benzodiazepines are often prescribed to treat the opioid induced anxiety and depression. Subsequently, Adderall is prescribed to treat the combined opioid and benzodiazepine depression. When a medical professional writes these prescriptions, patients and doctors alike often fail to make the essential connection and interactions between these medications and the consequent aversive effects experienced [19,20].

Patients are unaware that prescribed medications can be addictive and perpetuate their own use despite adverse consequences. This lack of awareness is partially attributable to physicians' lack of knowledge and skill regarding prescribing these medications and failure to educate their patients about the addictive risks and consequent harms.

Overdoses from opioid medications, both lethal and nonlethal are common. The majority of opioid overdose deaths occur in the home, a minority appear to be intentional. Recent studies indicate disordered breathing during non-REM sleep increases with opioid dose. The potent effect of opioids in depressing central respirations in both animals and humans has been well documented. Opioids impair cognition and depress mood, additionally contributing to poor insight and judgment. Lack of control and compulsive use due to addiction lead to a loss of control and dangerous use of opioid medications and adverse consequences [9,19,21]

In clinical settings, the risks-benefit equation for the use of opioids for chronic non-cancer pain is substantially unbalanced. Risks include but are not limited to loss of family and community, lifelong disability, dependence, addiction, serious adverse events, overdose morbidity, and mortality. The sole benefit is pain relief and is only effective in short-term prescribing of opioids. The severity of the imbalance is result of an underappreciated longer-term physical dependence and addiction risk associated with long-term disability and the underuse of best practices and universal precautions by health care providers [19,22,23].

Primary care physicians are the principal opioid prescribers in practice and they lack important training regarding risks involved with opioids. Current prescribing practices have been associated with substantial morbidity and mortality of epidemic proportions. In fact, the most common risk factor to become addicted to opioids is seeking medical care. It is essential that health care providers are promptly required to be educated in the addictive nature and inherent dangers of opioids. Recently, there has been an increased emphasis on pain recognition and lack of adequate pain care.

Many procedural and pharmacological modalities as well as adjunctive methods like acupuncture and relaxation training have been recently developed to improve function of patients with chronic pain. Concurrent with increased emphasis on pain management, here has been a quick and significant expansion in prescribing of short and long acting opioids in pharmacological treatments. In spite of these substantial increases, an estimated 40% of patients with chronic pain do not achieve adequate pain relief [24,25]

Addiction

Although there is evidence for substantial pain relief from opioid medications in the short term, there is not significant evidence for improved physical function or maintenance of pain relief for prescribing over longer periods of time. Mechanisms for loss of analgesic efficacy include the development of pharmacologic tolerance and opioid-induced hyperalgesia, addiction and dependence [2,10,26]. Additionally, under serious questioning is the premise that tolerance

can be overcome by dose escalation. The true incidence rate of dependence and addiction in the public is unknown.

However, 50% of patients taking opioids for at least 3 months are still on opioids 5 years later due likely to addiction [27-29]. Dangerously, there is a not a clear understanding for these addicted and dependent states of opioid use. Physicians lack knowledge on the pharmacological properties of opioids, notably their inherent addiction potential. This lack of knowledge and application in clinical practice makes it hard to identify the role of addiction in efficacy of these medications; opioids are not efficacious largely because they are addicting [30].

Chronic use of opioid causes brain abnormalities which become the underlying cause of opioid dependence and addiction. The abnormalities that produce addiction are wide-ranging and complex and may involve environmental effects as well as genetic predisposition in brain pathways that were abnormal prior to opioid administration.

These abnormalities can produce cravings that lead to relapse long after an individual is no longer opioid dependent. When administered, opioids attach to mu receptors on brain cells. This ligand binding triggers biochemical brain processes that induce pleasure, the same reward transductance that occurs when an individual eats or has sex. Opiates activate the mesolimbic reward system, motivating individuals to use the drug simply for pleasure. Activation of the mesolimbic reward system sends signals to the ventral tegmental area to release dopamine in the nucleus accumbens. Dopamine release in the nucleus accumbens is directly responsible for pleasure and it promotes continued drug use and subsequent addiction [31].

Repeated exposure to opioids induces the brain mechanisms of dependence causing daily use to avert the unpleasant drug withdrawal. Clinically, opioid withdrawal is a chief factor driving opioid dependence and addiction creating a vicious cycle. One way to view of opioid addiction is the "changed set point" model: essentially, drug use alters physiological settings or baselines. Based on the assumption that mesolimbic reward pathways are naturally set to release enough dopamine in the nucleus accumbens to produce normal levels of pleasure. This model suggests that opioids induce addiction by changing this set point such that the release of dopamine is reduced when normally pleasurable activities occur and opioids are not present. Additionally in the locus ceruleus, a set point alteration occurs such that norepinephrine release is increased during withdrawal [32].

When opioids are unavailable and desired, cravings can be attributable to cortical glutamate neurotransmitters. As excitatory glutamate activity increases during cravings, dopamine is released from the ventral tegmental area, increasing drug wanting and norepinephrine will be released from the locus ceruleus leading to increased symptoms of opioid withdrawal.

The addiction and misuse of opioids are on the rise and have been shown to have serious and grave consequences. For example, unintentional prescription opioid overdose deaths have been increasing since the year 2000. A staggering 2.1 million people in the United States had a substance use disorder related to prescription opioid pain medications in 2012. There is an array of factors that likely to contribute to breadth and depth of the current prescription opioid epidemic [33,34].

These factors include the rise in the number of prescriptions written and administered, increased social acceptance for using opioid medications for non-medical and medical purposes and the aggressive market practices of pharmaceutical companies. The United States consumes more than 80 percent of the world's supply of opioids. This alarming number elucidates that something about US opioid policy must change to improve management of pain as opioids are not solving the pain problem. Until the latter part of the 1990s, long term opioid prescribing (beyond three months) was prohibited in most states but our current policies for indefinite length in prescribing opioid medications are causing widespread failure in the treatment of pain due to opioid addiction [35].

Addiction to prescription opioid medications is an enormous and widespread public health problem. Overdose deaths relating to opioid pain medications have increased and now exceed deaths involving heroin and cocaine combined. In 2013, there were 43,982 total drug overdose deaths in the United States. 16,235 were attributed to prescription analgesics and 6,235 were attributed to heroin. Thus, opioids accounted for 28,470 or 64.7% of all drug related deaths in 2013 [36].

Notably, the increased rate of opioid medications prescribed has been followed by alarming increases in the negative consequences related to their pharmacological and addictive properties. These negative consequences include but are not limited to: mortality, overdose morbidity, serious adverse events, dependence/addiction, lifelong disability, and loss of family and community. For example, in 2013, 207 million prescriptions were written for prescription opioid pain medications. Prescription opioid use is also taxing on the economy. It has been estimated that medical and nonmedical use of opioid pain medications unnecessarily costs insurance companies as much as $72.5 billion a year for adverse consequences related to opioid medications [6,37,38].

On the 2012 list of top ten medications prescribed, 3 of them were Hydrocodone opioids (HYCD/APAP). There were a total of 129,068,000 prescriptions of Hydrocodone made by three different manufacturers: Actavis, Mallinckrodt and Qualitest Products.

Oxycodone, the second most frequently prescribed opioid behind Hydrocodone rose from 18.8% in 2007 to 24.4% in 2011 of all prescription pills dispensed [39].

Opioid addiction should be viewed as a chronic medical disorder, such as hypertension, schizophrenia, and diabetes. As with the other diseases, a cure is unlikely but long term treatment can decrease the disease's adverse effects and improve day to day functioning [40].

Costs

Between 1999 and 2010, opioid sales in the United States quadrupled. Enough opioid pain relievers were prescribed in 2010 to medicate every American adult with a dose of 5 mg of hydrocodone every 4 h for 1 month [41]. The cost associated with all types of pain, both direct and indirect, is estimated to be $560 to $635 billion annually in the United States. The use of pain relievers for medical and nonmedical purposes (without and prescription) is now the second most common form of drug addiction, exceeded by only marijuana use [42]. Of the emergency department visits for use of drugs, the majority involved opioid pain relievers 47.8%. White individuals accounted for 71.6% of the ED visits, blacks accounted for 10.9% and Hispanics accounting for 9.2%. The fourfold increase in the sale of these drugs between 1999 to 2008 paralleled the overdose rate which also increased fourfold in the period of 1999-2008 [38,43].

Hansen and his colleagues studied the economic cost of nonmedical use of prescription opioids and found that it totals more than $50 billion annually [38]. Ninety four percent of these costs were associated with crime and lost productivity. OxyCotin, oxycodone, hydrocodone, propoxyphene and methadone accounted for two thirds of this economic burden. Much of the so called non-medical use of prescription opioid likely was associated with medical use or originated from medical use [44,45].

Aside from the cost of the drug itself, opioid dependence is very expensive. High prevalence of costly medical and psychiatric comorbidities and high utilization rates of medical and psychiatric services and other prescription drugs causes the mean annual direct health care costs for opioid users to be more than 8 times higher than nonusers, $15,884 and $1,830 respectively. This leaves the excess annual cost burden of opioid use to be $14,504 per patient. This includes hospital inpatient, physician-outpatient, and drug costs. Mean drug costs for opioid users was more than 5 times higher than costs for nonusers driven by higher drug utilization, included but not limited to opioids, by opioid users [38,45].

Opioids and Disability

In a study of disabled Medicare beneficiaries under the age of 65, there was a significant overall rise in prescription opioid consumption by individuals [46]. This increase was not driven by overall use in more individuals using opioids but rather the proportion of individuals using opioids chronically, at the least 6 and generally 13 prescriptions per year. The authors state that the effectiveness of such a sustained and high dose is supported by scant evidence in this study. Overall, from 2007-2011, opioid use rates were relatively steady in the population but still alarmingly high. Among beneficiaries opioid use was prevalent among 43.9% in 2007, 44.7% in 2010 and 43.7% in 2011.

Also noteworthy is that among the chronic users studied, 38% were depressed. This common and chronic use of opioids observed is inconsistent with the growing evidence of hazards associated with such use and prescribing practices [14].

The United States has increased opioid consumption by more than 600% in the last 20 years. Yet we have not decreased our suffering from pain. A study in JAMA indicates that Americans suffered as much disability from back and neck pain in 2010 as they did in 1990 before the escalation in opioid prescribing. Some anecdotal evidence suggests chronic opioid therapy may be beneficial in a few select people. However a multitude of epidemiological studies suggest that it is doing more harm than good [1,47].

In 2010, Kidner et al. studied a Minnesota population of chronic pain patients [12]. The study population was divided into low, medium, high and very high opioid users classified by mg of opioids administered per day. He found that 69% percent of opioid users in all opioid subgroups showed a disability profile. Notably, the proportion of those on disability increased with subgroup dose; those in the very high group had higher disability rates than those in the lower sub groups. Patients who took opioids were more than 1 and a half times as likely to produce the disability profile.

Patients in the very high subgroup were nearly 3 times as likely to produce this profile. Webster et al. performed a retrospective cohort study of workers' compensation claims due to disabling lower back pain. This study assessed disability claimants and found that those who received more than 450 mg (morphine-equivalent amount) were on average disabled 69 days longer than those who did not receive early opioids (within first 15 days of treatment). They also had a three times greater risk of surgery [48].

Franklin and his colleagues examined whether prescription of opioids within 6 weeks of low back injury was associated with work disability at 1 year [49]. They found that more than one third of the workers received an opioid prescription within the first six weeks, with about 50% received at the first medical visit. They concluded that prescription of opioids for more than 7 days for workers with lower back injury was a significant risk factor for long term-disability.

Prescription Opioid Medications leads to Heroin Use

In addition to the negative effects prescription opioids have on emotional, physical, mental and behavioral wellbeing, they often lead to dangerous addictions to street drugs. Heroin, falls into the opioid family and nearly half of people who inject heroin report prior addiction to prescription opioids. Hydrocodone, oxycodone and heroin all bind to the same mu receptors and initiate and induce the development of tolerance, dependence and addiction. To someone who is addicted to opioids, prescription opioids are essentially an oral form of heroin. A study in the Archives of General Psychiatry followed 581 heroin addicts for 33 years from 1964-1977. Their results showed that heroin addicts only had a 50% survival rate [50-52].

Psychiatric effects

A study by Sullivan and his colleagues in 2005 found that depressive, anxiety and drug dependence disorders are associated with increased use of opioids in the general population. They also found that depressive and anxiety disorders are more common and more strongly associated with prescribed opioid use than any other drug dependence disorders.

In 2013, 16,235 deaths were directly attributed to prescription analgesics. Heroin overdose caused an additional 6,235. A person experiencing opioid overdose has decreased levels of consciousness, pinpoint pupils, slowed heart rate and respirations-sometimes to a stop, blue lips and nails due to lack of oxygen in the blood. Symptoms such as seizures and muscle spasms may also occur [53].

In 2011, Schepis and Hakes found evidence between nonmedical prescription opioid use and incident bipolar disorder among respondents with past psychopathology. Among those with no history of past psychopathology, they also found association between lifetime nonmedical prescription opioid use and incident depressive, bipolar and anxiety disorder [54].

Reid et al. studied the use of opioids in two primary care populations: a Virginia primary care clinic (VA) and an urban hospital based primary care center in the north-eastern US (PCC). In their study populations of chronic non-cancer pain patients they found rates of individual comorbidities were a staggering 44% and 54% for depressive disorder and 20% and 21% for anxiety disorder among VA and PCC patients respectively. This prevalence of psychiatric comorbidities in these study populations is substantial [21].

DSV-V classifies major depressive disorder as a prominent and persistent depressed mood causing clinically significant distress or impairment in social, occupational or other important areas of functioning that is not attributable to the psychological effects of a substance or another medical condition. The inherent nature of opioids is that they cause anxiety. Thus, it is impossible to independently

diagnose major depressive disorder in a patient that is using or in withdrawal of opioid medications. In cases such as these substance/medication-induced depressive disorder is a more appropriate diagnosis in which the symptoms of a prominent and persistent disturbance in mood characterized by depressed mood or markedly diminished interest or pleasure in activities developed during or soon after opioid intoxication or withdrawal or after exposure to the medication [55,56].

Similarly, the DSM-V defines generalized anxiety disorder as a condition where panic attacks of anxiety are predominant in the clinical picture and these disturbances cannot be attributable to the physiological effects of a substance or another medical condition [57]. Opioids cause and exacerbate anxiety symptoms; thus, it is impossible to independently diagnose an individual on opioids with generalized anxiety disorder.

Substance/medication-induced anxiety disorder would be the appropriate diagnosis in which panic attacks or anxiety is predominant in the clinical picture but these symptoms developed during or soon after substance intoxication or withdrawal or exposure to medication and where the involved substance is capable of producing the relevant symptoms. [55,58,59].

Suicide is a common cause of death among prescription opioid and heroin users alike. Risk factors for suicide include current ideation, intent, plan, access to means, previous attempts, alcohol and substance use/dependence, current or previous history of psychiatry diagnosis, impulsivity and poor self-control, hopelessness (presence, duration, severity) and recent losses, whether it be physical, personal or financial. All these factors are highly associated with opioid use disorder, which in turn contributes to suicidal behaviors [60].

Opioid Induced Hyperalgesia

Currently, we define opioid-induced hyperalgesia as a state of nociceptive sensitization caused by exposure to opioids. The condition is characterized by a paradoxical response whereby patient receiving opioids for the treatment of pain actually becomes more sensitive to painful stimuli and has pain induced or caused by the opioids [61-63]. The type of pain experienced might be the same as the underlying pain or might be different from the original underlying pain. Commonly the area of pain is more diffuse and is of higher quantity but lesser quality and harder to locate. Opioid induced hyperalgesia is a distinct, definable, and characteristic phenomenon that contributes to and explains the loss of opioid efficacy in patients along with opioid addiction [36,64-67].

Neurobiology of Opioid Medicaitons

Neural systems involved in physical dependence and analgesia are distinct from those that induce addictive behavior [68]. Dopaminergic pathways involving the nucleus accumbens (NAcc) are involved in drug induced reward and evidence shows interactions between opioids and dopamine function to increase opioid-induced reward. Although the mechanisms by which opioids produce initial transient euphoria, tranquility and other mood alterations are not clear, dopaminergic pathways, involving the nucleus accumbens are likely key players in the drug-induced reinforcement. There is ample evidence for interactions between opioids and dopamine in mediating opioid-induced reward and compulsive use as in addictive use [32,69].

Opioids function by binding to mu receptors, which are widely distributed in the central and peripheral nervous systems as well as being embedded in the gastrointestinal tract. Activation of the mu receptor causes the behavior experienced by users that ultimately drives addictive use. Opioids bind to the mu receptor inducing a signaling cascade in which the associated G protein activates, reducing cAMP. Less cAMP causes blockage of sodium and calcium channels, preventing an electrochemical gradient from increasing thereby decreasing excitability along the cell membrane in pain pathways. Opioids do nothing to eliminate or inhibit pain transmission pain but rather temporarily decrease the individual's perception of it and induce apathy to pain stimuli [32,69].

Dea Scheduling

Opioids are classified as a Schedule II drug on the U.S. Schedules of Controlled substances. Drugs under this classification are recognized to have a high potential for addiction. According to scheduling, Schedule II drugs do have a currently accepted medical use in the United States but continued use of the substance leads to severe psychological and physical dependence. Other drugs in this schedule include cocaine, methylphenidate, amphetamine, amphetamine mixed salts, methamphetamine, dextromethamphetamine, opium, fentanyl, methadone, oxycodone, oxymorphone, morphine, hydromorphone, codeine, hydrocodone, secobarbital, pethidine, diphenoxylate, phencyclidine, short acting barbituates, Nabilone and Tapendtadol. Prescription opioid dependence is especially debilitating to daily life. Opioid users often cease working and collect disability from the government and private sources to live on. In severe cases, opioid users have to depend on others to perform daily tasks for them and take care of their hygiene [70].

Physician Monitor

In 2009, the FDA sent letters to manufacturers of various long-acting and extended-release opioids asking them to develop risk evaluation strategies to address the opioid epidemic as an attempt to control opioid prescribing to undermine adverse consequences and addiction. Following up, they issued a directive in 2011 requiring stakeholders to develop comprehensive strategies within 120 days to address those concerns. A bill was introduced into congress to change the voluntary aspect of continuing medical education to a mandatory 16 hours of training every 3 years to obtain DEA certification to prescribe these drugs. This training would require education in the treatment and management of opioid-dependent patients, pain management guidelines, and early detection of opioid addiction. DEA certification is required for a physician to prescribe a wide spectrum of drugs, including opioids [71].

Most primary care physicians do not feel competent to treat alcohol-and drug-related disorders. Physicians generally do not like to work with patients with these disorders and do not find treating them rewarding. Despite large numbers of such patients, the diagnosis and treatment of alcohol- and drug-related disorders are generally considered peripheral to or outside medical matters and ultimately outside medical education. There is substantial evidence that physicians fail even to identify a large percentage of patients with these disorders [72,73].

Essential role models are lacking for future physicians to develop the attitudes and training they need to adequately approach addiction as a treatable medical illness. Faculty development programs in addictive

disorders are needed to overcome the stigma, poor attitudes, and deficient skills among physicians who provide education and leadership for medical students and residents. The lack of parity with other medical disorders gives reimbursement and education for addiction disorders low priority.

Medical students and physicians can also be consumers and patients with addiction problems. Their attitudes and abilities to learn about alcohol- and drug-related disorders are impaired without interventions. Curricula lack sufficient instruction and experiences in addiction medicine throughout all years of medical education. Programs that have successfully changed students' attitudes and skills for treatment of addicted patients continue to be exceptional and limited in focus rather than the general practice in U.S. medical schools. [74,75].

Physcian Education

The American Academy of Family Physician has developed a guideline to teach residents how to care for patients with chronic pain [45]. Skills they are instructed in include understanding the pathophysiology of chronic pain, evaluating a patient's opioid abuse risk utilizing risk assessment tools, establishing opioid contracts with patients, interpreting urine toxicology screens, performing chart reviews and adjusting treatment plans based on those reviews, treating and monitoring patients at high risk of abuse, prescribing narcotic alternatives and performing selected joint injections. As laudable as these goals are, it is extremely problematic that addiction potential is not on this list.

There is a serious lack of physician education regarding the inherent addicting nature of opioids. Uneducated physicians push opioids onto patients as a band-aid for pain and then it is wrongfully assumed that patients bear full responsibility for the opioid epidemic.

The AAFP opposes mandated continuing medical education as a prerequisite to DEA or other licensure due to the limitations on patient access to legitimate pain management and other clinical needs that many occur. So essentially, the AAFP does not want physicians to be educated about opioids because it will surely limit opioid prescribing. Frankly, that is exactly what needs to happen. If family physicians learned about the lack of efficacy and dangerous, addictive nature of opioid treatment there would be a positive, limiting dampening effect on prescribing in harmful ways. With less long-term prescribing of opioids, pain relief and function would improve and adverse consequences would decrease and the identification of addictive use in patients would be easier for health care providers [45].

Additionally, poor public health concerns and information about addiction furthers the problem. Patients rely on their physicians to educate them regarding their health conditions and relevant treatment benefits and risks. When physicians are uneducated in prescribing addicting drugs and not informing about risks and benefits of medications, patients suffer physically and psychologically and wrongly bear full responsibility for their addictions.

It is a myth that most people treated with opioids never become addicted, and addiction does not develop if you are prescribing opioids for pain. Pain is important, it not only serves as a warning sign to protect one's self but additionally it motivates the patient to identify the cause of the pain and take action. Physicians must realize that opioids merely mask this pain but do nothing whatsoever to fix it. Patients on opioid medications have poor motivation to correct or treat the underlying pain source. On the contrary, they develop more pain from hyperalgesia, tolerance and dependence of opioids.

Recommendations for prescribing opioid medications

1. Long term prescribing of opioid medications should be discouraged to avoid adverse consequences including increased morbidity and mortality.

2. Short term prescribing should be implemented with skill and knowledge of opioid risks and benefits.

3. Physicians' strict compliance with controlled substance laws and regulations: to prescribe, dispense, or administer controlled substances, the physician must be registered with the DEA, licensed by the state of practice and comply with applicable federal and state regulations will function to avoid initiating and maintaining addicting and dangerous use and assist in attenuating the opioid epidemic.

4. Physicians must fully assess patients and routinely use prescription drug monitoring programs (PDMPs) to effectively identify individual patients who are suffering from addictive use of opioids.

Physicians must receive education regarding controlled substances.

Reccomendations for policy regarding opioids in the treatment of pain

Dr. Thomas Friedan, the director of the Centers for Disease Control and Prevention noted that the deaths from prescription painkiller overdose have tripled in the last decade. He reports that prescription painkillers are meant to help people with severe pain however they are highly addictive. He suggests that doctors should limit prescriptions giving only a 3 day supply for acute pain, then seeking alternative treatments and that for chronic pain, narcotics should be the last resort [76,77].

It must be understood that chronic pain is often intractable and that the current state of medical therapies, including opioid analgesics, do not provide for complete elimination of chronic pain. The existence of persistent and disabling pain does not in and of itself constitute evidence for treatment to inherently addicting and dangerous opioid medications. Indeed, some cases of intractable pain actually result from over treatment in terms of procedures and medications, particularly opioids. It is imperative that treatment plans utilizing alternative, non-opioid medications be developed and implemented in the treatment of chronic pain [76,77].

Overwhelming evidence shows that long-term prescription of opioids for chronic non-cancer pain is not efficacious for pain relief and it actually causes increased reported pain symptoms. Additionally, opioids are inherently pharmacologically addictive and disabling. Reforms in health care professional education, clinical prescribing standards and pharmaceutical company policies must be made immediately to truncate the harmful effects of the opioid epidemic. The negative effects are extremely widespread and supported by strong evidence. Opioids are highly addictive medications yet physicians continue to prescribe them and dependent patients take them despite the harmful effects and lack of efficacy [78-80].

Substantial alterations in the field of healthcare must occur to reverse this trend. Health policy for prescribing opioid medications for clinical conditions of pain must be revised to include an analysis of risks and benefits of prescribing addicting medications.

Medical schools, medical education programs, and state continuing medical education programs should be required to meet standards of education on addiction medicine for adequate knowledge and skill in prescribing these inherently dangerous medications. Additionally, policy and legislation against drug manufacturers should be vigorously pursued in cases where they fail to warn or deceive the public on the dangers of controlled substances.

References

1. Kissin I (2013) Long-term opioid treatment of chronic non-malignant pain: Unproven efficacy and neglected safety? J Pain Res 6: 513-529.
2. Ballantyne JC, Mao J (2003) Opioid therapy for chronic pain. N Engl J Med 349: 1943-1953.
3. Boudreau D, Von Korff M, Rutter CM, Saunders K, Ray GT, et al. (2009) Trends in long-term opioid therapy for chronic non-cancer pain. Pharmacoepidemiol Drug Saf 18: 1166-1175.
4. Strassels SA (2009) Economic burden of prescription opioid misuse and abuse. J Manag Care Pharm 15: 556-562.
5. Paulozzi L, Baldwin G (2012) CDC grand round: Prescription drug overdoses-A US epidemic. MMWR Morb Mortal Wkly Rep 61: 10-13.
6. Markenson JA, Croft J, Zhang PG, Richards P (2005) Treatment of persistent pain associated with osteoarthritis with controlled-release oxycodone tablets in a randomized controlled clinical trial. Clin J Pain. 21: 524-535.
7. Noble M, Tregear SJ, Treadwell JR, Schoelles K (2008) Long-term opioid therapy for chronic non-cancer pain: A systematic review and meta-analysis of efficacy and safety. J Pain Symptom Manage 35: 214-228.
8. Ballantyne JC, Shin NS (2008) Efficacy of opioids for chronic pain: A review of the evidence. Clin J Pain 24: 469-478.
9. Paulozzi LJ, Budnitz DS, Xi Y (2006) Increasing deaths from opioid analgesics in the United States. Pharmacoepidemiol Drug Saf 15: 618-627.
10. Eriksen J, Sjøgren P, Bruera E, Ekholm O, Rasmussen NK (2006) Critical issues on opioids in chronic non-cancer pain: An epidemiological study. Pain 125: 172-179.
11. Teater D (2014) Evidence for the efficacy of pain medications. National safety council.
12. Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, et al. (2007) Systematic review: Opioid treatment for chronic back pain: Prevalence, efficacy and association with addiction. Ann Intern Med 146: 116-127.
13. Moore PA, Hersh EV (2013) Combining ibuprofen and acetaminophen for acute pain management after third-molar extractions: Translating clinical research to dental practice. J Am Dent Assoc 144: 898-908.
14. Maldow D, Miller NS, Matthews A (2016) Do current policies and practices for prescribing opioid medications solve chronic pain problems. Psychiatr Ann 10: 500-505.
15. Radcliff K, Freedman M, Hilibrand A, Isaac R, Lurie JD, et al. (2013) Does opioid pain medication use affect the outcome of patients with lumbar disc herniation? Spine (Phila Pa 1976) 38: E849-860.
16. Paulozzi LJ, Mack KA, Hockenberry JM, Division of unintentional injury prevention and control, CDC (2014) Vital signs: Variation among states in prescribing of opioid pain relievers and benzodiazepines-United States, 2012. MMWR Morb Mortal Wkly Rep 63:563-568.
17. Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, et al. (2008) Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA 300: 2613-2620.
18. Okie S1 (2010) A flood of opioids, a rising tide of deaths. N Engl J Med 363: 1981-1985.
19. Clausen T, Waal H, Thoresen M, Gossep M (2009) Mortality among opiate users: Opioid maintenance therapy, age and causes of death. Addiction 104: 1356-1362.
20. Degenhardt L, Bucello C (2011) Mortality among regular or dependent users of heroin and other opioids: A systematic review and meta-analysis of cohort studies. Addiction 106: 32-52.
21. Warner M, Chen LH, Makuc DM (2009) Increase in fatal poisonings involving opioid analgesics in the United States, 1999-2006. NCHS Data Brief, pp: 1-8.
22. Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN (2011) Opioid dose and drug-related mortality in patients with nonmalignant pain. Arch Intern Med 171: 686-691.
23. Dhalla IA, Mamdani MM, Sivilotti ML, Kopp A, Qureshi O, et al. (2009) Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. CMAJ 181: 891-896.
24. Katz MH (2010) Long-term opioid treatment of non-malignant pain: A believer loses his faith. Arch Intern Med 170: 1422-1424.
25. Chou R, Fanciullo GJ, Fine PG, Miaskowski C (2009) American pain society-American academy of pain medicine opioids guidelines panel. Clinical guidelines for the use of chronic opioid therapy in chronic non-cancer pain. J Pain 10: 113-130.
26. Parsells Kelly J, Cook SF, Kaufman DW, Anderson T, Rosenberg L, et al. (2008) Prevalence and characteristics of opioid use in the US adult population. Pain 138: 507-513.
27. Kahan M, Srivastava A, Wilson L, Gourlay D, Midmer D (2006) Misuse of and dependence on opioids: Study of chronic pain patients. Can Fam Physician 52: 1081-1087.
28. Saffer K, Colombo C, Brown D, Mundt MP, Fleming MF (2007) Addiction severity index in a chronic pain sample receiving opioid therapy. J Subst Abuse Treat 33: 303-311.
29. Naliboff BD, Wu SM, Schieffer B, Bolus R, Pham Q, et al. (2011) A randomized trial of 2 prescription strategies for opioid treatment of chronic non-malignant pain. J Pain 12: 288-296.
30. Ballantyne JC, LaForge KS (2007) Opioid dependence and addiction during opioid treatment of chronic pain. Pain 129: 235-255.
31. Miller NS, Lion D (2003) Biology of opiates: Affects prevalence of addiction, options for treatment 33: 558-564.
32. Koob GF, Volkow ND (2010) Neurocircuitry of addiction. Neuropsychopharmacology 35: 217-238.
33. Alexander GC, Kruszewski SP, Webster DW (2012) Rethinking opioid prescribing to protect patient safety and public health. JAMA 308: 1865-1866.
34. Zgierska A, Miller M, Rabago D (2012) Patient satisfaction, prescription drug abuse and potential unintended consequences. JAMA 307: 1377-1378.
35. Fleming MF, Balousek SL, Klessig CL, Mundt MP, Brown DD (2007) Substance use disorders in a primary care sample receiving daily opioid therapy. J Pain 8: 573-582.
36. Wheeler E, Jones TS, Gilbert MK, Davidson PJ, Centers for disease control and prevention (CDC) (2015) Opioid overdose prevention programs providing naloxone to laypersons - United States, 2014. MMWR Morb Mortal Wkly Rep 64: 631-635.
37. Mercadante S, Ferrera P, Villari P, Arcuri E (2003) Hyperalgesia: An emerging iatrogenic syndrome. J Pain Symptom Manage 26: 769-775.
38. Hansen RN, Oster G, Edelsberg J, Woody GE, Sullivan SD (2011) Economic costs of nonmedical use of prescription opioids. Clin J Pain 27: 194-202.
39. Bartholow M (2012) Top 200 Drugs to memorize, current for 2017. Pharmacy Tech Test 1: 1-7.
40. Kosten TR, George TP (2002) The neurobiology of opioid dependence: Implications for treatment. Sci Pract Perspect 1: 13-20.
41. Paulozzi LJ, Mack KA, Hockenberry JM, Division of unintentional injury prevention, national center for injury prevention and control, CDC (2014) Vital signs: Variation among states in prescribing of opioid pain relievers and benzodiazepines - United States, 2012. MMWR Morb Mortal Wkly Rep 63: 563-568.
42. Gaskin DJ, Richard P (2012) The economic costs of pain in the United States. J Pain 13: 715-724.

43. American academy of family physicians (2012) Pain management and opioid abuse: A public health concern (Position Paper). American Academy of Family Physicians.
44. White AG, Birnbaum HG, Mareva MN, Daher M, Vallow S, et al. (2005) Direct costs of opioid abuse in an insured population in the United States. J Manag Care Pharm 11: 469-479.
45. American Academy of Family Physicians (2012) Pain management and opioid abuse: A public health concern (Position Paper). American Academy of Family Physicians.
46. Morden NE, Munson JC, Colla CH (2014) Prescription opioid use among disabled Medicare beneficiaries: Intensity, trends and regional variation. Med Care 52: 852-859.
47. Kidner CL, Gatchel RJ, Mayer TG. (2010) MMPI disability profile is associated with degree of opioid use in chronic work-related musculoskeletal disorders. Clin J Pain 26: 9-15.
48. Webster BS, Verma SK, Gatchel RJ (2007) Relationship between early opioid prescribing for acute occupational low back pain and disability duration, medical costs, subsequent surgery and late opioid use. Spine 32: 2127-2132.
49. Franklin GM, Stover BD, Turner JA, Fulton-Kehoe D, Wickizer TM (2008) Early opioid prescription and subsequent disability among workers with back injuries: The disability risk identification study cohort. Spine 33: 199-204.
50. Liebschutz JM, Alford DP (2011) Safe opioid prescribing: A long way to go. J Gen Intern Med 26: 951-952.
51. Denisco RA, Chandler RK, Compton WM (2008) Addressing the intersecting problems of opioid misuse and chronic pain treatment. Exp Clin Psychopharmacol 16: 417-428.
52. Jamison RN, Ross EL, Michna E, Chen LQ, Holcomb C, et al. (2010) Substance misuse treatment for high-risk chronic pain patients on opioid therapy: A randomized trial. Pain 150: 390-400.
53. Martins SS, Fenton MC, Keyes KM, Blanco C (2012) Mood/Anxiety disorders and their association with non-medical prescription opioid use and prescription opioid use disorder: Longitudinal evidence from the national epidemiologic study on alcohol and related conditions. Psychol Med 42: 1261-1272.
54. Reid MC, Bennett DA, Chen WG, Eldadah BA, Farrar JT, et al. (2011) Improving the pharmacologic management of pain in older adults: Identifying the research gaps and methods to address them. Pain Med 12: 1336-1357.
55. American psychiatric association (2013) Diagnostic and statistical manual of mental disorders. 5th ed. Arlington, VA: American psychiatric association.
56. Childress AR, Ehrman RA (1994) Can induced moods trigger drug-related responses in opiate abuse patients? J Subst Abuse Treat 11:17-23.
57. NBC New York. Fatal overdoses from pain-killers triple in decade.
58. Sullivan MD, Edlund MJ, Steffick D, Unützer J (2005) Regular use of prescribed opioids: association with common psychiatric disorders. Pain 119: 95-103.
59. Ahmadi J, Majdi B, Mahdavi S, Mohagheghzadeh M (2004) Mood disorders in opioid-dependent patients. J Affect Disord 82: 139-142.
60. Miller NS (2006) prescription opiate medications: Clinical assessment and treatment of addiction, tolerance and dependence. Psychiatric Annals 36: 390-396.
61. Chu LF, Clark JD, Angst MS. (2006) Opioid tolerance and hyperalegsia in chronic pain patients after one month of oral morphine therapy: A preliminary prospective study. J Pain 24: 469-478.
62. Chu LF, Clark JD, Angst MS (2008) Opioid-induced hyperalgesia in humans: Molecular mechanisms and clinical considerations. Clin J Pain 24: 479-496.
63. Chen L, Malarick C, Seefeld L, Wang S, Houghton M, et al. (2009) Altered quantitative sensory testing outcome in subjects with opioid therapy. Pain 143: 65-70.
64. Mitra S (2008) Opioid-induced hyperalgesia: Pathophysiology and clinical implications. J Opioid Manag 4: 123-30.
65. Mao J (2006) Opioid-induced abnormal pain sensitivity. Curr Pain Headache Rep 10: 67-70.
66. Fishbain DA, Cole B, Lewis JE, Gao J, Rosomoff RS (2009) Do opioids induce hyperalgesia in humans? An evidence-based structured review. Pain Med 10: 829-839.
67. Angst MS, Clark JD (2006) Opioid-induced hyperalgesia: A qualitative systematic review. Anesthesiology 104: 570-587.
68. Koob GF, Bloom FE (1988) Cellular and molecular mechanisms of drug dependence. Science 242: 715-723.
69. Volkow ND, Koob GF, McLellan AT (2016) Neurobiologic advances from the brain disease model of addiction. N Engl J Med 374: 363-371.
70. Miller NS (2006) Failure of enforcement controlled substance laws in health policy for prescribing opiate medications: A painful assessment of morbidity and mortality. Am J Ther 13:527-533.
71. Reisfield GM, Sloan PA (2012) Physician identification of opioid diversion: A difficult diagnosis. J Opioid Manag 8: 5-6.
72. Passik SD (2009) Issues in long-term opioid therapy: unmet needs, risks, and solutions. Mayo Clin Proc 84: 593-601.
73. Grady D, Berkowitz SA, Katz MH (2011) Opioids for chronic pain. Arch Intern Med 171: 1426-1427.
74. Miller NS, Sheppard LM, Colenda CC, Magen J (2001) Why physicians are unprepared to treat patients who have alcohol- and drug-related disorders. Acad Med 76: 410-418.
75. Miller NS, Sheppard LM, Magen J (2001) Barriers to improving medical education and training in addiction medicine. Psychiatr Ann 31: 649-656.
76. The white house (2016) Continued rise in opioid overdose deaths in 2015 shows urgent need for treatment.
77. Centers for disease control and prevention (2016) CDC releases guideline for prescribing opioids for chronic pain.
78. Brushwood DB, Rich BA, Coleman JJ, Bolen J, Wong W (2010) Legal liability perspectives on abuse-deterrent opioids in the treatment of chronic pain. J Pain Palliat Care Pharmacother 24: 333-348.
79. Streltzer J, Johansen L (2006) Prescription drug dependence and evolving beliefs about chronic pain management. Am J Psychiatry 163: 594-598.
80. Starrels JL, Becker WC, Alford DP, Kapoor A, Williams AR, et al. (2010) Systematic review: Treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. Ann Intern Med 152: 712-720.