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An Original Contribution

Prevalence of Illicit Drug use in Patients without Controlled Substance Abuse in Interventional Pain Management

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Drug abuse with illicit drugs and licit drugs has been increasing steadily over the past decade. A recent National Household Survey on Drug Abuse found statistically significant increases between 2000 and 2001 in the use of multiple drugs, including marijuana, cocaine, and non-medical use of pain relievers and tranquilizers. Prescription controlled substance abuse is a major issue in chronic pain management. Various means suggested to avoid or monitor abuse in patients in treatment include urine/serum drug screening whenever requested, along with other precautions including one prescribing physician and one designated pharmacy, etc.

Based on the present evidence, physicians assume that patients adhering to controlled substance agreements and without obvious dependency behavior do not abuse either illicit or licit drugs. Thus, it is accepted that there is no necessity to perform routine urine/drug testing in this specific group of the patient population.

One hundred patients undergoing interventional pain management and receiving controlled substances were randomly selected for evaluation of illicit drug abuse by urine drug testing. They were selected from a total of 250 patients who were identified as non-abusers of prescription drugs.

Results showed that illicit drug abuse in patients without history of controlled substance abuse was seen in 16 patients. Thirteen of the 16 patients tested positive for marijuana and 3 patients tested positive for cocaine. Only one patient tested positive for a combined use of both marijuana and cocaine.

This study showed that, in an interventional pain management setting, there is significant use of illicit drugs (16%) with 13% use of marijuana and 3% use of cocaine in patients who are considered as non-abusers of prescription controlled substances and those who are adherent to controlled substance agreements. However, if cocaine is considered as a hardcore drug in contrast to marijuana, abuse of hardcore illicit drugs is only 3%.

Keywords: Drug abuse, illicit drugs, licit drugs, prescription controlled substances, controlled substance agreement, opioid abuse, marijuana, cocaine, methamphetamine

Over the past decade, there has been a steady increase in the use of particular drugs or groups of illicit drugs, such as marijuana and cocaine, and the non-medical use of prescription drugs (1-14). Based on the 1997 National Household Survey on Drug Abuse (NHSDA), it is estimated that 76.9 million Americans, age 12 and older, had used an illicit drug at least once in their lives (6, 7). This represents 36.6% of the nation's household population age 12 and older. This survey also indicated that the non-medical use of prescription drugs exceeds that of all illicit substances except for marijuana and hashish (1, 6-14). Further, the National Institute of Health-National Institute on Drug Abuse (NIH-NIDA) reported that in 1999, about 14.8 million Americans were current users of illicit drugs (6-11). The 2001 National Household Survey on Drug Abuse (1), found statistically significant increases between 2000 and 2001 in the use of multiple drugs including marijuana (4.8% to 5.4%), cocaine (0.5% to 0.7%), and non-medical use of pain relievers (1.2% to 1.6%) and tranquilizers (0.4% to 0.6%). In 2001, an estimated 15.9 million Americans age 12 years or older (7.1% of the population) used an illicit drug during the month immediately prior to the survey interview. By comparison, in 2000, the survey found that 6.3% of this population were current users of illicit drugs (1).

The National Household Survey on Drug Abuse of 2001 reported the number of persons reporting use of OxyContin® for non-medical purposes at least once in their lifetime increased four-fold from 1999 to 2001. The estimates were 221,000 in 1999; 399,000 in 2000; and 957,000 in 2001. An estimated 2.4 million Americans used marijuana for the first time in 2000 (1). Between 1990 and 1996, the estimated number of new users increased from 1.4 million to 2.5 million. The number of persons with substance dependence or abuse increased from 14.5 million (6.5% of the population) in 2000 to 16.6 million (7.3%) in 2001 (1). Between 2000 and 2001, there was a significant increase in the estimated number of persons needing treatment for an illicit drug problem from 4.7 million in 2000 to 6.1 million in 2001. It was also shown that adults who used illicit drugs were twice as likely to have serious mental illness (SMI) as adults who did not use an illicit drug. Marijuana is the most commonly used illicit drug. In 2001, it was used by 76% of current illicit drug users. Further, 44% of current illicit drug users in 2001 (7.0 million Americans) used illicit drugs other than marijuana and hashish, with or without using marijuana as well. Of the 7.0 million current users of illicit drugs other than marijuana, 4.8 million were current users of psychotherapeutic drugs. Of those who reported current use of any psychotherapeutics, 3.5 million used pain relievers, 1.5 million used tranquilizers, 1.0 million used stimulants, and 0.3 million used sedatives.

The true extent of prescription drug abuse is unknown. The estimates from a national survey indicate that the principle drug of abuse for nearly 10% of the US patients in treatment is a prescrip-

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tion drug (12). The NHSDA shows that the initiation of non-medical prescription type drug use has been increasing (1). The annual number of new users of pain relievers has been increasing since the mid-1980s, from about 400,000 initiates to 2 million in 2000. New users of stimulants increased from more than 200,000 in 1991 to almost 700,000 in 2000. New users of tranquilizers have been increasing since the mid-1980s, but the largest increase has been recently, from more than 700,000 new users in 1999 to almost 1 million users in 2000 with increases noted from 2000 to 2001. The number of new users of sedatives remained around 100,000 per year between 1988 and 1994. However, starting in 1995, the numbers rose from 111,000 to 175,000 in 2000 (15). In 2001, 36 million Americans (16% of persons age 12 or older) had used prescription-type drugs non-medically at least once in their lifetime. The most common category of prescription-type drugs used non-medically by youths and young adults in the past year was pain relievers. Pain relievers include codeine, methadone, meperidine hydrochloride, hydrocodone bitartrate, and oxycodone.

It was shown that those youths and young adults who used prescription-type drugs non-medically in the past year had a higher rate of other illicit drug use in the past year as well. Sixty-three percent of youths and young adults who had prescription-type drugs non-medically in the past year had also used marijuana in the past year compared with 17% of youths and young adults who had not used prescription-type drugs non-medically in the past year. Lynskey et al (2) demonstrated significant associations between early cannabis use and later drug use and abuse/dependence. According to the Drug Abuse Warning Network (DAWN) (9), the incidence of emergency department (ED) visits related to narcotic analgesic abuse has been increasing in the US and since the mid-1990s, and more than doubled between 1994 and 2001. In 2001, there were an estimated 90,232 ED visits related to narcotic analgesic abuse, a 117% increase since 1994.

Manchikanti et al (16) in a randomized clinical evaluation showed a prevalence of opioid abuse in interventional pain management practice settings as 24% with frequent abuse in 12% of the patients. Polatin et al (17) showed current substance abuse of 19% and lifetime prevalence of 36% in chronic low back pain. Chabal et al (18) showed that 34% of the chronic pain patients met one abuse criteria and 27.6% of the patients met three or more of the abuse criteria. Many of the patients who are abusing prescription drugs may also abuse illicit drugs. Multiple means suggested to avoid or monitor abuse in patients in the treatment include: 1) one prescribing doctor and one designated pharmacy, 2) urine/serum drug screening when requested, 3) no early refills and no medications called in, 4) if medications are lost or stolen, then a police report could be required before considering additional prescriptions, and 5) finally, discontinuation of drug therapy for violation of a documented doctor/patient agreement resulting from abuse of the drugs. Thus, the question arises; should urine/serum drug screening be performed on all the patients randomly or on only the patients with abuse patterns? It is not known at the present time the prevalence of illicit drug usage in patients receiving controlled substances in interventional pain management settings or for that matter, in any setting. Further, it is also not known if illicit drug abuse exists in patients adherent to their controlled substance agreements and who seem not to be abusing the drugs by means available other than urine/drug testing.

Based on the present evidence, adherence to the controlled substance agreement, a clean report on doctor shopping, or not obtaining prescriptions outside the agreement, patients are considered as not requiring urine/drug testing. This group of patients is presumed not to abuse either illicit or licit drugs. It is expected that abuse of illicit drugs in this group of population will be absent or extremely low. Thus, we have accepted that if a patient presents with appropriate history, no signs of abuse on history and physical examination, shows improvement in functional status, does not escalate the dosage, and no evidence of prescription abuse or doctor shopping is detected, it is not necessary to perform urine/drug testing. However, some authors claim that all patients should undergo random urine/drug testing irrespective of their prescription usage pattern (19-21).

This evaluation was undertaken to test the prevalence of illicit drug abuse in patients without abuse of controlled substances by means of urine testing. This randomized clinical trial evaluated the usage of illicit drugs in 100 patients without known controlled substance abuse.

Methods

One hundred patients undergoing interventional pain management but also receiving controlled substances, including opioids, were randomly selected for evaluation of illicit drug use by means of urine drug testing. A total of 250 patients identified without history of drug abuse as evaluated by history, physical examination, doctor shopping, prescription substance abuse, escalation of dosage, and appropriate response to controlled substance usage (stable without dependency) were included in the allocation. Patients were divided into 5 batches of 50, twenty patients were randomly selected by computer allocation in each group. Each patient was provided with a serial number. All patients had a prior controlled substance agreement, and were willing to participate in the study. The evaluation was randomized. Urine drug testing was performed in 100 patients. The person obtaining the consent, and the person performing the testing were different. The results were blinded to the evaluating author, statistician, the patient, and the other members of the study.

All the tests were performed at the practice location utilizing the Rapid Drug Screen™ (American Biomedia Corporation, Kinderhook, New York). Rapid Drug Screen is a one-step, lateral flow immunoassay for the simultaneous detection of up to 9 abused drugs by urine analysis. Each analysis occupies a separate channel in a test cord. This is intended for use in the qualitative detection of the various drugs. Rapid Drug Screen is a competitive immunoassay utilizing highly specific reactions between antibodies and antigens for the simultaneous detection of cocaine, opiates, amphetamines, cannabinoids, barbiturates, benzodiazepines, methamphetamine, phencyclidine, and tricyclic antidepressants in urine. The testing was performed to detect the four most commonly abused drugs, namely marijuana, cocaine, methamphetamine, and amphetamine.

Fresh urine specimens with sufficient volume in the cup were evaluated. Based on the temperature strip attached to the bottom of the specimen cup, for fresh urine specimens, a reading between 90° to 100° F (32-38°C) was considered a

viable sample. The protocol also included that there should be a sufficient amount of urine to test in the container within the specified blue area on the cup label. If the urine was below the blue area on the cup or above or below the blue area on the card, the results were considered as invalid and were not utilized in the study. False-positives for methamphetamine were excluded by positive history of drugs resulting in false-positive results.

Data were collected using a preprinted format without patient identification. Following the collection of the data, all the patients negative for illicit drug usage were included in Group I. Group II consisted of all the patients with abuse of one or more drugs.

Results

One hundred patients were included in the study, derived randomly from 250 patients undergoing interventional pain management. All the patients participated in the study. All specimens were collected and were able to be tested for the presence or absence of 4 drugs. All the results were valid and were double-blinded.

Table 1 shows the prevalence of illicit drug abuse in patients without history of controlled substance abuse. The results showed that 13 patients tested positive for marijuana or tetrahydrocannabinol (THC). Three patients tested positive for cocaine. Three patients tested false-positive for methamphetamine. None of the patients tested positive for amphetamine. Thus, a total of 16 patients tested positive for illicit drugs. There was only one patient who tested positive for both marijuana and cocaine.

Table 1. Illicit drug abuse in patients without history of prescription drug abuse

Drug	Prevalence (n=100)
Tetrahydrocannabinol (THC) marijuana	13
Cocaine	3
Methamphetamine	0
Amphetamine	0
Total Abuse	16
Combined THC and Cocaine	1

Discussion

This randomized, double-blind, clinical evaluation showed an unexpected prevalence of 16% use of illicit drugs in patients considered as non-abusers of prescription controlled substances. However, the major prevalence was for marijuana with 13%. Amphetamine, methamphetamine, cocaine, and combination of more than one drug was seen in only 0%-3% of the patients. This study established illicit drug usage among patients without abuse of prescription controlled substances to be frequent for marijuana in interventional pain management settings.

Among all the illicit drugs, marijuana is the most widely abused and readily available illicit drug in the United States, with an estimated 11.5 million current users (22). At least one-third of the US population has used marijuana some time in their lives. The drug is considered a "gateway" to the world of illicit drug abuse. Various reasons attributed to its widespread use are relaxed public perception of the harm, popularization by the media and by groups advocating legalization, and the trend of smoking of marijuana-filled cigars known as "blunts." The Drug Enforcement Administration (DEA) (22) believes that the internet also contributes to marijuana's popularity. Websites exist that provide informal and links extolling the virtues of marijuana. These sites provide forums for user group discussion, post documents and messages for public discussions and advocate the legal sale of marijuana. Several websites advertising the sale of marijuana and providing instructions on home growth have also been identified (22). Lynskey et al (2) showed that associations between early cannabis use and later drug use and abuse/dependence may arise from the effects of the peer and social context within which cannabis is used and obtained. Stein (23) found that Americans want marijuana to be illegal, but not really enforced. A TIME/CNN poll in 2002 found that 34% of Americans want it to be totally legalized, the proportion of Americans doubling since 1986 (23). Further, 80% think marijuana for medical purposes is acceptable, whereas 72% think people caught with it for recreational use should be fined, not jailed (23). Eight states allow medical marijuana, and a handful of states have reduced the sentences for pot smokers to almost nothing. It is also viewed by the laypublic to be associated with the belief that health risk from occasional use of marijuana is mild and it might ease certain ills (24). In particular, early access to and use of cannabis may reduce perceived barriers against the use of other illegal drugs and provide access to these drugs. Thus, patients may be using marijuana along with prescription controlled substances. Lynskey et al (2) showed that the association with early cannabis use was causal. However, the mechanisms by which this association arises remains unclear. Pharmacological mechanisms and hypotheses assume that exposure to cannabis induces subtle biochemical changes that encourage drug-taking behavior (25). This hypothesis is supported to some extent by findings of similarities between THC and heroin on the opioid receptor mechanism (26). Further, chronic treatment with THC also induces cross tolerance to amphetamine (26) and opioids in rats (26, 27). Other proposed mechanisms include initial experiences with marijuana, which are frequently rated as pleasurable (28), may encourage continued use of marijuana and also broader experimentation. Seemingly safe early experiences with marijuana may reduce the perceived risk of, and therefore barriers to, the use of other drugs and experience with and subsequent access to marijuana use may provide individuals with access to other drugs as they come into contact with drug dealers (29) or prescription controlled substances. NHSDA of 2001 (1) reported a significant decline in perception of risk of marijuana and increased perception of easy availability.

According to the 2000 Domestic Cannabis Eradication/Suppression Program (DCE/SP) statistics, the five leading states for indoor growing activity were California, Florida, Oregon, Washington and Wisconsin. However, DCE/SP statistics also indicate that the major outdoor growing states in 2000 were California, Hawaii, Kentucky, and Tennessee. All these states accounted for approximately three quarters of the total of eradicated outdoor cultivated plants. The DEA also reports that prices for commercial-grade marijuana have remained relatively stable over the past decade ranging from approximately $400 to $1,000 per pound in the US southwest border areas to between $700 to $2,000 per pound in the midwest and northeastern United States (22). In

contrast, prices of cocaine and heroin ranged from $12,000 to $35,000 per kilogram and $50,000 to $200,000 per kilogram in most metropolitan areas in the United States respectively.

Nationwide research in marijuana popularity is also seen in patients receiving prescription controlled substances in interventional pain management settings. This is based to a great extent on the reasons described by the DEA with its perception of low harm, popularization by media, advocacy for legalization, indoor and outdoor growing of marijuana with ease, and finally, the internet-based activities. Many Americans also perceive that marijuana is an innocent drug, which is commonly used and basically portrays a phenomenon that it is not an illicit drug. For example, as the vast majority of those who use marijuana do not experience any legal consequences of their use, such use may act to diminish the strength of legal sanctions against the use of all drugs (2). The fact that legalization is being considered seriously and there are various web sources describing its indoor and outdoor growing, also supports public perception. It has been described that experience with and subsequent access to marijuana use may provide individuals to access to other drugs as they come into contact with drug dealers (29, 30). This argument provided a strong impetus for the Netherlands to effectively decriminalize marijuana use in an attempt to separate it from the hard drug market. It has been claimed that this strategy may have been partially successful as rates of cocaine use among those who have used marijuana are lower in the Netherlands than in the United States (31).

Numerous consequences of marijuana use include frequent respiratory infections, impaired memory and learning, increased heart rate, anxiety, panic attacks, tolerance and physical dependence (32, 33); impairment of infant motor development with use of marijuana during the first month of breast-feeding (34); symptoms of chronic tobacco smoking, including daily cough and phlegm, chronic bronchitis symptoms, frequent chest cold and abnormal functioning of lung tissues in chronic marijuana smokers (35); and impaired skills related to attention, memory and learning in people who use marijuana heavily, even after discontinuation of its use for at least 24 hours (35). Marijuana is usually smoked as a cigarette (called a joint) or in a pipe or bong. Further, it has been shown that early initiation of marijuana use is a significant risk factor for other drug use and drug-related problems. In 1999, there were 222,000 marijuana-related admissions to publicly funded substance abuse treatment programs in the United States, representing 14% of all such treatment admissions (5). Thus, the increases in treatment seeking have been paralleled by heightened concerns about the long-term consequences of chronic marijuana use (36, 37) and recognition of the need for treatment and other interventions to ameliorate the effects of drug dependence, which is best characterized as a chronic, recurrent condition (38). Early marijuana use with increased risk for escalation to other drug use and drug dependence continues to be a major focus of concern (2). Stage theory posits that there is an invariant sequence in initiation and use of drugs, with use of marijuana preceding the use of "hard" drugs such as cocaine and heroin (39-42). This theory has been highly influential in drug policy debates and has provided a major rationale for sustaining prohibition against marijuana (43), as it is assumed that delaying or preventing early marijuana may reduce risks of other illicit drug use (2). Thus, many studies using various types of analyses have reported that early initiation to marijuana remains a significant risk factor for both the use of other drugs and experiencing drug-related problems (44-48). In 2001, 11.9% of the past year marijuana users used the substance on 300 or more days in the past 12 months. This translates to 2.5 million persons using marijuana on a daily or almost daily basis over a 12-month period (1). Among the past month users, about a third (32% or 3.9 million persons) used marijuana more than 20 days in the past month (1).

Cocaine is available as white crystalline powder or crack or rock cocaine. Powdered cocaine is generally snorted or dissolved in water and injected where as crack cocaine is usually smoked (49). Cocaine is the second most commonly used illicit drug in the United States. About 10% of Americans over the age of 12 have tried cocaine at least once in their lifetime, about 2% have tried crack and nearly 1% is currently using cocaine (49-51). Cocaine is powerfully addictive (52). Smoking crack can cause severe chest pains with lung trauma and bleeding (53). The mixing of cocaine and alcohol increases the rate of sudden death (53) and cocaine-related deaths are often a result of cardiac arrest or seizures followed by respiratory arrest (54). In 2001, an estimated 1.7 million (0.7%) of Americans age 12 or older were current cocaine users and an additional 460,000 (0.2%) were current crack users.

Methamphetamine and amphetamine are also known as meth, poor man's cocaine, crystal meth, ice, glass, etc. Methamphetamines and amphetamines are used by injection, snorting, smoking, or oral ingestion (55). During 2000, 4% of the US population reported trying methamphetamine at least once in their lifetime (56). The abuse of methamphetamine and amphetamines is considered to be concentrated in the western, southwestern and midwestern United States. Methamphetamine and amphetamines cost from $3,500 to $21,000 per pound. Retail prices range from $400 to $3,000 per ounce. Numerous consequences of methamphetamine and amphetamine use include addiction, psychotic behavior, and brain damage (57); withdrawal symptoms including depression, anxiety, fatigue, paranoia, aggression, and intensive cravings (57), violent behavior, anxiety, confusion, insomnia, auditory hallucinations, mood disturbance, delusions, and paranoia with chronic use (58), and damage to the brain similar to Alzheimer's disease, stroke, and epilepsy (58).

Thus, it appears that marijuana is less toxic and most commonly used with the general acceptance of the public. However, it is an illicit drug and also is associated with significant consequences. In contrast, cocaine which is seen in only 3% of the patients in this particular group, are associated with serious consequences. Thus, it appears that it may be necessary to randomly monitor patients who are thought to be without any illicit drug usage, however, only for marijuana. Random evaluation for marijuana is less expensive and more affordable. If medical community believes marijuana is not a hardcore drug like cocaine and if its use in combination with controlled substances is safe, monitoring may not be needed.

Random drug testing may be performed in many ways. Rapid drug screening is performed easily and inexpensively.

Rapid drug screening utilizes competitive immunoassay utilizing highly specific reactions between antibodies and antigens for the simultaneous detection of multiple substances. It is a one-step immunoassay. The test device consists of a membrane strip with an immobilized drug conjugate. Quality control is provided for these testings. Limitations for this procedure include that it is only a preliminary qualitative test result. However, for further evaluation, a more specific alternate quantitative analytical method to obtain a confirmed analytical result should be used. Further screening, if performed, should be by DS-9 test (drug screen-9), which may be performed either by the enzyme-multiplied immunoassay technique (EMIT) assay or the fluorescent polarization immunoassay (FPIA). Qualitative detection of the drugs by rapid drug screen are for amphetamines 1,000 ng/mL, cocaine 300 ng/mL, marijuana or cannabinoids 50 ng/mL as recommended screening cut-off concentrations by the Substance Abuse Mental Health Services Administration (SAMHSA).

Conclusion

The study showed that there is significant use of illicit drugs an in interventional pain management setting, with 13% attributed to marijuana and 3% to cocaine in patients who are considered as non-abusers of prescription controlled substances with controlled substance agreements. However, amphetamines were found in 0% of the patients and combined use of cocaine and marijuana was found in only one patient. Therefore, patients considered to be non-abusers of controlled substances may reasonably be randomly tested for marijuana by an inexpensive qualitative testing.

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