

DOES RANDOM URINE DRUG TESTING REDUCE ILLICIT DRUG USE IN CHRONIC PAIN PATIENTS RECEIVING OPIOIDS?

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Background: Prescription drug abuse and illicit drug use are common in chronic pain patients. Adherence monitoring with screening tests, and urine drug testing, periodic monitoring with prescription monitoring programs, has become a common practice in recent years. Random drug testing for appropriate use of opioids and use of illicit drugs is often used in pain management practices. Thus, it is expected that random urine drug testing will deter use of illicit drugs, and also improve compliance.

Objectives: To study the prevalence of illicit drug use in patients receiving opioids for chronic pain management and to compare the results of illicit drug use with

the results from a previous study.

Design: A prospective, consecutive study.

Setting: Interventional pain management practice setting in the United States.

Methods: A total of 500 consecutive patients on opioids, considered to be receiving stable doses of opioids supplemental to their interventional techniques, were studied by random drug testing. Testing was performed by rapid drug screen. Results were considered positive if one or more of the monitored illicit drugs including cocaine, marijuana (THC), methamphetamine or amphetamines were present.

Results: Illicit drug use was evident

in 80 patients, or 16%, with marijuana in 11%, cocaine in 5%, and methamphetamine and/or amphetamines in 2%. When compared with previous data, the overall illicit drug use was significantly less. Illicit drug use in elderly patients was absent.

Conclusion: The prevalence of illicit drug abuse in patients with chronic pain receiving opioids continues to be a common occurrence. This study showed significant reductions in overall illicit drug use with adherence monitoring combined with random urine drug testing.

Key Words: Chronic pain, controlled substances, illicit drug use, substance abuse, opioids, urine drug testing.

Marijuana, methamphetamine, diverted pharmaceutical drugs, and cocaine continue to be the primary drug threats in the United States. The National Survey on Drug Use and Health (NSDUH) of 2004 (1) showed that in 2004, 91.1 million Americans, or 7.9% of the population aged 12 or older, were current illicit drug users. In this survey, current drug use was defined as use of an illicit drug during the month prior to the survey interview. Marijuana was the most commonly used illicit drug in 2004, with a rate of 6.1% (14.6 million current users). There were 2.0

million current cocaine users, 467,000 of whom used "crack." Hallucinogens were used by 929,000 persons, and there were an estimated 166,000 heroin users. In addition, in 2004, 6.0 million persons were current users of psychotherapeutic drugs taken non-medically (2.5%). These included 4.4 million who used pain relievers, 1.6 million who used tranquilizers, 1.2 million who used stimulants, and 0.3 million who used sedatives. However, there were significant increases in the lifetime prevalence of use from 2002 to 2004 in several categories of pain relievers among those aged 18 to 25. Specific pain relievers with statistically significant increases in lifetime use were hydrocodone and oxycodone products. The number of individuals abusing pain medications for the first time grew from 628,000 in 1990 to 3 million in 2000. The highest increase was seen for oxycodone at 345% (1).

In a July 2005 report (2), the National Center on Addiction and Sub-

stance Abuse at Columbia University (CASA) stated that abuse and addiction of controlled prescription drugs – opioids, central nervous system depressants, and stimulants – have been stealthily, but sharply, rising. Between 1992 and 2003, while the US population increased 14%, the number of people abusing controlled prescription drugs jumped 94% – twice the increase in the number of people abusing marijuana, five times in the number abusing cocaine, and sixty times the increase in the number abusing heroin. Controlled prescription drugs like OxyContin®, Ritalin®, and Valium® are now the fourth most abused substances in America behind only marijuana, alcohol, and tobacco. The CASA report (2), also presented a 212% increase from 1992 to 2003 in the number of 12- to 17-year-olds abusing controlled prescription drugs and the increasing number of teens trying these drugs for the first time. The report also illustrated that new abuse of prescrip-

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tion opioids among teens was up an astounding 542%, more than four times the rate of increase among adults. Furthermore, disturbing statistics also show that teens who abuse opioids are likely to use other drugs including alcohol, marijuana, heroin, Ecstasy, and cocaine at rates respectively of 2, 5, 12, 15, and 21 times that of teens who do not abuse such drugs. Controlled prescription drug abuse and addiction are considered epidemic with 15.1 million people admitting to abusing prescription drugs – more than the combined number of those who admit abusing cocaine (5.9 million), hallucinogens (4 million), inhalants (2.1 million), and heroin (0.3 million). Past use of illicit drugs and illicit pain relievers among persons aged 12 or older was 4.9% of the population or 11,671,000 for non-medical use of pain relievers based on 2003 Substance Abuse and Mental Health Services Administration (SAMHSA) survey (3, 4). The population using psychotherapeutic drugs for non-medical purposes was 6.3% of the US population or 14,986,000 (3).

It has been reported that the principle drug of abuse for nearly 10% of youths in drug treatment programs is a prescription drug (4). It was concluded that diagnosis of abuse, drug dependency, and drug addiction occur in a significant proportion of chronic pain patients (5). Opioids are by far the most abused drugs. However, other controlled substances, along with illicit drugs are also used by many chronic pain patients. Multiple investigators have shown a prevalence of drug abuse in 9% to 41% of patients receiving opioids for chronic pain (6-21). Similarly, illicit drug use is also a common phenomenon in chronic pain patients. Illicit drug use in patients without controlled substance abuse was found in 14% to 16%, whereas illicit drug use was found in patients with controlled substance abuse in 34% of the patients (9, 13). Based on their type of insurance, the prevalence of illicit drug use among individuals with chronic pain were shown to be highest in patients on Medicaid (11). Other investigators (12, 18) also showed significant illicit drug use in patients with chronic non-malig-

nant pain treated with opioids.

In a study evaluating patterns and trends of illicit drug use among individuals with chronic pain (11), prevalence of illicit drug use was shown to be 17% in patients covered by third-party insurance, 10% in patients on Medicare, with or without a third-party insurance 24% in patients on Medicare and Medicaid, and 39% in patients only on Medicaid.

In recent years, adherence monitoring with screening test(s), urine drug testing, periodic monitoring with prescription monitoring programs, has become a common practice. Random urine drug testing for appropriate use of opioids, and use of illicit drugs is commonly used in pain management practices (21). It is expected that random urine drug testing will deter use of illicit drugs and also improve compliance.

This prospective evaluation was undertaken to study the prevalence of illicit drug use in patients receiving opioids for chronic pain management.

METHODS

The study was conducted in an interventional pain management practice. A total of 500 consecutive patients on opioids were studied. Following the initial selection, the evaluation consisted of a review of the charts and gathering of information with regards to controlled substance intake. All the patients were considered to be receiving stable doses of either hydrocodone, oxycodone, methadone, or morphine as supplemental to their interventional techniques. Opioids were not the mainstay of treatment.

All patients signed an informed consent for random drug testing and publication of results without the identification of individuals. Appropriate precautions were taken to protect the privacy and identity of patients participating in this evaluation. Inclusion criteria were patients willing to participate, in stable condition, and in a pain management program encompassing interventional techniques and opioid drug administration. Exclusion criteria were inability to understand the consent, refusal to sign the consent, refusing to un-

dergo random drug testing, and unstable pain control.

Patients were considered positive if they were positive for one of the monitored illicit drugs including cocaine, marijuana (THC), amphetamines or methamphetamine. The drug testing was performed by rapid drug screen. Positive drug screen for cocaine was considered definite by rapid drug screen. Positive methamphetamine, amphetamine, or marijuana were also checked for false-positives with a follow-up laboratory evaluation and evaluation of history of drugs causing false-positive results. The results of positive THC were confirmed with laboratory testing, if a patient was on Protonix® (Pantoprazole) or denied using marijuana. The results confirmed by laboratory evaluation were considered as final.

Rapid drug screen was performed on all the patients participating in the study. Rapid drug screen is a 1-step, lateral flow immunoassay for the simultaneous detection of up to nine drugs by urine analysis. Each analysis occupies a separate channel, intended for use in the qualitative detection of various drugs.

Data from a previous study (11) evaluating the prevalence of illicit drug use among individuals with chronic pain was utilized to compare the present data.

Data were recorded in a database using Microsoft® Access® 2003. The SPSS version 9.0 software was used to generate the frequency tables and chi-squared statistic was used to test the significant difference among groups. Fisher's Exact test was used wherever the expected value was less than 5. Prevalence and 95% confidence intervals were calculated. Results were considered statistically significant if the *P* value was less than 0.05.

RESULTS

Patient Flow

A total of 500 patients were evaluated with a rapid drug screen during 2005. Their urine was tested for the following drugs: cocaine, opioids, methadone, oxycodone, amphetamines,

Table 1. Demographic characteristics

Gender	Male	41% (205)
	Female	59% (295)
Age	Mean ± SEM	48.5 ± 0.55
Height (inches)	Mean ± SEM	66.8 ± 0.19
Weight (lbs.)	Mean ± SEM	184.5 ± 2.24
Duration of pain (years)	Mean ± SEM	10.7 ± 0.37
Insurance Status	Medicare only or with third party	31% (154)
	Medicare and Medicaid	17% (85)
	Medicaid	14% (69)
	Third party	33% (166)
	No insurance	5% (26)

Table 2. Prevalence of illicit drug use

Drug	Prevalence n=500 (%)
Marijuana (Tetrahydrocannabinol (THC)) 95% CI	11% (54) 8% - 14%
Cocaine 95% CI	5% (24) 3% - 7%
Methamphetamine and / or Amphetamines 95% CI	2% (11) 1% - 4%
Total Abuse 95% CI	16% (80) 13% - 20%

Total numbers may not correlate as some patients were positive in more than one substance abuse category

Table 3. Prevalence of illicit drug use based on insurance

	Third Party (192)	Medicare w/wo third party (154)	Medicare & Medicaid (85)	Medicaid (69)	Total (500)
Marijuana	14%* (26)	5% (7)	12%* (10)	16%* (11)	11% (54)
95% CI	9% - 19%	2% - 9%	6% - 21%	8% - 27%	8% - 14%
Cocaine	6%* (11)	1% (2)	8%* (7)	6% (4)	5% (24)
95% CI	2% - 10%	0% - 5%	3% - 16%	1% - 14%	3% - 7%
Methamphetamine and / or Amphetamines	4% (8)	1% (1)	1% (1)	1% (1)	2% (11)
95% CI	1% - 8%	0% - 4%	0% - 6%	0% - 8%	1% - 4%
Total Abuse	20%* (38)	6% (9)	21%* (18)	22%* (15)	16% (80)
95% CI	14% - 26%	2% - 11%	13% - 31%	13% - 33%	13% - 20%

() Number of patients

*Indicates significant difference with Medicare with/without third party insurance

methamphetamines, cannabinoids, benzodiazepines, barbiturates, and phencyclidine.

Data were evaluated in 500 patients from a sample of 566 patients eligible to participate in the study. Of the 566 patients, 66 patients refused to participate in the study.

Demographic Characteristics

Table 1 illustrates demographic characteristics encompassing gender, age, height, weight, duration of pain, and insurance status. The results showed that 59% of the patients were female, the mean age was 48.6 years and the mean duration of pain was 10.7 years. Even then, 48% of the patients were on Medicare and 31% of the patients were receiving Medicaid either as supplemental insurance or as the main insurance. For evaluation purposes, patients without insurance were combined with third party insurance.

Prevalence of Illicit Drug Use

Table 2 illustrates overall prevalence in 80 patients or 16% with marijuana in 11%, cocaine in 5%, and methamphetamine/amphetamine in 2%.

Prevalence Based on Insurance

Table 3 shows prevalence of illicit drug use based on insurance. Overall prevalence of illicit drug use was 6%, 22%, 21%, and 20% based on the coverage by Medicare with or without third party, Medicaid, Medicare and Medicaid, and third party insurance consecutively.

Table 4 and Figure 1 illustrate illicit drug use based on age. Illicit drug use was highest in patients in the age group of less than 45 and lowest in patients aged 65 or higher.

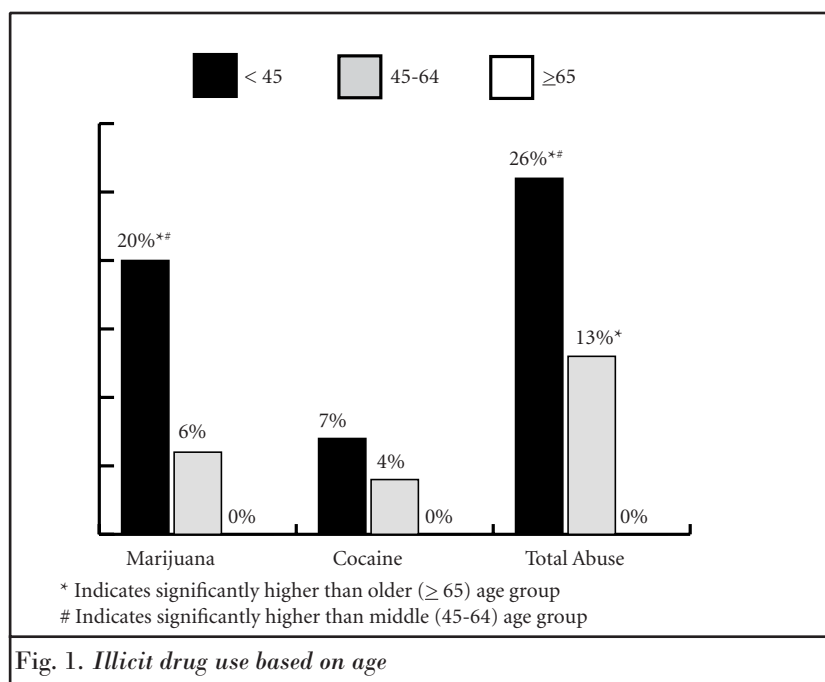
Table 5 illustrates the data of comparative evaluation of illicit drug use in the present study with a previously referenced study (11). The overall illicit drug use prevalence was significantly less compared to the data from the previous study (16% vs 22%). It was also significantly less in patients on Medicaid (22% vs 39%). Marijuana use was also less in the present study (16% vs 34%) in Medicaid patients.

Table 4. *Illicit drug use based on age*

	< 45 years (188)	45 – 64 Years (254)	≥ 65Years (58)	Total (500)
Marijuana	20% ^{**} (38)	6% (16)	0%	11% (54)
95% CI	14% - 27%	8% - 17%	-	8% - 14%
Cocaine	7% [*] (13)	4% (11)	0%	8% (24)
95% CI	3% - 12%	2% - 8%	-	3% - 7%
Methamphetamine and/ or Amphetamines	4% (7)	2% (4)	0%	2% (11)
95% CI	1% - 8%	0% - 4%	-	1% - 4%
Total Abuse	26% ^{**} (48)	13% [*] (32)	0%	16% (80)
95% CI	19% - 33%	8% - 17%	-	13% - 20%

* Indicates significant difference with older (≥ 65) age group

Indicates significant difference with middle (45-64) age group

Fig. 1. *Illicit drug use based on age*

DISCUSSION

This prospective evaluation suggests that random urine drug screening reduced illicit drug use. This study identified illicit drug use among 16% of the patients in a heterogeneous group of patients. In the past, illicit drug use in patients without a history of controlled substance abuse was shown to be present in 14% to 16% of the patients (9, 13). In contrast, illicit drug abuse in patients with a history of controlled substance abuse was present in 34% of the patients (9). In a study based on in-

surance coverage, the illicit drug use ranged from 10% to 39% with overall illicit drug use in 22% of the patients (11). This study showed overall reduction in illicit drug use and reduction in marijuana use in Medicaid patients. The elderly (age ≥ 65 years) were not abusing illicit drugs.

To our knowledge, this is the first study to examine patterns and trends in illicit drug use among individuals with chronic pain with enhanced adherence monitoring, which included random drug testing. This study showed signifi-

cant reductions in illicit drug use compared to the previous studies conducted at least two years earlier (9, 11, 13). However, the patterns of illicit drug use are consistent with previous evaluations which found the highest proportion in patients on Medicaid and patients on Medicare and Medicaid.

Among all the illicit drugs used in the United States, marijuana is the most widely used and readily available illicit drug. A National Survey on Drug Use and Health of 2004 (1) showed marijuana continues to be the most commonly used illicit drug in 2004, with a rate of 6.1% (14.6 million current users). The 2004 NSDUH survey (1) showed that 2.1 million persons have used marijuana for the first time within the past 12 months – approximately 6,000 per day. The average age at the first use among the 2.1 million recent marijuana initiates was 18 years. Most of the recent initiates (64%) were younger than age 18 when they first used. It is stated that at least one-third of the US population has used marijuana at some time. The Drug Enforcement Administration (DEA) (22) has suggested numerous reasons that marijuana use is widespread, including a relaxed public attitude regarding its potential harm, popularization by the media, and by groups advocating legalization, the current trend of smoking marijuana-filled cigars known as “blunts,” and the internet. Even though, marijuana has been the most common illicit substance used over several decades (23, 24), its deleterious effects are not well appreciated. Marijuana use is associated with impaired educational attainment (23), reduced workplace productivity (25), and increased risk of use of other mood enhancing substances (26). Marijuana use also has been shown to play a major role in motor vehicle accidents (27), and to cause adverse effects on cardiovascular and respiratory systems (28, 29). The use of marijuana or hashish produces feelings of relaxation and well-being and impairs cognitive function and performance of psychomotor tasks (30). Symptoms of withdrawal include restlessness, irritability, and insomnia (31). However, overdose can induce panic attacks and psy-

Table 5. Comparative evaluation of illicit drug use in present study with a previous study (11)

	Third party		Medicare w/wo third party		Medicare & Medicaid		Medicaid		Total	
	Present study (192)	Previous study (100)	Present study (154)	Previous study (100)	Present study (85)	Previous study (100)	Present study (69)	Previous study (100)	Present study (500)	Previous study (400)
Marijuana	14%*(26)	11% (11)	5% (7)	8% (8)	12%*(10)	20% (20)	16%*(11)	34% (34)	11%*(54)	18%(73)
95% CI	9% - 12%	5%- 17%	2% - 9%	3%-11%	5% - 21%	12%-28%	8% - 27%	25% 43%	8% - 14%	14%-22%
Cocaine	6%*(11)	7% (7)	1% (2)	4% (4)	8%* (7)	6% (6)	6% (4)	8% (8)	5%(24)	6%(25)
95% CI	2% - 10%	2%- 12%	0% - 5%	0% -8%	3% - 16%	1% - 11%	1% -15%	3% - 13%	3% - 7%	4% - 9%
Methamphetamine and / or Amphetamines	4% (8)	3% (3)	1% (1)	2% (2)	1% (1)	4% (4)	1%(2)	3% (3)	2% (11)	3%(12)
95% CI	1% - 8%	0% - 6%	0% - 4%	0% -5%	0% - 6%	0% - 8%	0% - 8%	0% - 6%	1% - 4%	1% - 5%
Total Abuse	20%*(38)	17% (17)	6% (9)	10%(10)	21%*(18)	24% (24)	22%*(15)	39% (39)	16%*(80)	22%(90)
95% CI	14%-26%	10%-4%	2%-11%	4% -6%	13%-31%	16% -32%	12%-33%	29% 49%	13%-20%	18%-27%

() Number of patients

* Indicates significant difference with Medicare with or without third party insurance

Indicates significant difference with previous study (within the same insurance group)

chosis (32).

Marijuana is considered as a “gateway” to the world of illicit drug abuse. Associations between early cannabis use and later drug use and abuse/dependence have been demonstrated which may arise from the effects of the peer and social context within which cannabis is used and obtained (26). As with previous reports (9, 11, 13), marijuana was the most commonly used illicit drug in this study. A total of 11% of the study population used marijuana with 16% of Medicaid patients, 12% of Medicare and Medicaid patients, and 14% of third party insured patients, with only 5% of the patients on Medicare with or without third party coverage.

Cocaine is the second most commonly used illicit drug in the United States. Based on the 2004 National Survey on Drug Use and Health, there were 2.0 million current cocaine users, 467,000 of whom used “crack” (1). Further, in 2004, an estimated 1.0 million persons had used cocaine for the first time within the past 12 months – approximately 2,700 per day. Cocaine is a potent blocker of the dopamine-norepinephrine and serotonin-uptake transporters (30). It is also a powerful

addictive (33). The mixing of cocaine and alcohol increases the rate of sudden death. Cocaine-related deaths are often a result of cardiac arrest or seizures followed by respiratory arrest (33). Cocaine is readily available throughout the United States, with greatest availability in the densely populated areas. The present study showed overall 5% prevalence of cocaine abuse in chronic pain patients on opioids compared to 6% in the previous study.

Amphetamine and methamphetamine are known as meth, poor man’s cocaine, crystal meth, ice, glass, etc. Short-term administration of amphetamine and methamphetamine produces euphoria, a feeling of well-being, and alertness, as well as increased arousal, concentration, and motor activity. However, long-term use causes irritability, aggressive, and stereotyped behavior, and paranoid-like psychosis (30). Amphetamine and methamphetamine abuse was seen in this study in 2% of the patients.

Even though there are extensive data on the use of illicit drugs in the general population, there are few data documenting use of illicit drugs in patients taking prescription-controlled substances. Consequently, there are no

theories predicting that abuse of prescription-controlled substances increases the rate of illicit drug use. This relationship has been noted with marijuana and controlled substance usage, but not vice versa. However, the same mechanisms may apply in illicit drug use of patients with chronic pain on controlled substances. Further, chronic treatment with THC induced cross-tolerance to opioids in rats (26). Additionally, with advocacy for marijuana, perceptions about marijuana may be similar to controlled substances, with the impression that marijuana is not only pleasurable, but also safe. Previously it was demonstrated that there was increased use of illicit drugs in patients with controlled substance abuse (9).

This study may be criticized for utilizing previous data for comparison purposes. Since the data was accumulated in the same setting with a large number of patients in each group, the authors felt that this usage was appropriate. One may also criticize random drug testing by the use of rapid drug screen. The rapid drug screen is performed easily and inexpensively. This test utilizes a competitive immunoassay technique for the simultaneous detection of multiple illicit substances. The

test device consists of a membrane strip with an immobilized drug conjugate. Quality control is provided with the test. Further screening may use the DS-9 test (Drug Screen-9), which can be performed either by the Enzyme-Multiplied Immunoassay Technique (EMIT) or the Fluorescent Polarization Immunoassay (FPIA).

While drug testing may be performed by either testing the urine, serum, or hair, urine testing is considered to be the best for detecting the presence or absence of certain drugs due to specificity, sensitivity, ease of administration, and cost. Even then, controversies exist regarding the clinical value of urine drug testing, partly because the most current methods are designed for, or adapted from, forensic or occupational deterrent-based testing for illicit drug use and are not necessarily optimized for clinical applications in chronic pain management. However, with an appropriate level of understanding, urine drug testing can improve a physician's professional ability to manage therapeutic prescription of drugs with controlled substances, and to diagnose substance abuse or appropriate intake of drugs, thereby leading to proper treatment in chronic pain.

CONCLUSION

Based on this study, the prevalence of illicit drug abuse in patients with chronic pain receiving opioids continues to be high. However, this study showed significant reductions in illicit drug use with adherence monitoring combined with random urine drug testing in this population. This study also showed absence of illicit drug use in the elderly.

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