ISSN: 2641-6271
DOI: 10.33552/OAJAP.2023.07.000668
Open Access Journal o
Addiction and Psychology
Iris Publishers

Research Article

Observations on Prescribed Drugs for Pain Patients

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Received Date: August 09, 2023

Published Date: September 18, 2023

Abstract

Background: The Clinical Laboratory Institute has Published guidelines for testing drugs in urine to monitor compliance.

Objective: We wished to compare our observations on the frequency of positive drug use from our urine test data with the panel of tests recommended by CLSI C-63 Laboratory Support for Pain Management programs.

Study Design: We examine the frequency of positive drug test data from 2016 to 2022 from medical practices designated as pain. Setting: Reference laboratory performing urine drug testing for pain practices.

Methods: Our test menu differed from the more exhaustive one listed in the CLSI document. Results: there was good correlation with those drugs prescribed for pain, but not for the psychotropic ones as many were not included in our test panel. We found several drugs taken by patients that were not listed in the CLSI document.

Limitations: Our comparison was limited by our 80-drug test menu.

Conclusion: The CLSI document offers guidance, but the list must be tailored for the practices served by the laboratory.

Keywords: Pain patients; Drug therapy; Urine drug testing

Background

The CLSI (Clinical Laboratory Standards Institute) has proposed a list of drugs that should be tested for their presence to ensure patient compliance with their pain medications [1]. We wished to compare the CLSI recommendations with our observed positive drug tests in this population. We offer a panel of 80 drugs and metabolites in our definitive urine drug test [2]. For this analysis we matched the medical practice designation with the drugs observed by urine drug testing. The data is from our laboratory which performs drug testing for pain clinics and rehabilitation centres. This correlation should result in a good indicator of the drugs used in the medical practice of treating these patients. The CLSI recommendations and our observations should correlate.

Study Design

Permission to perform the study was granted from WCG IRB WCG IRB, 1019 39th Ave., SE Suite 120, Puyallup, WA 98374, USA. The patient population was selected from those medical practices designated as pain medicine [3,4]. This included pain/ortho, pain management, primary care pain, internal medicine, primary family medicine, pain orthopedics, physical medicine and pain, sports medicine.

Methods

The laboratory tested 611,329 specimens from 2016 to 2022. The method of analysis was that of Krock K, et al. [3]. The computational methods and data storage were that of Pesce AJ, et al. [2]. The medical practice designations were obtained from our billing information. The calculation of observed frequency was based on the number of times that drug was observed in the years 2020 to 2022.

Results

The tier 1 drugs in the CLSI document that we test for are Amphetamine, Methamphetamine, Methylenedioxymethamphetamine (MDMA), Methylenedioxyamphetamine (MDA), Methylenedioxyethylamphetamine, (MDEA), Phenobarbital, Alprazolam, Clonazepam, Diazepam, Lorazepam, Oxazepam,

Temazepam, Benzoylecgonine, Δ9-tetrahydrocannabinol (THC), 6-acetylmorphine (6-AM), Buprenorphine, Codeine, Fentanyl, Hydrocodone, Hydromorphone, Morphine, Oxycodone, Oxymorphone, Tapentadol, and Tramadol. Not included in the CLSI document are the metabolites norhydrocodone, noroxycodone, 7-aminoclonazepam, alpha-hydroxyalprazolam, o-desmethyl tramadol, and norbuprenorphine which are used to indicate that the patients are taking the prescribed drug.

For the pain medication patients, the observed drug positive finding for each medication is tabulated in Table 1. The list is truncated at forty-six observations. The lowest frequency is about 2.5% of the most prevalent treating drug, hydromorphone, The next most prevalent was oxycodone. Hydrocodone was the third most prevalent. The oxymorphone frequency was due to its role as a metabolite of oxycodone as well as being a separate prescribed drug. Gabapentin was also prevalent as a pain medication. The illicit drug fentanyl was present in less than 10% of our observations. However, THCA was present in about 25% of our positive specimens.

Table 1: Pain Management testing, From CLSI Table 8: Tiers of drug testing.

Tier	When to Order	Drug Class	Example Drug or Drug Metabolite*	Precision Observation
I	Routine Monitoring	Amphetamines	Amphetamine	29,349
			Methamphetamine	6,369
			Methylenedioxymethamphetamine (MDMA)	161
			Methylenedioxyamphetamine (MDA)	175
			Methylenedioxyethylamphetamine (MDEA)	24
		Barbiturates	Amobarbital	Not tested
			Butalbital	240
			Phenobarbital	80
			Pentobarbital	Not tested
			Secobarbital	Not tested
		Benzodiazepines	Alprazolam	42,655
			Chlordiazepoxide	Not tested
			Clonazepam	As 6-amino 30,219
			Clorazepate	Not tested
			Diazepam	As nordiazepam 28,654
			Estazolam	Not tested
			Flurazepam	Not tested
			Halazepam	Not tested
			Lorazepam	16,776
			Medazepam	Not tested
			Midazolam	Not tested
			Oxazepam	40,327
			Prazepam	Not tested
			Temazepam	34,180
			Triazolam	Not tested
		Cannabinoids	Δ9-tetrahydrocannabinol (THC)	8490
		Cocaine	Cocaine	Not tested
			Benzoylecgonine	14,426
		Opiates/Opioids	6-acetylmorphine (6-AM)	1,422
			Buprenorphine	26,784
			Codeine	14,677
			Dihydrocodeine	Not tested
			Fentanyl	21,741
			Hydrocodone	216,881
			Hydromorphone	238,819
			Morphine	69.735
			Oxycodone	232,391
			Oxymorphone	217,293
			Tapentadol	6,749
			Tramadol	57,299

II	**High-risk patients with known history of abuse for this medication or prevalence of drug use is endemic to local region, risky polypharmacy, multiple providers, or if prescribed and patient shows lack of efficacy or toxicity**	**Alcohol**	Ethanol or metabolite	55,009
II	**High-risk patients with known history of abuse for this medication or prevalence of drug use is endemic to local region, risky polypharmacy, multiple providers, or if prescribed and patient shows lack of efficacy or toxicity**	**Alcohol**	Ethanol or metabolite	55,009
		Anticonvulsants	Carbamazepine	Not tested
			Felbamate	Not tested
			Gabapentin	106,951
			Lacosamide	Not tested
			Lamotrigine	Not tested
			Levetiracetam	Not tested
			Oxcarbazepine	Not tested
			Phenytoin	Not tested
			Pregabalin	29,940
			Rufinamide	Not tested
			Tiagabine	Not tested
			Topiramate	Not tested
			Valproic acid	Not tested
		Antidepressants	Amitriptyline	6,161
			Citalopram	6295
			Clomipramine	Not tested
			Desipramine	Not tested
			Doxepin	Not tested
			Duloxetine	10,425
			Fluoxetine	3,754
			Imipramine	113
			Nortriptyline	Not tested
			Paroxetine	1,542
			Sertraline	4,912
			Venlafaxine	
		Synthetic cathinones	Compounds ever-changing, too numerous to list	Not tested
		Antitussive	Dextromethrophan	5842 Dexthorphan 8,409
		Dissociative anesthetic	Ketamine	622
		Hallucinogens	Lysergic acid diethylamide (LSD)	Not tested
			Phencyclidine	Not found
		Muscle relaxants	Carisoprodol	4,781
			Meprobamate	6,387
				Cyclobenzaprine 43,760
		Narcotic painreliever	Propoxyphene	51

III	**As Clinically Indicated**	**OTC analgesic**	Acetaminophen	Not tested
			Salicylate	Not tested
		Antihistamine	Certirizine	Not tested
			Chlorpheniramine	Not tested
			Diphenhydramine	Not tested
			Loratidine	Not tested
		Antipsychotics	Amisulpride	Not tested
			Amoxapine	Not tested
			Chlormethiazole	Not tested
			Clopenthixole	Not tested
			Chlorpiprazine	Not tested
			Chlorprothixene	Not tested
			Cloxazepine	Not tested
			Clozapine	Not tested
			Distraneurine	Not tested
			Dixyrazine	Not tested
			Chlorpromazine	Not tested
			Fluentixol decanoate	Not tested
			Fluphenazine	Not tested
			Haloperidole	Not tested
			Loxapine	Not tested
			Melperone hydrochloride	Not tested
			Methotrimeprazine	Not tested
			Olanzapine	Not tested
			Oxilapine	Not tested
			Perphenazine	Not tested
			Phenothiazine	Not tested
			Pimozide	Not tested
			Quetiapine	2415
			Risperidone	594
			Sulpiride	-
			Thioridazine	
			Tiapride	
			Trifluoroperazine	
			Ziprasidone	
			Zotepine	
		Synthetic cannabinoids	Compounds ever-changing, too numerous to list	-
	Not listed		mitragynine	4,655
			methylphenidate	2,766
			fluoxetine	3,754
			bupropion	6,118
			Meperidine	202
			pentazocine	96
			propoxyphine	51
			6-betanaltrexol	499
			naltrexone	-
			Naloxone	8,170
			Zolpidem	12,941
			Phentermine	10,101

The drug propoxyphene was observed infrequently as this has been removed by the FDA as a prescription drug. However, alcohol use must be considered in pain management testing. In this case about 23% of the positive specimens were positive for the alcohol use maker ethyl sulfate.

Discussion

For the pain medications we expected hydrocodone to be the most prevalent prescribed drug as this was the most prescribed opiate in the general population.

There are a number of available surveys showing the most prescribed drugs in the US population. These are Vitamin D, Amoxicillin, Levothyroxine, Lisinoprill, Ibuprofen, Amphetamine/dextroamphetamine, Amlodipine, Albuterol HFA, Prednisone, and Gabapentin [5]. These observations are based on population prescribing information and may not reflect what drugs are being prescribed for specific medical conditions. It is possible to establish specific drugs used to treat medical conditions by examining the medical practices. Pain management is somewhat unique because most of the patients undergo urine drug testing. We decided to examine the drug treatment of patients being given medications for pain management. We postulate that the information of drug test results may constitute a more accurate estimation of the actual patient's use of their prescriptions but may also reveal non-prescription drug use.

We chose to examine the presence of this drug and other opiates in pain management medical practices.

Results

In this study, hydrocodone was the most prescribed opiate. One of the reasons for performing medical urine drug tests is to determine if the patient is taking other non-prescribed drugs. For the pain treated patients the most observed drug was hydromorphone, this is a metabolite of hydrocodone, and morphine as well as a prescription drug. The incidence of illicit drug use was significant (about10%) However the use of alcohol as measured by the frequency of positive ETS in specimens was about 23% far greater than any other non-prescribed drug. We observed drugs not listed in the CLSI guidelines which included mitragynine, methylphenidate, fluoxetine, bupropion, meperidine, 6-betanaltrexol, naltrexone, naloxone, zolpidem, and phentermine.

Limitations

Our study was limited to the opiate drugs, hydrocodone, oxycodone, morphine, and the opiate agonists, methadone, buprenorphine. We also tested for the illicit drugs heroin, fentanyl, cocaine, and THCA.

Conclusion

The major drugs found were opiates showing compliance, however, alcohol use was prevalent, but the incidence of illicit drug use was low.

Acknowledgement

All the authors are employees of Precision Diagnostics LLC.

Conflict of Interest

There are no conflicts of interest.

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