When poll is active respond at

PollEv.com /jasonlane545

CASE 1

- 27 yo male presented to ED previous night feeling ill after stopping multiple substances.
- Recent substance use includes 6-month history of:
  - Fentanyl smoking 4-6 times a day; last use the previous morning, about 24 hours prior to our initial interview
  - ETOH, half a liter of whisky per day, last drink about 36 hours prior to our initial interview
  - “Xanibars” from street, 2-3 tablets 3-4 times a day; last use about 48 hours prior to our interview.
- + ETOH withdrawal seizures after a prior period of heavy use.
- He received 2mg IV lorazepam in ER about 10 hours earlier
- Currently: T 98.9, P103, 152/104, R18, 99% RA; appeared anxious, agitated, flushed, sweaty and moderately tremulous at rest. Pupils appeared normal for light.

NEXT STEP

A. Complete the history and physical
B. Give intravenous benzodiazepine
C. Give intravenous phenobarbital
D. Begin buprenorphine induction
E. Give benzodiazepine and buprenorphine

Patient received 4mg lorazepam IV (consecutive 2mg doses) while the team completed the history and physical

Vitals normalized, symptoms improved, patient became drowsy but interactive after the lorazepam

PERTINENT ADDITIONAL HISTORY

PMH: ETOH withdrawal seizures 8 months ago; Bipolar 2 disorder

PSH: None

All: None

Home meds: None

FH: + AUD (parent)

Soc: Lives with parents, not employed

EFORCE: No prescriptions

Previous rehab: 8 months ago for ETOH and bzd

Substance Use History:

ETOH: half a bottle of whisky per day (last drink was 2 days ago). Began drinking age 14, intermittent periods of detox/rehab, last 8 months ago
Sedatives: ”Xanibars” purchased illicitly, 2-3 tablets 3 – 4 times a day (last time use was 2 days ago). Began in late teens, intermittent periods detox/rehab, last 8 months ago.
Opioids: Fentanyl (the last time used was 1 day ago) began after most recent rehab (about 6 months ago. Prior to this had intermittent use of oral opioids since age 16. No prior MAT.
Stimulants: None
Cannabis: None
Hallucinogens/Dissociatives: None
Tobacco: 1 PPD

INITIAL PHYSICAL AND LABS

- Gen: Anxious, agitated prior to lorazepam, drowsy but easily arousable and interactive afterwards, oriented x 3
- HEENT: Pupils normal for light, mild nasal congestion
- Lungs: CTAB
- CV: RRR, S1 S2 with no murmurs
- Abd: Soft, non-tender.
- MSK: No joint swelling or redness, no muscle wasting or tenderness
- Skin: No piloerection, moderately sweaty, no rash, no ulcers

- CBC normal
- Chem 20 remarkable for AST 248, ALT 72
- ETOH < 10
- Urine drug screen negative: Opiates, benzodiazepines, amphetamine, barbiturates, cocaine, methadone, PCP, THC
- Urine fentanyl confirmation pending (usual turnaround 3 days)

DAY 1 TREATMENT

A. Continue benzodiazepines
B. Stop benzodiazepines, start phenobarbital
C. Continue benzodiazepines, start buprenorphine
D. Stop benzodiazepines, start phenobarbital and buprenorphine

Patient was placed on lorazepam 2mg IV q6 hours for the first 24 hours

Symptoms remained improved, with 1 added dose of Ativan the evening of day 1 for return of tremulousness/CIWA 13, improved afterwards

DAY 2

- Tremors remain improved
- Reports increased anxiety which he rates as severe, agitation, nausea, muscle aches
- Pupils normal, nasal congestion and mild tearing are present, mild goosebumps present on upper arms
- 48 hours past last reported use of fentanyl

DAY 2 TREATMENT

A. Continue same dose benzodiazepines, start buprenorphine induction
B. Decrease scheduled benzodiazepines, start buprenorphine induction
C. Change benzodiazepines to CIWA triggered only, start buprenorphine induction
D. Decrease benzodiazepines, wait for worsening opioid withdrawal prior to starting buprenorphine
E. Decrease benzodiazepines, wait for urine fentanyl confirmation to start buprenorphine

Patient received 2mg buprenorphine with some improvement in symptoms. Additional 2mg doses given for total of 8mg day 1, with marked improvement in symptoms

BZD dose decreased and transitioned to oral taper

DAY 3

- Visible tremors at rest and anxiety return, requests IV ativan
- Current treatment includes lorazepam 1mg po q6 and buprenorphine 12mg (day 2 induction)
- RN states she has observed the tremors are only present when others are in his room
- T97.9, P79, 122/80, R18

DAY 3 TREATMENT

A. Increase benzodiazepines due to the anxiety and tremors
B. Give an additional 4mg buprenorphine
C. Change benzodiazepines to OAWS triggered dosing only
D. Consult psychiatry and explore symptoms further
E. Consult psychiatry and discuss consequences of drug seeking behavior

Psychiatry was consulted, noted the history of bipolar 2, reported patient was grateful for his care and feeling much better. Started Depakote and aripiprazole.

DAY 4-6

- BZDs tapered to off
- Buprenorphine advanced to 16 mg daily
- Continued to report feeling much better and grateful for care
- LFTs improved, urine fentanyl confirmation returned positive day 4
- DC meds also included Depakote and aripiprazole. Acamprosate discussed but deferred.
- Transferred to PHP

Received: 1 March 2021 | Revised: 18 June 2021 | Accepted: 18 June 2021

DOI: 10.1002/dta.3119

SPECIAL ISSUE - SHORT COMMUNICATION

WILEY

What's in fake 'Xanax'?: A dosage survey of designer benzodiazepines in counterfeit pharmaceutical tablets

Karen Blakey[1] | Amanda Thompson[2] | Abbey Matheson[1] | Andrew Griffiths[2]

Drug Test Anal. 2022;14:525–530.

Analyzed 46 tablets from 20 seizures over a 6-month period (Australia)

Etizolam with most frequent (25 tablets, dose range 0.7 – 8.3 mg per tablet)

Alprazolam and flualprazolam next most frequent

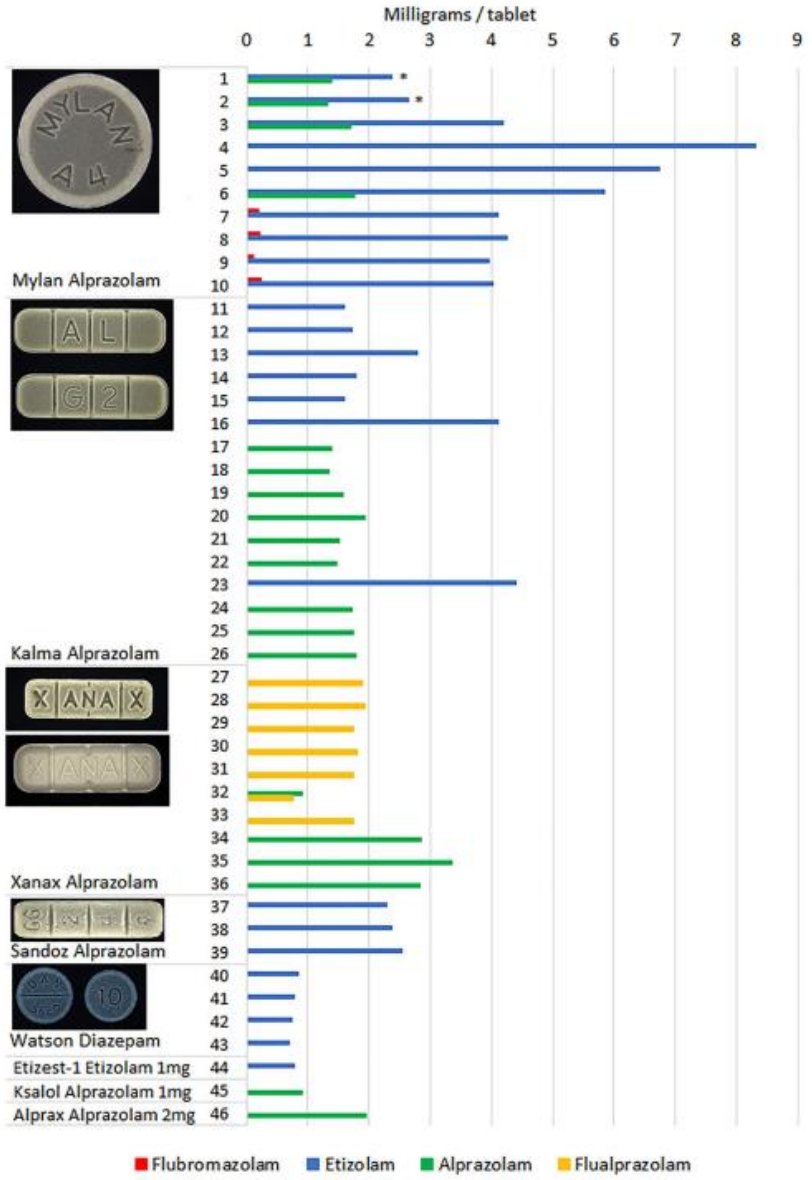


TABLE 1 Drugs detected in counterfeit benzodiazepine tablets seized in Queensland, Australia

Counterfeit presentation	Drugs identified
Mylan Alprazolam 2 mg 'Mylan A4'	Etizolam
	Etizolam, alprazolam, cyproheptadine, amantadine and promethazine
	Etizolam, alprazolam, cyproheptadine and 2-methyl-4′-(methylthio)-2-morpholinopropiophenone (MMTMP/Irgacure 907)
	Etizolam and alprazolam
	Etizolam and flubromazolam
Xanax Alprazolam 2 mg 'Xanax'	Etizolam
	Flualprazolam
	Flualprazolam and alprazolam
	Alprazolam
	Etizolam and doxepin
	Doxepin and 5-methoxy-*N*,*N*-dibutyltryptamine (5-MeO-DBT)
	Zopiclone
	Paracetamol
	No drugs detected
Kalma Alprazolam 2 mg 'AL|G2'	Etizolam
	Alprazolam
	No drugs detected
Sandoz Alprazolam 2 mg 'GG249'	Etizolam
Dava Pharmaceuticals Alprazolam 2 mg 'S903'	Clonazepam and lidocaine
Watson Diazepam 10 mg 'DAN5620'	Etizolam
Roche Diazepam 10 mg 'Roche 10'	Etizolam

Morbidity and Mortality Weekly Report

Notes from the Field

Illicit Benzodiazepines Detected in Patients Evaluated in Emergency Departments for Suspected Opioid Overdose — Four States, October 6, 2020–March 9, 2021

- 141 patients from 4 states (NY, PA, MO, OR) with suspected opioid overdose
- Tested biologic samples for illicit (unlawfully manufactured) bzds
- 21 + (15%)
- Clonazolam, Etizolam, Flubromazolam

TABLE. Detection of illicit benzodiazepines and opioids, initial naloxone administration, and outcomes among patients with suspected opioid overdose (N = 21) — Toxicology Investigators Consortium Fentalog Study Group, four states, October 6, 2020–March 9, 2021

Characteristic	No. (%) of patients
Illicit benzodiazepines detected	
Clonazolam	11 (52.4)
Etizolam	10 (47.6)
Flubromazolam*	2 (9.5)
Opioids detected	
Co-detected opioids†	20 (95.2)
Methadone	12 (60.0)
Fentanyl	6 (30.0)
Heroin	4 (20.0)
Codeine	2 (10.0)
Para-fluorofentanyl	2 (10.0)
Buprenorphine	1 (5.0)
Acetyl fentanyl	1 (5.0)
Medical course and outcome	
Naloxone administration§	16 (76.2)
Only 1 dose administered	9 (56.3)
≥2 doses administered	7 (43.8)
Known naloxone indication¶	15 (71.4)
Depressed level of consciousness	9 (60.0)
Respiratory depression	7 (46.7)
Decreased oxygenation	3 (20.0)
Decreased carbon dioxide expiration	2 (13.3)
Known naloxone response**	13 (61.9)
Improved level of consciousness	6 (46.2)
Increased respiratory rate	4 (30.8)
Improved oxygenation	1 (7.7)
Precipitated withdrawal††	1 (7.7)
No response	5 (38.5)
Respiratory and cardiac intervention	
Endotracheal intubation/Mechanical ventilation	1 (4.8)
Cardiopulmonary resuscitation	1 (4.8)

EMERGING THREAT REPORT Annual 2022

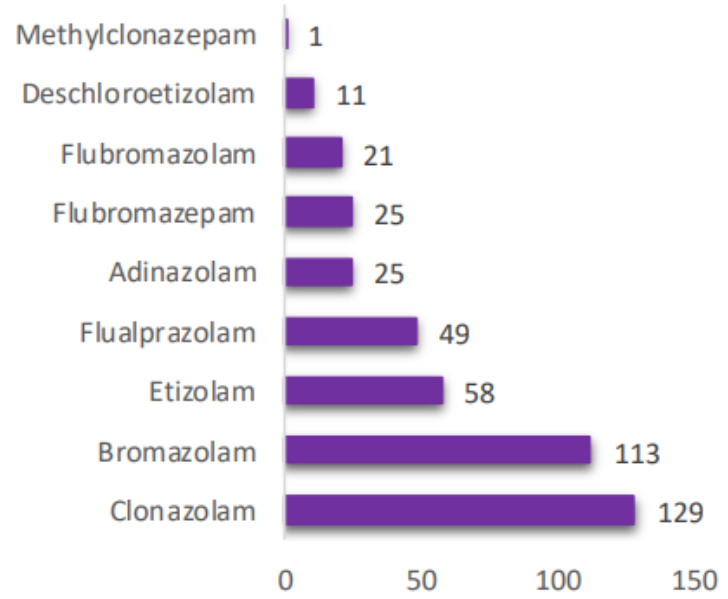
Drug Enforcement Administration

Special Testing and Research Laboratory

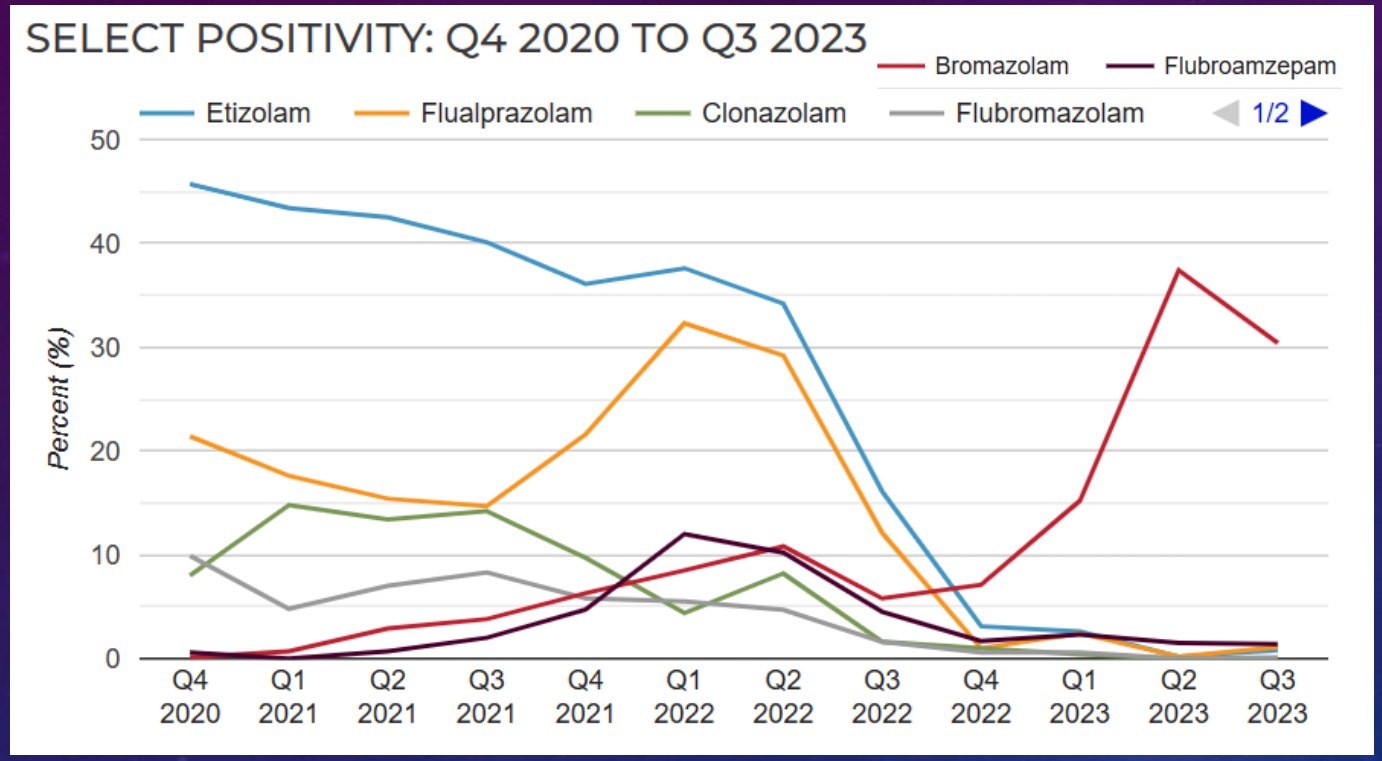
DEA-Emerging-Threat-Report-2022-Annual.pdf (umd.edu)

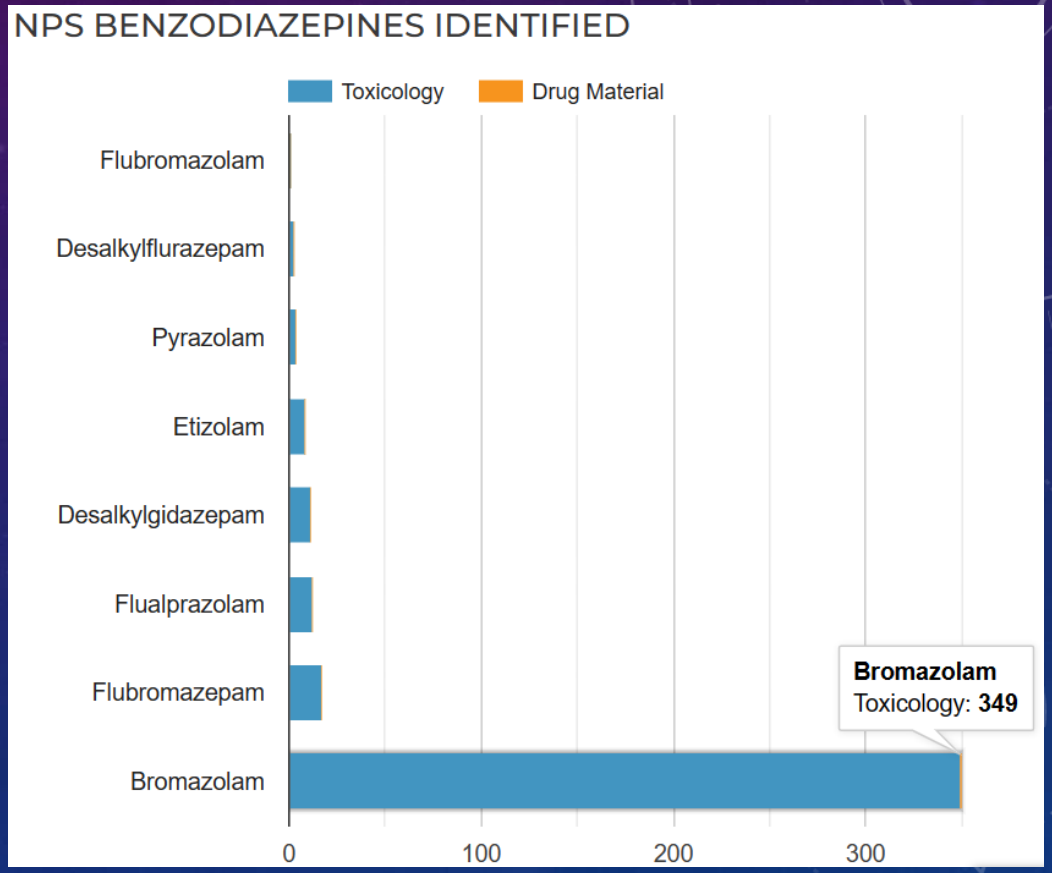
BENZODIAZEPINES

THERE WERE **375** IDENTIFICATIONS OF DESIGNER BENZODIAZEPINES DURING THIS REPORTING PERIOD. THIS REPRESENTS AN APPROXIMATELY **15%** INCREASE FROM CY2021. CLONAZOLAM AND BROMAZOLAM WERE THE MOST REPORTED DESIGNER BENZODIAZEPINES ACCOUNTING FOR APPROXIMATELY **56%** OF THE IDENTIFICATIONS.



cfsre The Center for Forensic Science Research & Education





https://www.cfsre.org/nps-discovery/trend-reports/nps-benzodiazepines/report/49?trend_type_id=1

VITROS BENZODIAZEPINE IMMUNOASSAY

Compound	Quantity (ng/mL) equivalent to 200 ng/mL of lormetazepam	% cross-reactivity*	Quantity (ng/mL) equivalent to 300 ng/mL of lormetazepam	% cross-reactivity*
tetrazepam	51	396	66	454
diazepam	52	385	71	422
prazepam	62	323	80	375
alprazolam	64	313	73	411
N-desmethyldiazepam / nordiazepam	78	256	97	309
1-N-hydroxyethylflurazepam	80	250	99	303
estazolam	81	247	100	300
α -hydroxyalprazolam	84	238	109	275
halazepam	88	227	110	273
ketazolam	92	217	121	248
α -hydroxytriazolam	98	204	150	200
α -hydroxyalprazolam glucuronide	98	204	129	232
N-desalkylflurazepam	103	194	138	217
triazolam	114	175	141	213
medazepam	118	169	163	184
nitrazepam	127	157	225	133
nitrazepam (GEN 8 and above)	289	69	525	57
midazolam	129	155	164	183
flunitrazepam	133	150	209	144
flunitrazepam (GEN 8 and above)	215	93	357	84
temazepam	146	137	203	148
flurazepam	175	114	223	134
clobazam	192	104	332	90
clobazam (GEN 8 and above)	414	48	825	36
oxazepam	220	91	319	94
clonazepam	245	82	475	63
clonazepam (GEN 8 and above)	469	43	887	34
clotiazepam	378	53	625	48

Ortho Clinical Diagnostics is not responsible for any editing, line alteration or other revision, intentional or otherwise, to this information.

Compound	Quantity (ng/mL) equivalent to 200 ng/mL of lormetazepam	% cross-reactivity*	Quantity (ng/mL) equivalent to 300 ng/mL of lormetazepam	% cross-reactivity*
lorazepam	590	34	1070	28
bromazepam	775	26	1320	23
demoxepam	925	22	1870	16
demoxepam (GEN 8 and above)	1777	11	3636	8
7-aminoflunitrazepam	930	22	1620	18
norchlordiazepoxide	2460	8	4700	6
temazepam glucuronide	3900	5	5750	5
chlordiazepoxide	4500	4	8000	4
7-aminoclonazepam	4800	4	10,100	3
lorazepam glucuronide	>10,000	<2	>10,000	<3
oxazepam glucuronide	>10,000	<2	>10,000	<3

* The VITROS BENZ Assay cutoff value (ng/mL) divided by the amount of cross-reactant (ng/mL) that produces a value e the cutoff value, multiplied by 100

WHICH BENZODIAZEPINE WAS OUR PATIENT TAKING?

A. Etizolam
B. Alprazolam
C. Bromazolam
D. Other
E. None

PATIENT

39 year old male presented to the ED involuntarily under the Baker Act.

Patient called police and stated that he was having intrusive/violent thoughts. Per wife patient was reportedly not taking his medications.

Patient was paranoid and anxious appearing. Complained of insomnia, headache, tingling sensation in hands/feet and light sensitivity.

Denies any nausea/vomiting.

Per Wife: patient has been stressed about starting a second job, had completed rehab in 2021 for inhalant abuse, and claims that since then he has not used any substances. Patient recently bought about 3-4 bags of cocaine and finished them within 2 days.

ADDITIONAL HISTORY

Lifetime Substance Abuse History:

Nicotine: Started smoking in college occasionally. DOLU 2 months ago prior to presentation

Cannabis: Started while in college, uses occasionally. DOLU 2 weeks ago prior to presentation.

EtOH:Started at 18 while in college. Usually Binged. Has a history if drinking until he passed out. Patient does not have a history of withdrawal seizures or ICU admissions. He states has not drank in about 1 month. DOLU 1 month ago prior to presentation.

S-H-A (Sedatives, Hypnotics, Anesthetics):Xanax for anxiety prescribed by psychiatrist. He uses 1 tab of 1 mg per patient every other day. has been using for years regularly. Does not take more than needed per patient. Usually drinks to help sleep. DOLU 1 day ago prior to presentation.

Opioids (Fentanyl, Heroin, Pain killers):Denies

Stimulants (Methamphetamine, Cocaine, etc..):Cocaine use started at age 25. Occasional use when drinking. Used 1 bag occasionally. only snorting. Used 4 days ago prior to presentation.

Dissociatives (PCP, ketamine, dextromethorphan, Nitrous Oxide, Salvia):Dextromethorphan, has used for 3 years regularly. He claims because he cannot sleep. Uses as much as he needs to feel better and sleep. Anywhere from 1/4 bottle to 1 bottle of OTC preparations of dextromethorphan or more, used daily.. DOLU 1 day ago prior to presentation. Also abused Nitrous Oxide in the past.

Psychedelics (LSD, Peyote/Mescaline, Psilocybin): Denies

PMH: Anxiety, Depression, Bipolar Disorder, Neuropathy

PSH: None

Allergies: None

Home Meds: OTC NyQuil, Lorazepam, Gabapentin

Family History: Uncle with Substance Use Disorder

EFORCSE: Lorazepam 1mg 15 tablets for 15 days. Last filled 08/26/2022.

PHYSICAL AND LABS

Gen: Poor eye contact, uncooperative

HEENT: pupils equal and reactive to light. No nasal discharge.

Lungs: CTAB

CV: RR, S1 S2 with no murmurs

Abd: soft, non-tender

MSK: No joint deformity. No muscle wasting or tenderness. Slight tremor of the hands appreciated.

Skin: warm, dry, no no evidence of infection

Psych: Anxious, restless. Blunted mood and affect.

Temp: 98, HR 127, O2 100% on RA, BP 144/95, RR: 18

CBC: WBC 12.02, Hemoglobin 17.0

CMP: Na 131, Bicarb 20, Cl 94,

CK: 451

UDS: Negative - amphetamines, barbiturates, benzos, cocaine, methadone, opiates, PCP, THC

Etoh: <10

DEXTROMETHORPHAN (DXM) MISUSE, POISONING

1.5 millions (Ages 12-25) misuse OTC cough and cold medication that contain DXM each year in the United States.

Co-ingestion of ethanol is commonly seen.

Recreational DXM: “going pharming”, “dexing”, “robodosing”, “robotripping”

Among young adults who misused DXM, of these individuals would try other illicit substances such as cannabis, inhalants, or hallucinogens

DXM is the D-isomer of the codeine synthetic analog, levorphanol. Active metabolite is dextrorphan.

Due to its structure it binds to the sigma opioid receptors in the medulla, does not bind to mu & delta opioid receptors.

Also has serotonergic activity at the 5-hydroxytryptophan 2 receptor.

In overdose, metabolite inhibits NMDA receptors producing neurobehavioral effects similar to ketamine and PCP. Also inhibits adrenergic neurotransmitter reuptake in peripheral and central nervous system causing tachycardia, hypertension, and diaphoresis.

DXM TOXICITY DOSE DEPENDENT

Neurobehavioral effects typically begin 30 to 60 minutes post-ingestion and persist for up to six hours.

Approximate range of doses:

Mild stimulation (first "plateau"): 1.5 mg/kg (adult dose: 100 to 200 mg)

Euphoria and hallucinations (second "plateau"): 2.5 to 7.5 mg/kg (adult dose: 200 to 400 mg)

Dissociative "out of body" state (third "plateau"): 7.5 to 15 mg/kg (adult dose: 300 to 600 mg)

Complete dissociation with unresponsiveness (fourth "plateau"): 15 mg/kg (adult dose: >600 mg)

MEDICATIONS TO AVOID DURING MANAGEMENT

A - Ativan

B - Haloperidol

C - Naloxone

D - Fluids

Parenteral neuroleptic medication (eg, haldol) should be avoided in patients with DXM overdose/poisoning due to risk of exacerbating hyperthermia or anticholinergic symptoms.

BZD (eg Ativan) preferred medication to control marked agitation or florid psychotic patients and those who develop seizures, serotonin syndrome.

Naloxone has reversed respiratory depression & coma in some patients who have had DXM poisoning/overdose

Fluids part of medical management, especially in those who develop rhabdomyolysis

HOSPITAL COURSE

Day 1:

- Lorazepam
- Normal Saline
- Supportive Care

Day 2:

- Continued w/ Normal Saline
- No longer requiring Lorazepam
- Supportive Care

POTENTIAL CO-INGESTANTS

- Acetaminophen
- Antihistamines
- Phenylephrine, similar decongestants

ROLE OF DXM TESTING

DXM poisoning/overdose diagnosis usually clinical

Rapid UDS to not detect DXM

DXM use can frequently cause false positive for PCP on rapid tests that utilize liquid chromatography

DISPOSITION

Most patients with uncomplicated dextromethorphan poisoning have resolution of symptoms within four to six hours after ingestion

Patients who are asymptomatic for six hours after ingestion of DXM, who have nontoxic acetaminophen concentrations, and who are not suicidal, may be discharged home.

POTENTIAL CONSEQUENCE OF CHRONIC INGESTION

A - Bromism

DXM produced as crystalline hydrobromide salt, leading to build up of bromide in the body. A.

B - Stroke

Cocaine may cause changes in cerebral vasculature which can cause sludging in vessels w/ consequent ↑thrombus formation.

C - Cerebellar Degeneration

Cerebellar Degeneration seen chronically in those who drink after 10 years or more, especially after excessive ethanol use. Clinically similar to WE.

D - Adrenal insufficiency

Chronic administration of opiates can potentially cause secondary adrenal insufficiency.