

Kratom: Emerging Findings and Treatment Considerations such as MI and Medication Strategies

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Disclosure Information

☀ Marissa Andres-Kim, MD

☀ “No Disclosures”

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☀ Actinogen Medical Limited

☀ Axsome Therapeutics

☀ Biogen

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☀ Janssen

☀ Karina Therapeutics

☀ Merck

☀ Prothena Biosciences

☀ Sage Therapeutics

☀ Tonix pharmaceuticals

Learning Objectives

Upon completion, participants will be able to

- ☀ Describe recent trends in Kratom use, including some effects that are commonly desired by its users.
- ☀ List at least three potential adverse medical and/or psychiatric effects of kratom use.
- ☀ Demonstrate at least three basic motivational interviewing techniques to address kratom use in patients.

Case 1

Jenni is a 32yo woman who comes into your clinic with concerns about depression, diffuse pain, and fatigue. She is otherwise healthy with no known history of substance use.

☀️ Would you screen her for Kratom?

Mitragyna speciosa



What is Kratom?

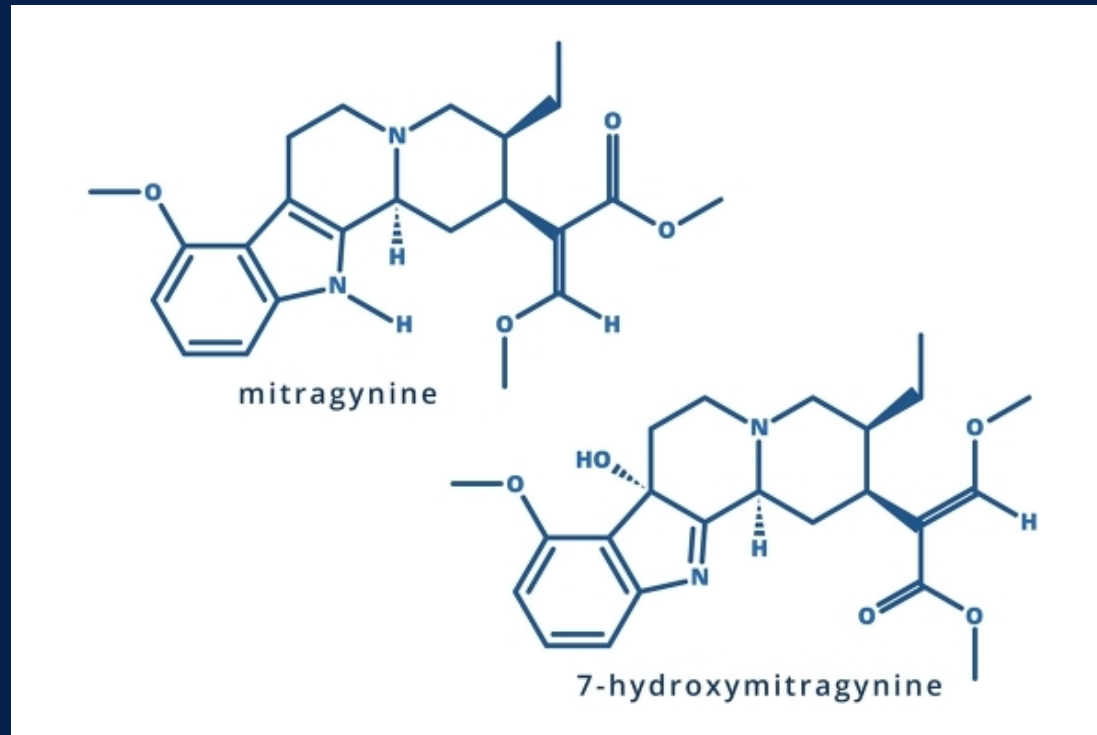
- ☀ Refers to the tree, which is native to Southeast Asia
- ☀ Also refers to products derived from its leaves
- ☀ Leaves can be chewed, brewed into a tea, or smoked

Effects of Kratom

☀ Stimulant effects at low-doses

☀ Opioid-like effects at high-doses

Mitragine and 7-hydroxymitragine



- Bioactive alkaloids
- Mu-opioid receptors
- Adrenergic, serotonin, and dopamine receptors

Prozialec, 2012

What is Kratom?

- ☀ Promoted as a performance - boosting wellness supplement
- ☀ Known as an herbal remedy for opioid withdrawal, pain, fatigue, depression, and anxiety

“Shop by Benefits”



**KRATOM
FOR ENERGY**



**KRATOM
FOR
RELAXATION**



**KRATOM
BODY & MIND**

Kratom is Legal “Drug of Concern”



- Legal in 44 states
- Local bans or restrictions
- Passed Kratom Consumer Protection Act in 12 states
- Illegal in 6 states



Kratom Products

Ease of Access in US

- ☀️ Available online and at retail headshops
- ☀️ Capsules, powder, tea bags, liquid concentrate, edible products or gummies



Kratom Users

- ☀ Oct 2016, cross-sectional online survey of 8049 Kratom Users
- ☀ Typical: White, male, 31-50yoa, married, college educated, employed, private insurance, \$35K+ household income



Grundmann, 2017

Prevalence of Kratom Use

2020 National Survey on Drug Use and Health (N=32,893)



Reported Kratom Use

Past 30 Days	Past 31+ Days
0.41%	1.40%

2020 National Survey on Drug Use and Health (N=32,893)

Kratom Users w/ Past Year	Past 31+ Days (~Lifetime Use)	Past 30 Days (~Recent Use)
Major Depressive Episode	25.3%	24.2%
Alcohol Use Disorder	30.1%	25.2%
Cannabis Use Disorder	28.9%	24.2%
Other Illicit Drug Use Disorder	12.8%	15.9%

Co-Occurring Disorders

Compared to Never Used
Kratom,

Lifetime Kratom Users
were more likely to have

- ☀ Major Depressive
Episode
- ☀ Alcohol, Cannabis, or
Other Illicit Drug Use
Disorder

Recent Kratom Users were
more likely to have

- ☀ Other Illicit Drug Use
Disorder

2019 National Survey on Drug Use and Health (N=56,136)

Other Illicit Drug Use

Kratom Users w/ Past Year	Lifetime Kratom Users	Prevalence Ratio
Opioids	8.9%	18.0
Methamphetamine	4.3%	12.5
Cocaine	4.0%	14.0
Prescription Stimulants	2.8%	16.5
Tranquilizer	3.6%	16.8
Hallucinogens	1.4%	16.8

- ☀ 1/3 of Kratom Users have at least 1 co-occurring substance use disorder
- ☀ Other Illicit Drug Use is associated with 3-5X higher likelihood for Kratom Use than those with Alcohol Use, Cannabis Use, or Major Depressive Episode

Audience Participation

- ☀ Which of the following is/are the most common reason(s) patients use Kratom?
 - ☀ A: Physiologic dependency on an illicit opioid
 - ☀ B: Physiologic dependency on a prescription opioid
 - ☀ C: Medical condition leading to acute/chronic pain
 - ☀ D: Emotional/mental condition
 - ☀ E: A+B
 - ☀ F: C+D

Reasons for Kratom Use

	Reasons for Kratom Use	Notes
68%	Acute or chronic pain (medical condition leading to acute or chronic pain)	Women, 21+yoa, out of work or unable to work
66%	Emotional or mental condition (anxiety, depression, PTSD)	Women, <41yoa, Medicare or Medicaid or uninsured
26%	Relieving withdrawal symptoms of current or prior use of illicit drugs (heroin, cocaine, amphetamines)	Men, 21-30yoa, not married, self-insured, Medicare, Medicaid, uninsured
8%	Relieving withdrawal symptoms of a current or prior dependency to legally prescribed opioids (pain killers)	21+yoa, partnered, Medicare, Medicaid, uninsured

Grundmann, 2017

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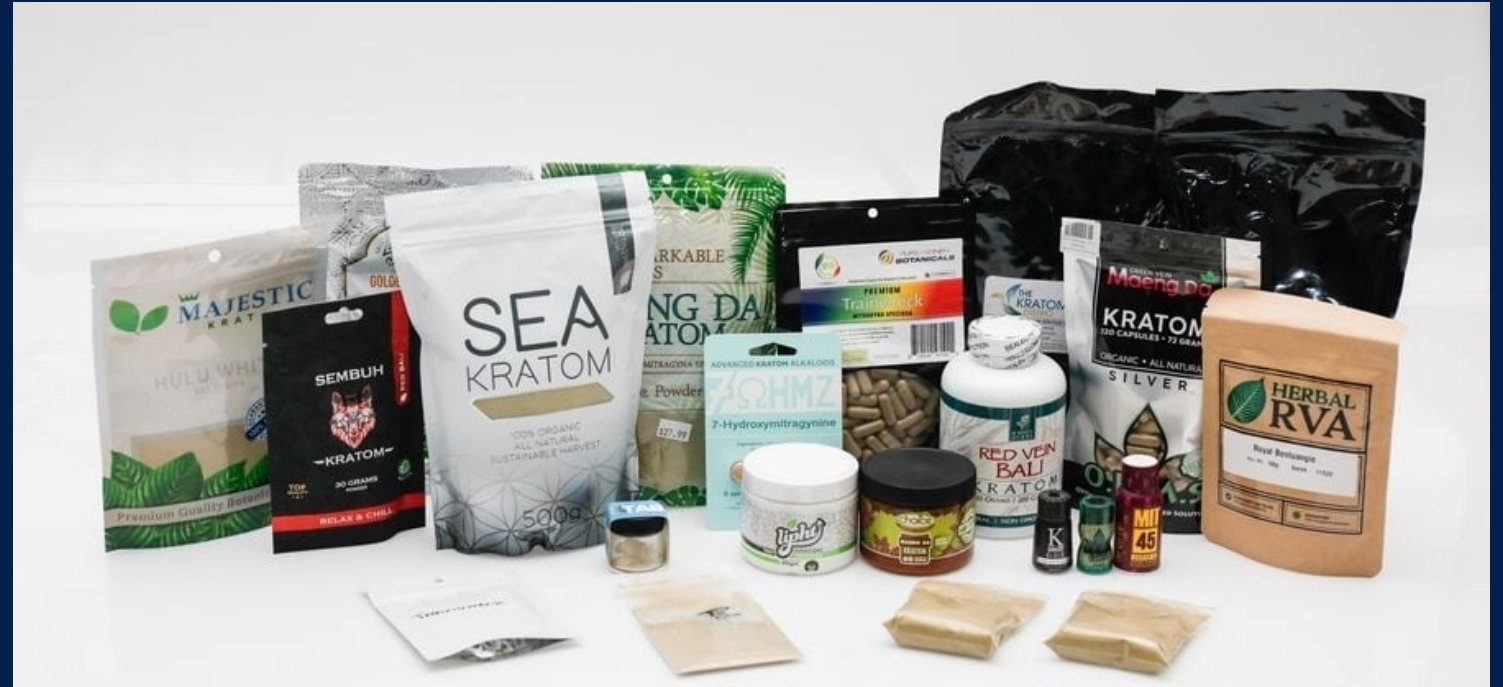
You ask her what she has tried for her symptoms. She tells you that, based on her friend's recommendation, she started using Kratom. It helped, but she has been needing more of it, daily.

☀️ What kind of psychoeducation can you offer her?

Risks of Kratom Use

- ☀ Non-standard compositions
- ☀ Lack of safety regulations
- ☀ Addiction
- ☀ Polysubstance Use
- ☀ Drug-drug interactions

Importance of Addressing Kratom Use



Safety Risks of Unregulated Kratom

- ☀ Adulteration with other drugs
 - ☀ Phenylethylamine
 - ☀ Hydrocodone, morphine, tramadol
- ☀ Contamination with toxic metals
 - ☀ Manganese
 - ☀ Lead
 - ☀ Nickel
- ☀ Contamination with microbes
 - ☀ Salmonella

 **WARNING**



Adverse Effects Associated with Kratom Use

US Poison Control Centers:

☀ Frequently Reported:

☀ Agitation, Tachycardia, Drowsiness,
Vomiting, and Confusion

☀ Also Reported:

☀ Seizure, Withdrawal, Hallucinations,
Respiratory Depression, and Coma

Reports of Hepatotoxicity, Kidney Injury, and
Death. Neonatal abstinence syndrome with in-
utero exposure.



Kratom is Addictive

Frequent use can lead to

- ☀ Dependence
- ☀ Tolerance
- ☀ Withdrawal

- ☀ Dose-dependent additive or synergistic effects with co-administered drugs
 - ☀ Stimulants: Tachycardia, Elevated Blood Pressure, Arrhythmias, Cardiac Arrest, Stroke
 - ☀ Opioids, Benzodiazepines: CNS depression, Respiratory suppression
- ☀ Increased risk of hepatotoxicity, coma, and death with polysubstance use
- ☀ 2D6 > 3A4 inhibition affecting co-administered medications



Exploring Reasons to Change Kratom Use

Desired Effects

- ☀ Stimulant
- ☀ Increased energy
- ☀ Pain relief
- ☀ Mitigate opioid withdrawal
- ☀ Euphoria
- ☀ Sedation

Adverse Effects

- ☀ Dependence, tolerance, withdrawal
- ☀ Weight loss, sleep disturbance
- ☀ Lethargy, breathing suppression
- ☀ Liver and kidney damage
- ☀ Psychiatric disturbance
- ☀ Contamination, adulteration
- ☀ Drug-Drug Interactions
- ☀ Seizure, coma, or death
- ☀ In-utero exposure

Why Do People Change?

- ☀️ Change is natural
- ☀️ Therapeutic conversations can facilitate change
- ☀️ The “fixing reflex” is common among clinicians

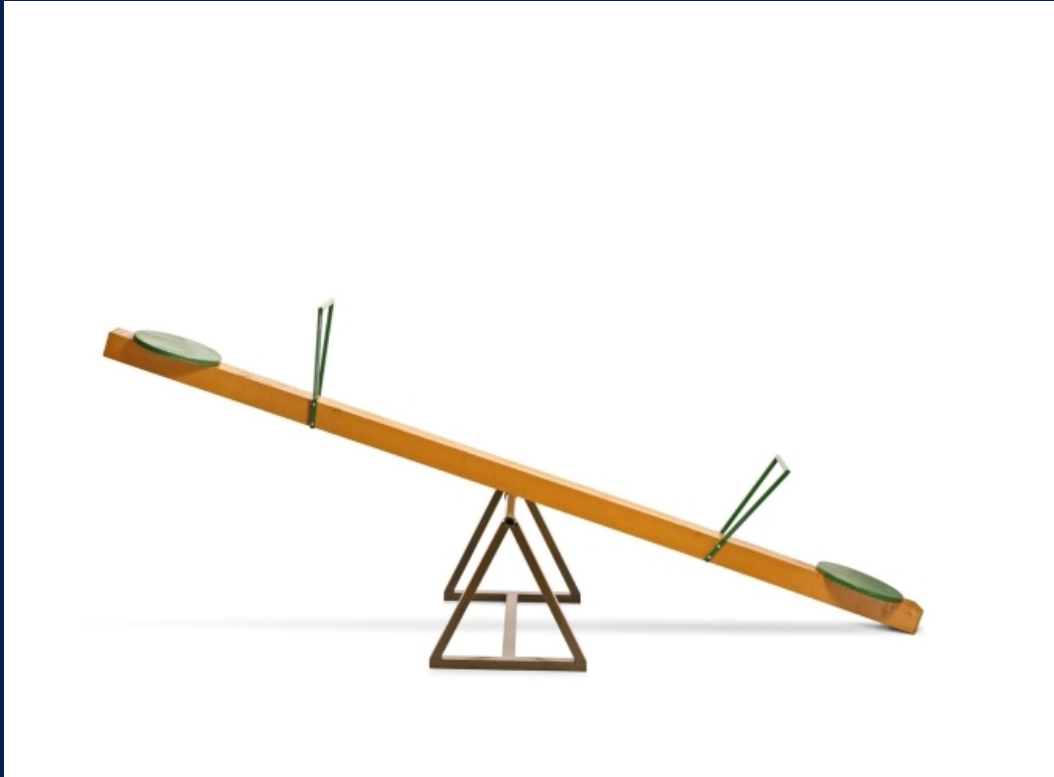


Ambivalence



- ☀️ Ambivalence is normal
- ☀️ Ambivalence needs to be explored, not confronted
- ☀️ Resolving ambivalence can be a key to change

Fundamental Idea #1



If there are two sides to an issue, and you take up one, you are inviting the other person to take up the other.

Fundamental Idea #2



In any conversation about something where there are two sides, we tend to

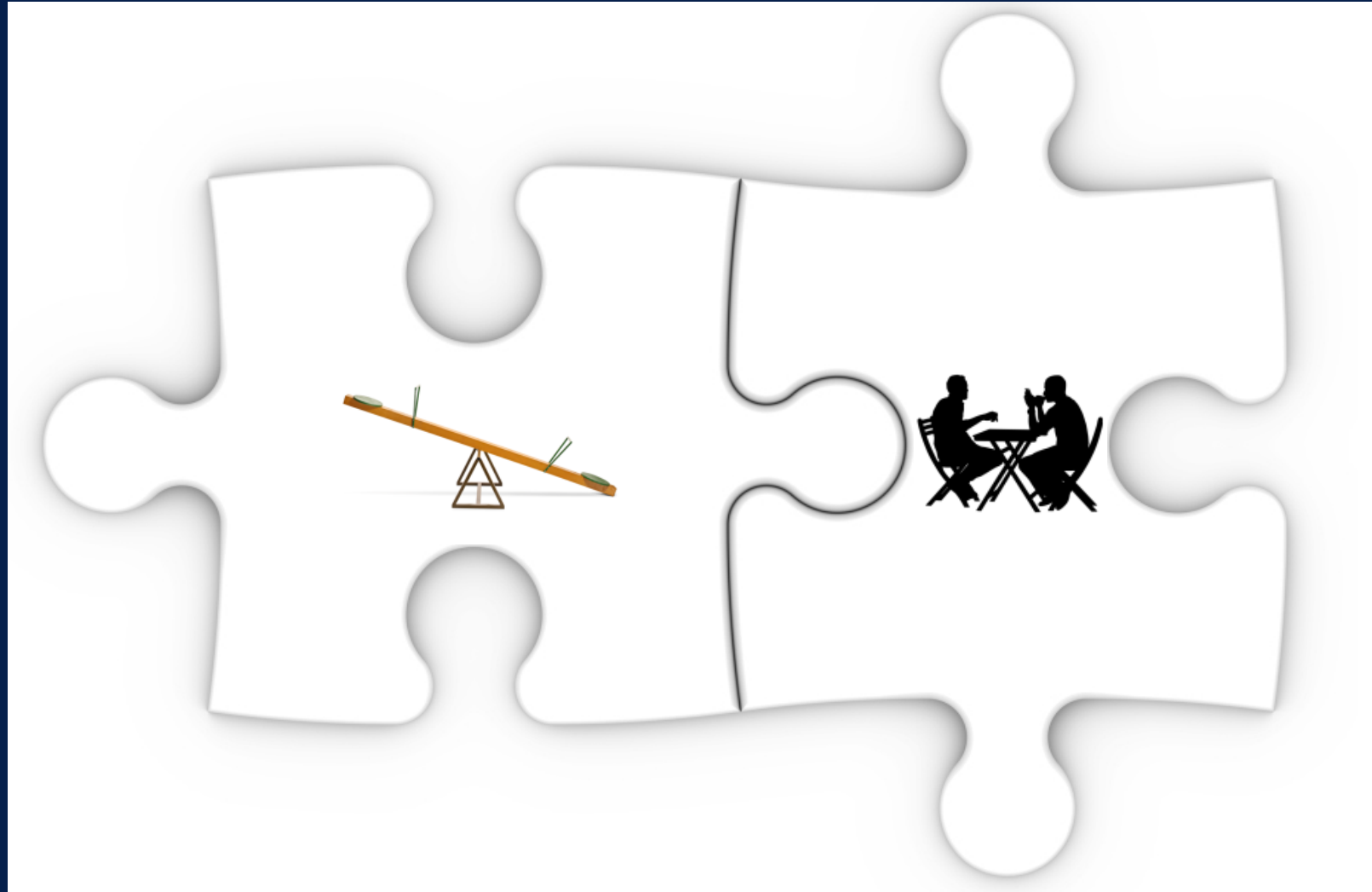
- **REMEMBER** *and*
- **ACT ON**

the things we heard ourselves say.

*Especially the things we said **LAST!***

The Paradoxical Effect of Coercion

*Put these
two ideas
together...*



A Continuum of Communication Styles

Directing



Guiding



Following



teach
assess
prescribe
lead



draw out
encourage
motivate



listen
understand
go along with

Miller & Rollnick, 2023

Four Foundational Tasks of MI

Planning* (how will we get there?)

Evoking (why are we going there?)

Focusing (where shall we go?)

Engaging (shall we walk together?)

Spirit of Motivational Interviewing

- ☀️ **C**ompassion
- ☀️ **A**cceptance
- ☀️ **P**artnership
- ☀️ **E**mpowerment



☀️ Miller & Rollnick, 2023

Core Skills (OARS + I&A)

MI is focused on strengthening the pros and softening the cons of healthful change

- ☀ **O**pen-ended Questions
- ☀ **A**ffirming (simple and complex)
- ☀ **R**eflecting (simple and complex)
- ☀ **S**ummarizing
- ☀ **I**nforming & **A**dvising (with permission, ask-offer-ask)

Case 2

- ☀️ 55-year-old man with chronic pain. Started using Kratom after a longstanding treatment with full agonist opioid medication was abruptly discontinued.
- ☀️ Role-play using MI skills to assess readiness for change.

Case 3

- ☀ Young man presents with psychosis, irritability, aggression, and with heavy use of both cannabis and kratom
- ☀ How would you assess kratom use and kratom's contribution to his illness?

Kratom Assessment

☀ Amount

- ☀ Quantity, dose, frequency, length of use, last time abstinence,

☀ Motivation

- ☀ Motivation to use, motivation to stop, repercussions, including cost

☀ Severity: cravings, tolerance, dependence, preoccupation, withdrawal, repercussions

☀ Comorbid symptoms

Kratom Withdrawal

- ☀ Mydriasis
- ☀ Nausea
- ☀ Sweating and chills
- ☀ Muscle and body aches
- ☀ Tremors and twitches
- ☀ Diarrhea
- ☀ Rhinorrhea
- ☀ Lacrimation
- ☀ Lacrimation
- ☀ Insomnia
- ☀ Restlessness
- ☀ Irritability/hostility
- ☀ Fatigue
- ☀ Anxiety
- ☀ Mood disturbances
- ☀ Hallucinations

Plan

- ☀ Most important: Psychoeducation

- ☀ Abstinence vs. Harm Reduction

- ☀ Motivation

- ☀ Most daily users used it in a problematic way, and that when it did become a problem, it was because they were trying to stop but couldn't because of withdrawal. (n=357 survey).

- ☀ Opioids unavailable

- ☀ Anxiety, mood, pain, psychosis, etc.

Recent Research

- ✱ No FDA approved treatments
- ✱ No randomized controlled trials
- ✱ Case studies, case series

Recent Research: Home initiation SL buprenorphine

2 case studies

- ☀ Taking 35 grams of kratom daily; 5 servings per day to avoid withdrawal
- ☀ Unsuccessful efforts to cut now
- ☀ Telehealth home initiation of buprenorphine-naloxone

- ☀ Buprenorphine-naloxone 2 mg–0.5 mg once while in moderate kratom withdrawal and were advised to repeat ½ film to 1 film every 2 h as needed to obtain comfort up to 8 mg–2 mg on the first day

- ☀ 1 patient used 2mg – 0.5mg daily and 2nd patient stabilized on 4mg –1mg BID
- ☀ Neither used kratom again during 2 years of follow up and both have functioned very well at work and interpersonally.

Long-Term Buprenorphine: A Case Series

- ☀ 28 patients: 17 males, average age 36y/o, Washington, Montana, North Dakota
- ☀ Average dose of 92 grams of kratom daily (0.06 - 850gram daily)
- ☀ All patients performed home induction after first appointment
- ☀ Wait 24 hours after last kratom use
- ☀ 4-8mg daily first day, and then 12-16mg.
- ☀ 3 patients stabilized on 4mg, 23 patients 8-16mg, 1 patient at 18mg, and 1 patient at 20mg.
- ☀ Six patients lost to follow-up
- ☀ After 4 weeks, 68% percent negative for kratom, after 8 weeks, 82 % negative, and at 12 weeks 82% negative

ASAM Survey to Chapter Presidents and Members

- ☀ Jan 2020, 711 participation invites sent.
- ☀ 82 responded (11.5%),
- ☀ 57 (82.6% endorsed having encountered patients with KUD
- ☀ 19 (27.5% had patients with only KUD (no past or comorbid
oud)
 - ☀ 17/19 used buprenorphine (6 with talk therapy)
 - ☀ 1 used methadone, 3 used naltrexone, 1 used buspirone

Methadone, Buprenorphine, and Clonidine Mitragnine Withdrawal in Rats

- ✦ Rats received mitragynine (30mg/kg) injected daily for 14 days
- ✦ Withdrawal assessed day 15 (24 hours after abstinence)
- ✦ Then given: methadone (1mg/kg), buprenorphine (0.8mg/kg), and clonidine (0.1mg /kg) over four days during withdrawal
- ✦ Withdrawal included: chewing, head shakes, exploring, digging, yawning, teeth chattering, wet dog shakes, writhing, squeaking, hostility, diarrhea
- ✦ Withdrawal attenuated significantly

Case 3

- ☀ Young man presents with psychosis, irritability, aggression, and with heavy use of both cannabis and kratom
- ☀ More history: multiple hospitalizations, diagnosed previously with schizophrenia, history of opioid use disorder (pain meds) treated with buprenorphine but was noncompliant.
- ☀ Also history of ADHD; overused stimulants. Wants amphetamine
- ☀ Reports using kratom to control his "adhd, hyperactivity....restlessness....", 5 times per day, tea,
- ☀ Since last hospitalization, has agreed paliperidone monthly injection and compliant with it

Case 3

- ✦ Young man presents with psychosis, irritability, aggression, and with heavy use of both cannabis and kratom
- ✦ Very motivated for treatment, because mom wants to kick him out for aggression and continuous agitation. He thinks that his aggression, irritability is because his ADHD and anxiety are not controlled.
- ✦ What other questions would you ask?
- ✦ How would you organize treatment?

Final Takeaways/Summary

- ✦ Sought out applications of Kratom include improvement in mood and energy, reduction in pain, and mitigation of withdrawal symptoms. However, risks of adverse health effects related to addiction, drug-drug interactions, and contamination/adulteration outweigh its use.
- ✦ Motivation Interviewing remains key therapeutic intervention to address Kratom use.
- ✦ Although there are no FDA approved treatments for Kratom use, medications for opioid use disorders show promise.

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