

#### Disclosures

I have no financial relationships with any commercial interest related to the content of this activity.

I will not discuss any off-label use of medications during this presentation.

#### Objectives

Define	Define the herbal extract Mitragyna Speciosa, also known as Kratom
Describe	Describe the pharmacology of Kratom
List	List three adverse physiologic effects of Kratom
Summarize	Summarize anesthetic implications for patients who use Kratom



Let's go back to the Tobocco/Vape Shops



#### Mitragyna Speciosa: Kratom

- Evergreen tree
- Member of the Plantae kingdom, Rubiaceae family
  - Cousin of the coffee plant
- Southeast Asia:
  - Cambodia, Thailand, Phillipines, Malaysia, Papua New Guinea, Vietnam
- Grows at low elevations near savannahs and swamps



#### More about Kratom...



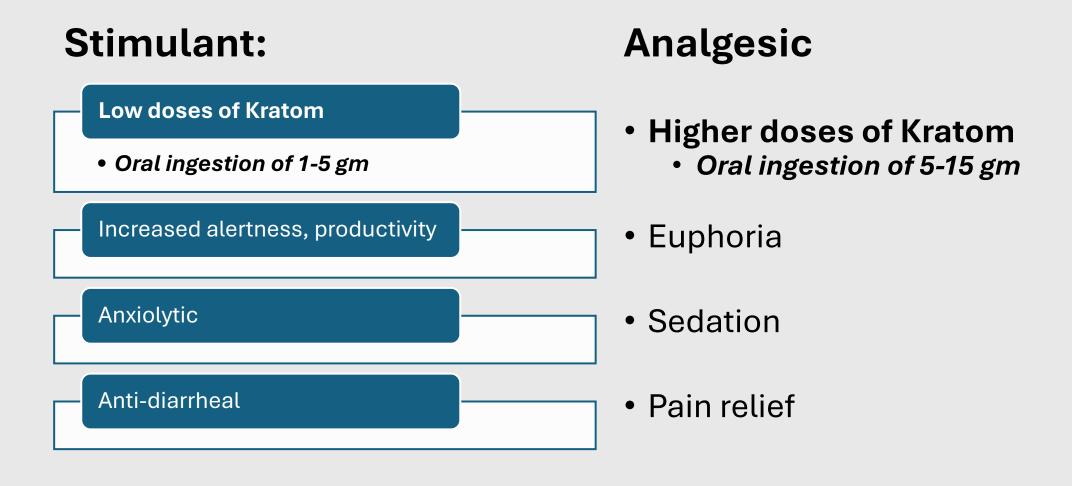
Trees grow 50 feet in height

Wood is harvested, used in construction

When in bloom, has cream colored flowers



#### What physiologic effects does it have?



#### How many people are using Kratom?

2022: 2 million users

2025: Estimates between 11-6 million (Medscape.com)

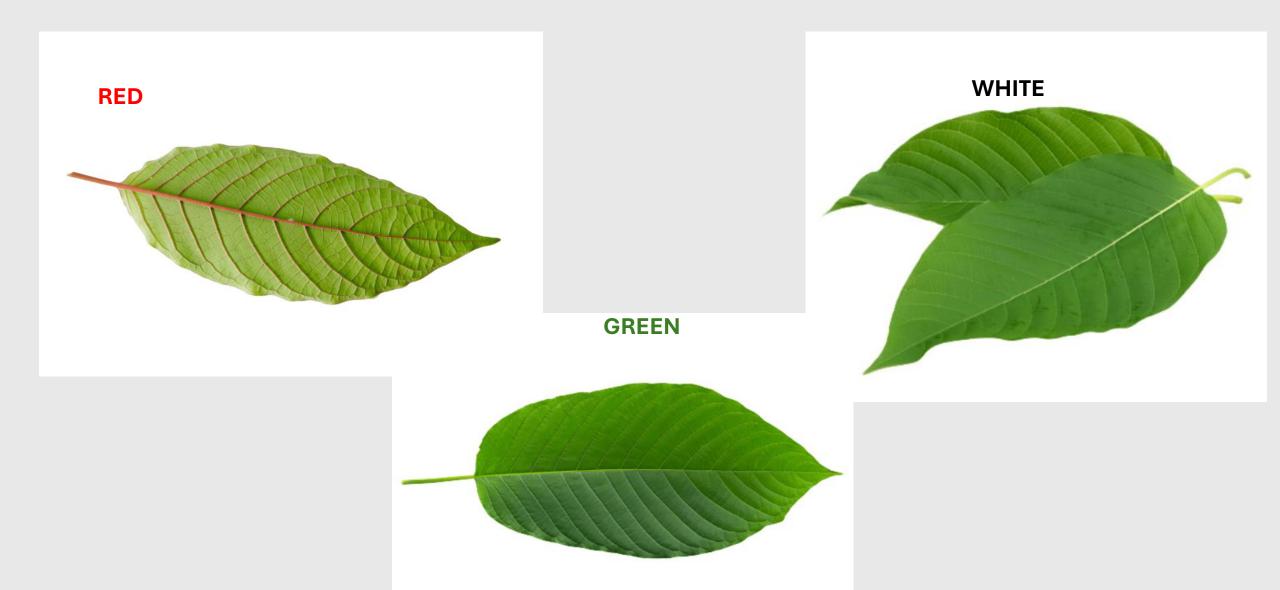
2024: 2.2 **billion** dollars in retail sales

#### Is it detected in a drug test?

Routine drug screens do NOT detect Kratom Can be detected by gas chromatography-mass spectrometry

Urine or hair samples used

#### 3 Strains -> Based on Leaf Veins!



## Oh wait, there's more...a yellow strain!

- Does not occur in nature
- White leaves are dyed yellow
  - Alters the effects of the plant
- Potent, euphoric
- Mood booster



#### The pharmacology behind the effects....

- Over 40 identified alkaloids isolated
  - 4 active alkaloids: Mitragynine, 7-Hydroxymitragynine, Speciociliatine, Corynantheidine
- Most abundant: Mitragynine
  - 60-65% of the dried leaves
- Most active: 7-Hydroxymitragynine
- Mostly responsible for the psychoactive and analgesic effects

- 7-Hydroxymitragynine is antinociceptive
  - "7-OH"
  - "7-Hydro" or "legal Morphine"
  - 5 times more potent than Morphine!
- G-protein based <u>agonist</u> at the <u>Mu</u> receptor
- Antagonist at the Kappa, Delta receptors

#### So...is Kratom considered an opioid?

 Opioid-like! Similar to Buprenorphine

 But unlike Fentanyl, Heroin, Morphine because is not a full agonist

 When Kratom binds to the Gprotein receptor, the effects with full agonists are not seen

#### Kratom also has these effects:

Inhibition of Cyclooxygenase-2 (COX-2) pathway

Inhibition of presynaptic Acetylcholine release, Adenosine release

Alpha-2 agonism

Calcium channel blockade

Serotonin (5-HT2A) antagonism

Dopamine (D1) antagonism

#### Which results in...and is used for:

Anti-inflammatory effect= pain (COX2)

Anxiolysis, vasodilation (a2 agonism)=relaxation, HTN, opioid

withdrawal

Analgesia, vasodilation (Calcium)= pain, sexual stamina

Decreased anxiety/depression (5HT2A)

Antipsychosis (D1)=Substance misuse, relief of PTSD

#### Pharmacokinetics: the alkaloids in Kratom

#### Mitragynine: lipophilic opioid

- Peak plasma concentration: 90 minutes
- Half-life: 23 +/- 16 hours

#### Hepatic metabolism

- Inhibit the Cytochrome P450 System
  - CYP2D6 (strongest), CYP3A4 (weak)

Kratom users have a highly variable reported drug effect

August 31, 2016



**Drug Enforcement Administration** 

@DEAHQ

## DEA Announces Intent To Schedule Kratom



#### DEA will ban kratom, a popular herbal supplement

MARK FRAUENFELDER / 9:18 AM WED AUG 31, 2016



#### DEA Withdraws Kratom Ban, Opens Formal Comment Period

www.forbes.com/sites/davidkroll/2016/10/13/dea-withdraws-kratom-ban-opens-formal-comment-period/

HEALTH REPORTING IN THE STATES

#### Kratom Gets Reprieve From Drug Enforcement Administration

www.npr.org/sections/health-shots/2016/10/12/497697627/kratom-gets-reprieve-from-drug-enforcement-administration

-**从**- News

#### DEA Withdraws Kratom Ban Notice After Public Outcry

The DEA's Notice of Intent to ban the herbal analgesic kratom led to an online campaign and subsequent withdrawal of the decision pending further action.

## However--Kratom sales are illegal in these states:

- Alabama
- Arkansas
  - Indiana
- Rhode Island
  - Vermont
  - Wisconsin



#### **OHIO POLITICS**

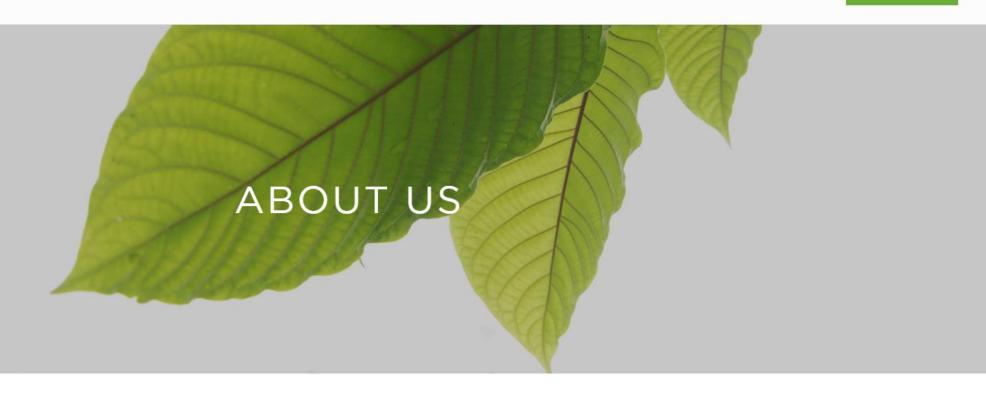
## DeWine seeks to ban sale of Asian plant, derivatives, citing 200 overdose deaths

Published: Aug. 25, 2025, 4:08 p.m.

Ohio kratom ban: Gov. Mike DeWine wants to declare it an illegal drug

AMERICAN KRATOM

ASSOCIATION



#### **OUR MISSION**

The American Kratom Association (AKA) is dedicated to protecting the rights of all Americans to legally consume safe kratom to better manage their overall health and well-being.

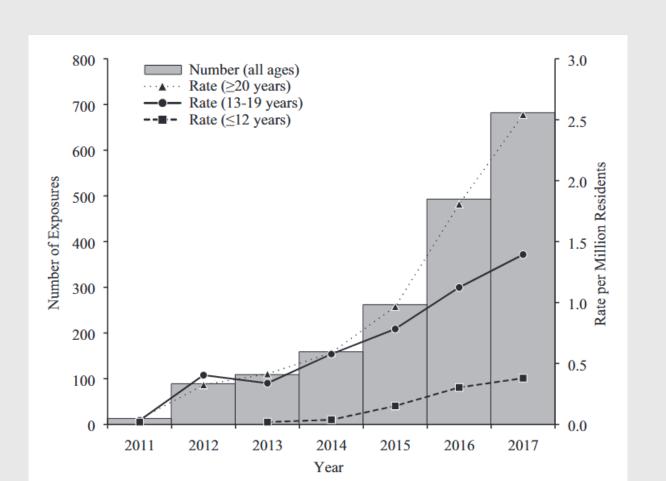
#### What are signs/symptoms of a Kratom overdose?

- GI: Nausea, vomiting, hepatotoxicity
- CV: HTN, tachycardia, prolonged QT, cardiac arrest
- Neuro: Drowsiness, confusion, agitation, hallucinations, seizures, coma
- Renal: Nephrotoxicity
- Deaths reported →
  - almost exclusively Americans
  - Adulterated or concentrated leaf extracts
  - Contaminated products from importers
  - Strong correlation with ingestion of illicit substances
    - Prescription opioids, cannabis, and others

#### Kratom exposures reported to United States poison control centers: 2011-2017

Sara Post<sup>a,b</sup>, Henry A. Spiller<sup>c,d</sup>, Thitphalak Chounthirath<sup>a</sup> and Gary A. Smith<sup>a,d,e</sup>

<sup>a</sup>Center for Injury Research and Policy, The Research Institute at Nationwide Children's Hospital, Columbus, OH, USA; <sup>b</sup>Northeast Ohio Medical University, Rootstown, OH, USA; <sup>c</sup>Central Ohio Poison Center, Columbus, OH, USA; <sup>d</sup>Department of Pediatrics, College of Medicine, The Ohio State University, Columbus, OH, USA; <sup>e</sup>Child Injury Prevention Alliance, Columbus, OH, USA



# Treatment for Kratom overdose:

#### Supportive

- Naloxone if indicated
- IV fluids
- Anticonvulsants
- Benzodiazepines
- N-acetylcysteine
- Ursodiol

#### Life-threatening organ failure management

- ACLS
- Liver transplant

#### What are withdrawal symptoms of Kratom?

Both physical and psychological!

GI: abdominal pain, anorexia, nausea/vomiting, diarrhea

CV: HTN, Tachycardia, hyperhidrosis and hot flashes

Neuro: Myalgia, myoclonus, insomnia, irritability, blurred vision

Symptoms present hours to days after last Kratom use!

- Abstinence: Naltrexone
- MAT (SUD): Buprenorphine-Naloxone
- Supportive:
  - IV Fluids
  - Benzodiazepines
  - Clomipramine
  - Clonidine
  - Gabapentinoids
  - Haloperidol
  - Hydroxyzine

## Treatment for Kratom Withdrawal

What does the literature say about anesthesia concerns in patients who use Kratom?

Let's look at a couple of case reports....



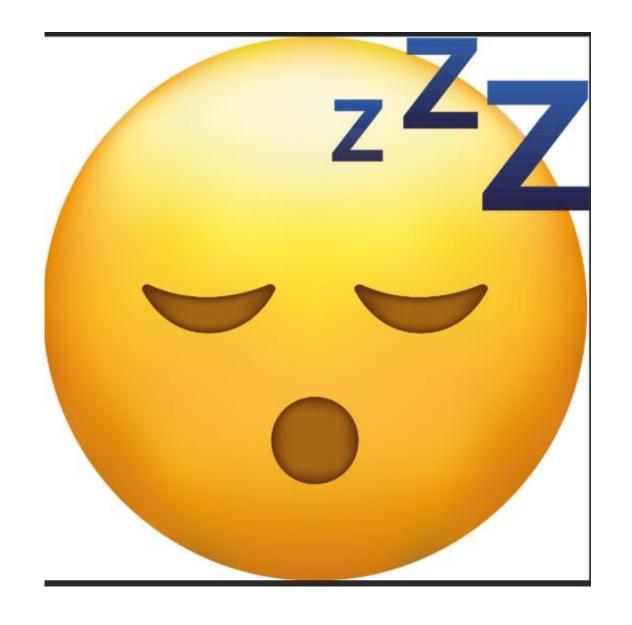
#### Kratom and General Anesthesia: A Case Report and Review of the Literature

Deborah J. Vermaire, MD, Deborah Skaer, BS Pharm, and William Tippets, DO

- 15-year-old male, lower back injury while playing basketball
- Unable to attend school, ambulated with a cane
- MRI: Central stenosis, bilateral recess compromise at L2-L3
- Scheduled for Lumbar Laminectomy L2-L3
- PMH: + snoring, weight 100 kg, otherwise healthy
- Meds: Gabapentin 400 mg TID, Naproxen 500 mg BID
- Mom revealed in preop interview patient was taking Kratom, ½ tsp 3-4 times per day x 3 months

## Induction, Maintenance, & Emergence

- Induction: Fentanyl, Lidocaine, and Propofol
  - No muscle relaxation, intubated
- Maintenance: Sevo and Fentanyl (250 mcg)
  - 100 mg Ketamine
  - 1000 mg IV Acetaminophen
  - 30 mg Ketorolac
  - 12 mg Decadron
  - 4 mg Zofran
- <u>Emergence</u>: Extubated and taken to PACU in stable condition



#### Postoperative Course

Night one: Hydromorphone PCA, Gabapentin, Naproxen, Acetaminophen POD 1: PCA D/C'd (received 5.4 mg Hydromorphone over 18 hours)

Oxycodone 10 mg q 4 hours prn

BP and HR ranges normal

Reaching PT goals

POD 2: D/C'd to home on Gabapentin, Naproxen, & Oxycodone Patient and parents counseled on the risk of using Kratom in conjunction with narcotics

Family opted to continue with Kratom and refrain from narcotics

#### **Anesthetic Challenges Posed by Heavy Kratom Users**

Elisa Lund <sup>1</sup>, Aaron B. Low <sup>2</sup>, Jennifer D. Allan <sup>1</sup>, Jose A. Puentes <sup>1</sup>, David N. Flynn <sup>1</sup>

Anesthesiology, University of North Carolina, Chapel Hill, USA
 Pediatric Anesthesiology, University of North Carolina, Chapel Hill, USA

Corresponding author: Elisa Lund, elisa\_lund@med.unc.edu

- 18-year-old male, bilateral idiopathic condylar resorption → retrognathia and OSA
- Scheduled for LeFort I Osteotomy with bilateral 5<sup>th</sup> rib resection, bilateral mandibular bone grafts, & genioplasty with genioglossus advancement
- PMH: Substance use  $\rightarrow$  occasional Cannabis, rare LSD
- OSA; no other PMH, weight 52 kg
- No medications, daily Kratom use up to 35 g/day

### Induction and Maintenance



- Induction: 150 mcg Fentanyl, 60 mg Lidocaine, 300 mg Proprofol
  - No loss of consciousness
  - Mask ventilated w 4-6% Sevoflurane
  - After LOC, 60 mg
     Succinylcholine → intubation
- <u>Maintenance</u>: Propofol infusion @ 150-200 mcg/kg/min + Remifentanil infusion @ 0.15-0.2 mcg/kg/min → BIS 50
  - After incision, MAP 60-110 mmHg
  - Boluses of Fentanyl and Dexmedetomidine
  - Infusions of Nicardipine and Esmolol required to achieve MAP<80 mmHg</li>
    - Continued until completion of surgery

#### Maintenance, continued

- Case was 9 hours in length
  - 5400 mg Propofol
  - 5.5 mg Remifentanil
  - 3200 mg Esmolol
  - 19 mg Nicardipine
  - 52 mcg Dexmedetomidine
  - 400 mcg Fentanyl
  - 2 mg Morphine
  - 800 mg Acetaminophen
  - Bupivacaine infiltration at sites by surgeon

- Prior to emergence:
  - Thoracic epidural placed in OR
  - Loading dose: 5 mL 1.5% Lidocaine with 1:200,000 Epinephrine
  - Infusion 0.125% Bupivacaine started at 7 mL/hour

## Emergence



## Agitation and emergence delirium, requiring:

20 mg bolus of Propofol

4 mcg boluses of Dexmedetomidine (20 mcg total)

25 mg Ketorolac

1 mg Lorazepam



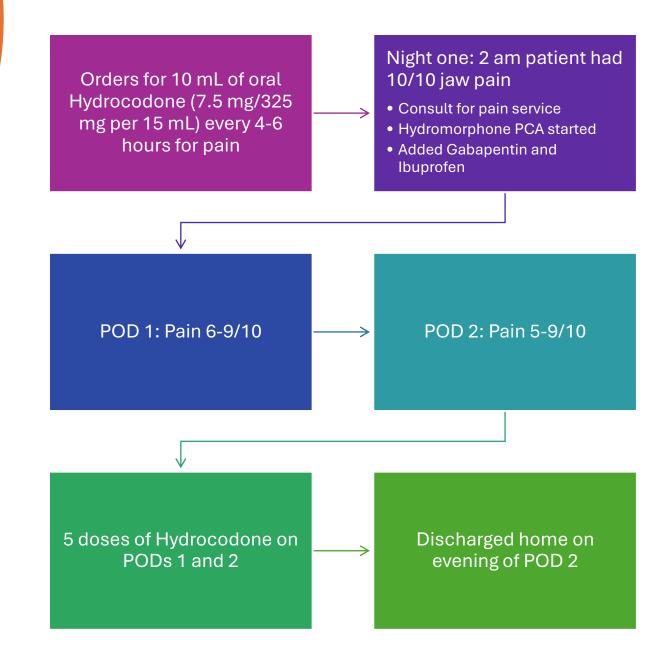
### Pain 10/10 at mandibular incision

5 mg oral Oxycodone solution

Pain → 8/10

Transferred to inpatient pediatric floor

#### Postoperatively:



#### In this case:

"Habitual, high-dose Kratom abuse likely contributed to the observed anesthetic resistance, due to upregulation of receptors in the central nervous system"

and

"Refractory pain was attributed to opioid resistance secondary to habitual Kratom use"

Lund et al (2022)

# Other takeaways:

- Patient complained of significant jaw pain, but not thoracic pain
  - Regional anesthesia?
- 2) In the PACU, his agitation resolved after he received Fentanyl, Dexmedetomidine, Lorazepam, & Oxycodone
  - This may have been appropriate treatment for withdrawal symptoms (although inadvertent)

### Kratom and Anesthesia Considerations

 NO guidelines currently exist
 for the anesthetic management of patients who use Kratom

#### But until they do.... Preoperatively:

#### Ask, ask, ask

- "Do you take anything additionally to your medications I see here, such as supplements that are not prescribed?"
- Vitamins or herbals?

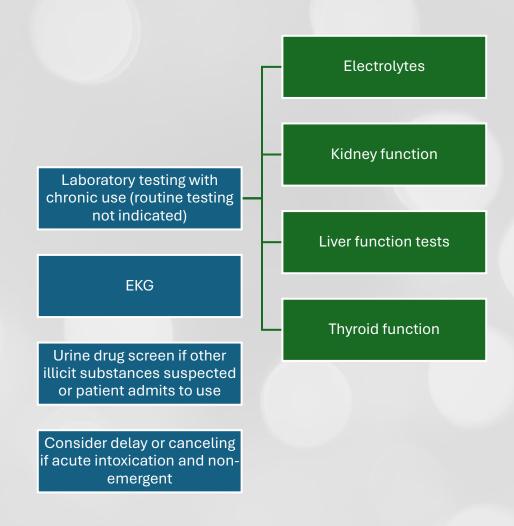
#### If you discover Kratom use:

- Dose
- Frequency
- History of adverse effects or withdrawal symptoms (looking for opioid cross-tolerance)
- Inquire about other illicit substances

# Consider counseling about pain management strategies

Kratom +
 opioids → oversedation,
 respiratory depression,
 and possible death

### Preoperatively, also consider:



#### Additionally:

1

Consider weaning from Kratom prior to surgery

2

Avoid abrupt withdrawal

3

Consult an addiction specialist with heavy Kratom users

#### Intraoperatively...be prepared!

Interactions between Kratom and anesthesia

Vigilance!

Consider the activity of Kratom at opioid, COX-2, alpha-2, Calcium, Serotonin, Acetylcholine, and Adenosine receptors

#### As part of your anesthetic, consider:



Regional anesthesia if possible

SAB or epidural Peripheral Nerve Blocks



Ketamine, Dexmedetomidine, Magnesium



Gabapentin, Acetaminophen, Ketorolac

#### Intraoperatively, you could see:

- Prolonged QT interval
- Hypotension
- Hypertension
- Prolonged neuromuscular blockade
- Prolonged emergence
- Emergence delirium

**EVEN...** 

Extrapyramidal symptoms or Serotonin Syndrome

#### Postoperatively

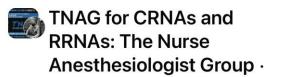
Education about drug interactions

Caution regarding continued Kratom use in the absence of safety data

Information about additives like bacterial and heavy metals

Referrals for patients interested in treatment

#### Social Media Consults



**Follow** Jan 1 · 💽

Has anyone taken care of a patient using Kratom chronically? Ortho case. The patient was told yesterday to stop. Surgery is scheduled two weeks from today. From what I have read, pain control can be an issue, and possibly there can be refractory hypertension. This is my first time hearing of this substance. Any insight is appreciated.

**\$\alpha \alpha \alpha** 

43 comments



#### TNAG for CRNAs and RRNAs: The Nurse Anesthesiologist Group

Michael Stovall · Dec 12, 2024 · 🖪

Any suggestions for heavy Kratom users? Best I can find is that they should wean off for at least 7 days before surgery. Not a well studied herbal and seems only case reports out there, no legit studies for recommendations

ம் Like

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Most relevant ~



Ryan Gundrum · 39w

I had a HEAVY user who cut his dose in half 3 days prior but still used the day of surgery. Did a lot of education up front to him about it and he did fine. I did not



#### Lauren Hostetler · 36w

All adjuncts. Regional block. Ketamine. Toradol. Ice.

Magnesium. Precedex.

Everything besides opiods

Reply













#### In conclusion

The use of Kratom is increasing in the United States

Kratom is a stimulant at low doses and has opioid-like effects at high doses

Patients who use
Kratom will
present as
patients needing
an anesthetic

There are no
current
anesthetic
guidelines in
place for patients
who use Kratom

# Conclusion, continued:

Patients need to be advised that their responses to anesthesia could be unpredictable and pain management may be challenging



Heavy Kratom use may need:

More narcotics

Multimodal analgesia

Regional or neuraxial anesthesia

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Thank you!!! I will be happy to answer any questions!

