Opioid-Like Kratom Use Booming, Cheap, Unregulated, and Addictive

By Leon Gussow, MD

The U.S. Food and Drug Administration confiscated 90,000 bottles of a liquid dietary supplement called Relak2pro from a company in northern Illinois in early January. The label said the product contained the medicinal herb kratom (pronounced KRAT-um), an ingredient the FDA said “could pose a risk to public health and have the potential for abuse.”

That same week, The New York Times published an article noting that opioid addicts sometimes use kratom for detoxification and to relieve withdrawal symptoms, but it was turning out that kratom itself can be addictive. (http://nyti.ms/IR8suUT.) Ed Boyer, MD, PhD, a toxicologist at the University of Massachusetts, remarked in that article, “It’s a fascinating drug, but we need to know a lot more about it. Recreationally or to self-treat opioid dependence, beware — potentially you’re at just as much risk [as with an opiate].”

Kratom is legal in the United States — sort of. An FDA alert from last December allows for seizure of specific products known to contain kratom, but does not ban the drug. The Drug Enforcement Agency has called the herb a “drug of concern” with no known medical use, but has not classified it as a Schedule I substance. Vermont, Tennessee, Wyoming, and Indiana, however, have banned kratom.

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Many clinicians are not all that familiar with the drug, if they have heard of it at all. Kratom is derived from leaves of Mitragyna speciosa, a tree native to Southeast Asia, especially Thailand and Malaysia. M. speciosa is from the same family as the coffee tree. Traditionally, local residents chew the leaves to relieve fatigue, increase sociability, and alleviate muscle aches. This is similar to the use of coca leaves in South America and khat in Africa and parts of the Middle East. Kratom has also been used as a cure for cough, diarrhea, and sexual dysfunction.

Widely Available
Kratom is available as a leaf, powder, or tea-like beverage. It can be legally sold over-the-counter as a dietary supplement in most states. The FDA ruled it has no medicinal value, so it cannot be sold or advertised with the claim that it treats or cures any disease. Kava bars — establishments that serve herbal beverages, often of the mind-altering variety — provide a number of concoctions containing kratom in some parts of the country. The drug is widely available for sale over the Internet, too. A recent Google search for “buy kratom” returned more than 600,000 hits. Prices vary widely depending on the strain, but one website listed its price at around $12 an ounce. (http://bit.ly/lwwCX0Q)

Kratom has a dose-dependent dual action that is somewhat unusual. It is a stimulant in low doses, causing an increase in alertness and stamina that at times can be accompanied by anxiety and irritability. But at higher doses, it causes opioid-like effects, including analgesia, pruritus, nausea, and constipation. Sedation and stupor may occur at very high doses, too. Respiratory depression tends to be less severe than that seen with opioids. At least three cases of seizures associated with exposure to kratom have been reported in the literature. Two of these involved co-ingestants — the stimulant modafinil (Provigil) in one case, the anticholinergic plant Datura stramonium (Jimson weed) in the other. No deaths in the United States have been attributed to kratom alone. Sweden reported nine deaths in 2010 that involved young people who ingested a legal herbal preparation called Krypton. This product contained kratom as well as caffeine and O-desmethyltramadol, the major active metabolite of tramadol. Adverse effects associated with chronic exposure to kratom have been reported — two cases of intrahepatic cholestasis in patients after they had ingested kratom powder for several weeks. Unfortunately, laboratory confirmation of exposure was obtained in only one of those cases. Providers also described anorexia, weight loss, constipation, hypothyroidism, and facial hyperpigmentation in patients with repeated exposure to kratom.

Supportive Care
Treatment for acute kratom toxicity is largely supportive. Naloxone may reverse some of the opioid-like effects of kratom (experience so far has been equivocal, but it may not be needed because respiratory depression tends to be mild in the absence of co-ingestants. The initial drug of choice for seizure activity is a benzodiazepine.

Kratom is clearly addictive, according to The New York Times article. Regular use can create cravings for the drug. Abstinence after chronic use can cause a withdrawal syndrome similar to that associated with opioids. Manifestations include irritability, restlessness, anxiety, yawning, lacrimation, rhinorrhea, abdominal pain, diarrhea, tremors, and diaphoresis.

More than 40 alkaloids and other compounds have been isolated from kratom leaves. The two major pharmacologically active alkaloids are mitragynine and 7-hydroxymitragynine (7-HMG). Both have a high affinity for opioid mu-receptors and are more potent than morphine. Mitragynine seems to affect serotonin and noradrenergic pathways in the spinal cord, and has a clonidine-like effect on post-synaptic alpha-2 receptors, perhaps augmenting its role in alleviating symptoms of opioid withdrawal.

Read more about kratom in the very good article, “The Pharmacology and Toxicology of Kratom: From Traditional Herb to Drug of Abuse” by Warner, et al. (Int J Legal Med 2016;130[1]:127.) This comprehensive review has an extensive list of references, and I highly recommend it. ENM

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