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Utox Update

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Kava

Case [1]

A 54-year-old man was hospitalized with altered mental status. He was lethargic and disoriented. His current medications included alprazolam, cimetidine, and terazosin. Vital signs were normal, and laboratory studies were negative for ethanol and positive for benzodiazepines. After several hours he became more alert and explained that he had been taking kava, a "natural tranquilizer" for the past 3 days. He denied overdosing on kava or alprazolam. The patient had a normal mental status prior to beginning treatment with kava. The kava most likely acted synergistically with the alprazolam to lower his mental status.

Background [2]

Kava, also known as kawa, ava, or awa is an herb derived from the roots of the plant *Piper methysticum* or "intoxicating pepper." A member of the pepper family, this plant is a large shrub that is cultivated in many Pacific Islands. The use of kava predates the written history of the people of many South Pacific Islands where a kava beverage was often used in ceremonial, religious, medicinal, and social events. This beverage was traditionally prepared by chewing or pulverizing the root of the kava plant, steeping it in water, and then filtering the liquid. Kava reportedly produces an intoxicating, calm, sociable, and euphoric feeling. Its popularity is growing in the United States and it is used to relieve anxiety, to improve sleep, and to produce muscle relaxation. It is available in dietary supplement stores in capsule and liquid form.

IN THIS ISSUE

Pharmacology [3,4]

The pharmacological activity of kava appears to be from kava lactones found in the lipid soluble portion of the root. There are over six kava lactones that have been identified. The major kava lactones are methysticin, kawain and dihyrokawain. Preparations from the raw root contain between 3-20% kava lactones. Following ingestion, kava has been shown to have anxiolytic, sedative, local anesthetic, skeletal muscle relaxant and anticonvulsant properties. Kava is not believed to affect benzodiazepine or GABA receptors, although the exact mechanism of action is not known.

Kava may antagonize dopamine. Dystonic reactions were reported in three patients who had taken kava. In one patient with a prior history of dystonic reactions a phenothiazine, involuntary neck extension and forceful deviation of the eyes occurred within 90 minutes of the first dose of kava. In a 22-year-old female, oral dyskinesia, torticollis and painful twisting of the trunk occurred four hours after a dose of kava. In a third woman oral dyskinesias occurred after the administration of kava three times daily for four days. In all three cases the symptoms either resolved spontaneously or were rapidly reversed with biperiden, an anticholinergic agent. There is little information on the pharmacokinetics of kava. Peak plasma concentrations occur in 1.8 hours. The half-life of kava lactones is about 9 hours and elimination of kava and its metabolites occurs through renal and fecal excretion.

Toxicology [3]

The first effect after drinking kava is a numbing or tingling of the mouth and sedative effects. "Kava dermopathy" appears after a few months of daily kava consumption. First reported by members of Captain Cook's expedition, it is a dry, scaly, ichthyformous rash appearing on the palms of the hands, the soles of the feet, the forearms, back, and shins. The cause of this dermopathy is unknown. It was hypothesized to be a niacin deficiency, however administration of nicotinamide was not shown to resolve this condition. Another hypothesis is that it relates to the interference of cholesterol metabolism. Chronic toxicity may also cause facial swelling and "bloodshot" eyes.

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These symptoms resolve several weeks after discontinuation of kava.

Mild gastrointestinal disturbances, visual accommodation disorders, pupil dilation, and disorders of equilibrium have also been associated with kava. A minimal toxic dose has not been established.

Drug interactions do occur with kava, as seen in the case presented above. Kava potentiates the effects of central nervous system depressants such as alcohol, barbiturates, and benzodiazepines. The anti-dopaminergic properties of kava may also cause an interaction with dopamine agonists such as levodopa, selegiline, and bromocriptine

Treatment

It is not known if gastric decontamination is useful in acute kava ingestions. Ipecac syrup is not recommended because of the potential for CNS depression. Activated charcoal may prevent absorption in an acute ingestion. Otherwise, treatment is symptomatic and supportive. Discontinuing use is the treatment for kava dermopathy. Adverse effects and toxicity from chronic kava use should resolve within a few weeks after discontinuation.

Summary

Kava has a long history as a ceremonial beverage in the South Pacific Islands. It has become more popular in Western societies and is available at health food stores in capsule or liquid form. Although kava is promoted as a natural alternative to anti-anxiety medications and sleeping pills, it should be used with caution and treated as a drug. Side effects of kava include extrapyramidal reactions, sedation and gastrointestinal distress. Chronic toxicity may cause kava dermopathy, which is reversible by abstinence. Patients using kava should avoid benzodiazepines, alcohol, and driving because of the depressant effects on the central nervous system.

Amber Overton, PharmD

References

1. Almeida JC, Grimsley EW. Coma from the health food store: interaction between kava and alprazolam. Ann Intern Med. 1996;125:940-941.
2. Singh YN, Blumenthal M. Kava: an overview. Distribution, mythology, botany, culture, chemistry, and pharmacology of the South Pacific's most revered herb. Herbalgram. 1997;39:34-55.
3. Pepping J. Kava: Piper methysticum. Am J Health Syst Pharm. 1999;56:957-960.
4. Anonymous. Kava monograph. In: Review of natural products. St. Louis, MO: Facts and Comparisons, 1999.

The Utah Poison Control Center thanks

McNeil Consumer Healthcare

for their generous contribution which allowed us to produce and distribute this newsletter.

What's New at the UPCC

Top notch staff: The UPCC is pleased to announce that 90% of the technical staff are now Certified Specialists in Poison Information. This means they have passed their national competency examination demonstrating their expertise in clinical toxicology. This examination is required of each specialist who has worked at least 2,000 hours at the poison control center and handled 2,000 exposure calls. Recertification is required every seven years. The only specialist who does not have this certification is eligible to take the examination in May 2002.

Scholarly activity: The UPCC will be sending six staff members to the upcoming North American Congress of Clinical Toxicology meeting in Montreal, Quebec. Three specialists in poison information and the medical director will be presenting the following poster presentations:

> Green DI, Caravati EM. Coma in a toddler from low-dose carisoprodol.
>
> Dahl B, Caravati EM, Dunson M. Surreptitious brodificoum poisoning.
>
> Caravati EM, Herman B. Treatment of severe ethylene glycol poisoning without hemodialysis.
>
> Grover J, Caravati EM. Right bundle branch block and delayed seizures associated with citalopram and fluoxetine ingestion.

If you would like additional information about these abstracts, please contact us at (801) 581-7504

Grant award: The UPCC was awarded a grant through the Maternal and Child Health Bureau of HRSA, Department of Health and Human Services under the Poison Control Centers Stabilization and Enhancement Grant Program. This three-year award will address space, medical direction and outreach education. As part of this grant program we will conduct a needs assessment for professional education, develop a customer satisfaction survey for health professional users of the UPCC as well as the public and will be developing a web site. Stay tuned for more details as we embark on this exciting endeavor.

A new number: Through assistance from the Centers for Disease Control and Prevention, the American Association of Poison Control Centers has launched a nationwide toll-free number for poison centers. The number is (800) 222-1222 and will route a caller to the nearest poison control center. The UPCC will eventually switch entirely to this toll-free number. Stay tuned for more details. The UPCC plans to "launch" this new number as part of its outreach program over the next year.

Ipecac at Home

Ideas for this column come from the specialists in poison information (SPI) who staff the phones at the Utah Poison Control Center (UPCC). The purpose of these articles is to address topics about which the UPCC receives multiple inquiries. In the last few months there have been several questions about the use of ipecac at home to treat unintentional poison exposures in children.

There is controversy within the toxicology community about the role of ipecac in the treatment of a poison exposure. The American Academy of Clinical Toxicology (AACT) published a position statement in 1997. It states that "There is no evidence from clinical studies that ipecac improves the outcome of poisoned patients and its routine administration in the emergency department should be abandoned. There are insufficient data to support or exclude ipecac administration soon after poison ingestion". However, some research demonstrated significant reduction in drug absorption following ipecac-induced emesis. Often this research is done in animal models or in healthy adult volunteers at sub-toxic doses, thus the information is difficult to apply to many overdose scenarios.

The UPCC currently considers the use of ipecac in a very limited set of pediatric exposures at home. Patients must be older than 12 months to be candidates for ipecac treatment at home. A specific set of substances (acetaminophen, ibuprofen, cough and cold preparations etc.) are considered appropriate for possible treatment with ipecac induced emesis.

The exposure must be unintentional, recent (within one hour of the call) and a maximum amount of exposure should be known. Ipecac is never used for caustic agents, unknown amounts of substances, hydrocarbons or substances that can decrease level of consciousness. All households where children live or visit are recommended to have an unopened bottle of ipecac in case of a poisoning emergency. The bottle does have an expiration date, check to make sure it has not expired. This prevents a delay in treatment, if it is on hand. It is always recommended that the caregiver call the UPCC before administering ipecac to prevent unnecessary or inappropriate use. Public education could prevent the use of inappropriate emetics such as fingers, spoons, mustard, salt and egg whites. While these seem to be antiquated remedies it is surprising how often they are used in a moment of panic at home. At this time, use of ipecac in a health care facility is rare and activated charcoal is typically the decontamination method of choice.

In conclusion, the UPCC recommends that all households with children have ipecac available but only use it after consulting the poison control center.

References

Quang LS Woolf AD: Past, present, and future role of ipecac syrup. Current Opinions in Pediatrics 2000, 12:153-162.

Position Statement: Ipecac Syrup. Clinical Toxicology 1997, 35 (7), 699-709

Meet the UPCC Staff

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PharmD, RPh, CSPI

I am a native of Utah and have lived along the Wasatch Front my entire life. I graduated from the University of Utah in Biology, Pharmacy and most recently finished my Doctorate of Pharmacy degree at the U. I have worked at the Utah Poison Center for over six years. My favorite part of the job is the satisfaction of helping others and that no two days are just alike.

Poison Exposures in Utah and in the US

This spring the UPCC published its 2000 Annual Report. This report highlights the nearly 40,000 human exposures reported to the Utah Poison Control Center in 2000. For a copy of the 2000 Annual Report, please call the UPCC Administrative Office at (801) 581-7504 or E-mail barbara.crouch@hsc.utah.edu.

The 2000 Report of the American Association of Poison Control Center's Toxic Exposure Surveillance System is published in the September 2001 issue of the *American Journal of Emergency Medicine*. This report highlights the over 2 million poison exposures reported by poison centers across the United States (including the UPCC). You can also find this report, as well as previous reports on the American Association of Poison Control Center's website at www.aapcc.org. Follow the links for Poisoning Data – Tess!

Both the UPCC report and the AAPCC report highlight that most poison exposures reported to poison control centers are unintentional and most involved children less than 6 years of age. Both reports are rich with data about the epidemiology of poison exposures in Utah and across the US. The national report also highlights 920 exposures that resulted in a fatal outcome. While fatal outcomes occur in less than 0.1% of all reports to poison centers, much can be learned by examining these cases in depth. The AAPCC report provides additional details about these cases to assist us in understanding more about the circumstances surrounding those exposures that result in a fatal outcome. A detailed table highlights the substances involved, age of the victim, route of exposure, reason for exposure and any serum concentrations of the offending agent. In addition, a number of the fatal outcomes are summarized in abstracts that are included with the report.

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Utah Poison Control Center Staff

Please send comments and suggestions for future articles to the editor of UTOX Update at:
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*CSPI denotes Certified Specialist in Poison Information.

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The largest number of deaths involved analgesics, antidepressants, sedative/hypnotics, stimulants and street drugs, cardiovascular agents and alcohols. The majority of exposures resulting in a fatal outcome were a result of an intentional exposure (79%) and involved those ages 20 and older (90%). There were 20 deaths in children less than 6 years of age. Analgesics were involved in 5 of these deaths, pesticides in 2. The remaining deaths involved one of the following: carbon monoxide, diphenhydramine, diphenoxylate/atropine, lead, methanol, norfloxacin, snake bite and valproic acid. There were 6 deaths in children ages 6-12 years. Tricyclic antidepressants were involved in 3 of the deaths, inhalant abuse in 2 and carbon monoxide in 1. There were 66 deaths in teenagers. Drugs of abuse were involved in 21 deaths, analgesics in 15, antidepressants in 9 and inhalant abuse was involved in 7. There were 2 deaths each involving plants, antipsychotic agents and cough and cold preparations and 1 death each involving carbon monoxide, carisoprodol, diphenhydramine, ethylene glycol, hydroxychloroquine, local anesthetics, sodium chloride, and valproic acid.

Litovitz TL, Klein-Schwartz W, White S, Cobaugh DJ, Youniss J, Omslaer JC, Drab A, Benson BE. 2000 Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 2001; 19:337-395.

Public Education Materials

Poison prevention display boards, brochures, telephone stickers, emergency action cards, videos, posters, and drug look-a-like displays are available. In addition, poison prevention education training will be offered to communities throughout Utah. Display materials and program development ideas, presentations and lesson plans to address the specific exposure problems in your community will be available. If you are interested in becoming a trainer in your area or you would like materials, please call Heather Foulger at (801) 585-7187 or email her at heather.foulger@hsc.utah.edu. Tell your colleagues or related health care agency personnel about this upcoming opportunity.

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