CASE REPORT
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Yohimbine: A New Street Drug

Following the ingestion of an alleged aphrodisiac known as "yo-yo," a 16-year-old girl experienced an acute dissociative reaction accompanied by weakness, paresthesias, and incoordination. Subsequent symptoms included anxiety, headache, nausea, palpitations, and chest pain. Hypertension, tachycardia, tachypnea, diaphoresis, pallor, tremors, and an erythematous rash were noted on physical examination. Serum epinephrine and norepinephrine levels were found to be elevated. Symptoms resolved spontaneously but lasted approximately 36 hours. The ingested substance was identified as yohimbine. The pharmacology of yohimbine and the treatment of yohimbine poisoning are discussed. [Linden CH, Vellman WP, Rumack BH: Yohimbine: A new street drug. Ann Emerg Med October 1985;14:1002-1004.]

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INTRODUCTION

Yohimbine has been used extensively as a "pharmacological probe" for the study of alpha-2 adrenergic receptors.[1] In contrast, clinical experience with this drug has been rather limited and its usefulness as a therapeutic agent remains to be determined. Although there is no evidence to support the alleged aphrodisiac properties of yohimbine, its CNS and sympathomimetic activity, as illustrated by this case, suggest that this drug may have a high potential for abuse.

CASE REPORT

At 10:00 PM on the day prior to admission, a 16-year-old girl ingested an estimated 250 mg of a white powder said to be yohimbine. The powder was given to her by a friend to test its purported aphrodisiac properties. It was said to have a bitter taste.

Twenty minutes following ingestion the patient noted weakness, generalized paresthesias, loss of coordination, and a dissociative state. She said that she felt separated from her body and physical surroundings, and she had difficulty remembering the events that occurred during the ensuing six hours. She also complained of a severe, squeezing headache associated with dizziness and tremors. The dizziness was described as a faint or weak feeling.

Four hours after ingestion the patient noted severe pressure-like substernal chest pain, which awakened her from a brief period of sleep. There were no associated symptoms except for continued anxiety, shakiness, and weakness. The chest pain resolved spontaneously after about two hours and the patient went back to bed.

On awakening the next morning the patient still felt weak and shaky and noted decreased hearing in her right ear. She subsequently developed nausea, diaphoresis, and intermittent palpitations. The squeezing headache recurred and was unrelieved by two aspirin tablets. The patient contacted the Rocky Mountain Poison Center at 4:00 PM, and she was advised to go to the nearest ED for evaluation.

On presentation vital signs were as follows: blood pressure, 150/80 mm Hg; pulse, 116; respirations, 24; and temperature, 37.2 C. Physical examination revealed an anxious, well-developed girl. She was pale and slightly diaphoretic, and she had fine tremors of the extremities. A raised, blotchy, erythematous rash was present over the upper back and a submucosal hemorrhage was seen in the right tympanic membrane. Except for tachypnea and

tachycardia, the remainder of the physical examination was unremarkable.

The patient was given oxygen, and cardiac monitoring was initiated. An ECG revealed sinus tachycardia. Arterial blood gases were as follows: pH, 7.44; PO_2, 75 mm Hg; and PCO_2, 36 mm Hg. A urinalysis was unremarkable. Blood, urine, and a sample of the alleged yohimbine were sent for toxicological analysis. She was then admitted and after three hours of bedrest, serum was sent for catecholamine levels. By the next morning the patient was asymptomatic except for decreased auditory acuity on the right side. She was afebrile, and blood pressure was 112/74 mm Hg, pulse was 64, and respirations were 14. No further symptoms were noted and the patient was discharged later in the day.

Toxicologic assay of the urine revealed salicylates, caffeine, and two unidentified alkaloids thought to be yohimbine metabolites. The serum salicylate level was less than 2 mg/dL and the serum caffeine level was less than 1 μg/mL. Serum catecholamine levels were as follows: norepinephrine, 788 pg/mL (normal, 150-550 pg/mL); epinephrine, 77 pg/mL (normal, < 75 pg/mL); and dopamine, 22 pg/mL (normal, < 75 pg/mL). The substance in the vial was identified as yohimbine by high-performance thin-layer chromatography.

DISCUSSION

Yohimbine, also known as aphrodine, corynine, hydroaergotocin, and quebrachine, is an indolealkylamine alkaloid obtained from the bark of Pausinystalia yohimbine (*corynanthe yohimbi*), which grows in tropical West Africa and the Congo. It is related structurally to reserpine and is also found in Rauwolfia root. Yohimbine is supplied in both powdered and tablet forms.[2] In this case, powdered yohimbine was obtained in bulk form from a mail-order company. The drug was advertised as an aphrodisiac in a pornographic magazine, and was available without a prescription. Yohimbine is known locally by the street name "yo-yo."

Pharmacologically yohimbine is classified as an alpha-2 adrenergic receptor antagonist.[1,3] In fact the selective interaction of yohimbine with alpha-2 receptors provides the basis for determining the function of these receptors; effects induced or inhibited by yohimbine are said to be mediated by alpha-2 adrenoreceptors.[1] Although the exact function, distribution, and location of alpha-2 receptors is currently under investigation,[1,3] it is clear that they modulate autonomic output from medullary brain structures. Alpha-2 receptors also may be involved in the local regulation of peripheral autonomic neurotransmission.[1]

Stimulation of central alpha-2 adrenergic receptors results in decreased sympathetic and increased parasympathetic (vagal) outflow from the CNS.[1,3] Sympathetic inhibition and vagal stimulation may result from feedback inhibition of presynaptic catecholamine release by free (synaptic cleft) neurotransmitters, direct postsynaptic inhibition of adenyl cyclase, or both.[3] Cardiovascular effects include decreased blood pressure, heart rate, and cardiac output.

Central alpha-2 receptor activation is the mechanism underlying the antihypertensive activity of agents such as clonidine, guanabenz, and the alpha-methyldopa metabolite alpha-methyl norepinephrine. Other central alpha-2 antagonists include the imidazoline derivatives naphazoline, oxymetazoline, tetrahydrozoline, and xylometazoline found in nasal and ophthalmic preparations. The additional alpha-1 receptor stimulant properties of these latter agents account for their vasoconstrictor action when applied topically.

Drugs that inhibit alpha-2 adrenergic receptors increase central epinephrine and norepinephrine turnover, resulting in increased sympathetic and decreased vagal outflow from the CNS.[1,3] Yohimbine and its diastereoisomer rauwolscine are selective alpha-2 receptor antagonists. Nonselective antagonists include agents such as dihydroergotamine, dihydroergotoxine, tolazoline, and phentolamine. Because of concurrent alpha-1 receptor inhibition, the autonomic response to these nonselective antagonists is often variable and dose-dependent.

The administration of yohimbine to human beings causes a variety of autonomic changes. Increased heart rate, increased blood pressure, mydriasis, perspiration, lacrimation, salivation, nausea, vomiting, and facial flushing were noted following IV yohimbine administration (0.5 mg/kg over a five- or six-minute period).[4,5] Such effects were observed to peak between five and 20 minutes and to last approximately one hour. Recent studies have reported similar effects from IV (0.016 to 0.125 mg/kg)[1] and oral (10 to 30 mg)[6,7] doses of yohimbine. Additional findings included anxiety, piloerection, rhinorrhea, urinary frequency, and hot and cold flashes. Elevated levels of plasma norepinephrine and the norepinephrine metabolite MHPG (3-methoxy-4-hydroxyphenylethene-glycol) also were observed.[1,6,7] With oral yohimbine effects were maximal between one and two hours postingestion and lasted three to four hours.

The symptoms, physical findings, and elevated serum catecholamine levels in our patient are consistent with the experimental data. Although speculative, it seems likely that our patient's headache, intratympanic membrane hemorrhage, and chest pain were hypertensive in etiology. The long duration of toxicity may have been a reflection of the magnitude of her overdose.

CNS excitation is a characteristic response to yohimbine.[4,7] Indeed the emotional reaction to this drug is so consistent that it has been used as a clinical model for anxiety in the testing of various anxiolytic agents.[8] Its hallucinogenic effects are said to be mild, but have not been well characterized. Our patient initially experienced a dissociative state similar to that which occurs in phencyclidine (PCP) intoxication.

Yohimbine, said to be "the refuge of aging Don Juans in the Victorian era,"[9] has historically been touted as an aphrodisiac. Although it may be of some benefit in the treatment of organic impotence,[10] there is no evidence that yohimbine has any power to arouse or increase sexual desire. Our patient denied having any such feelings and considered her overall experience with yohimbine an unpleasant one.

A number of drugs have been shown to alter the CNS and autonomic responses to yohimbine. Amobarbital, clonidine, and reserpine were found to attenuate both the psychic and sympathetic effects, whereas chlorpromazine and imipramine potentiated them.[4,6,11] Benzodiazepines, while useful in alleviating yohimbine-induced anxiety, had no effect on sympathetic hyperactivity.[7] Conversely atropine was noted to block the pressor response to yohimbine without altering the psychic reaction.[11]

Based on these studies and pharmacological considerations, the following treatment recommendations are suggested for yohimbine toxicity. Clonidine, an antagonist of yohimbine at the central alpha-2 adrenoreceptor level, would appear to be the agent of choice. Although not recommended for children, it may be effective in reversing both central and peripheral sympathetic excitation in adolescents and adults. A dose of 0.1 mg to 0.2 mg PO may be used initially. Several additional doses of 0.1 mg PO may be given at hourly intervals until vital signs normalize and symptoms resolve.

Beta-adrenergic blocking agents (eg, propranolol) would be expected to alleviate some of the peripheral manifestations of yohimbine toxicity, but could theoretically worsen hypertension by allowing unopposed alpha-adrenergic stimulation. The use of a beta-blocker in conjunction with an alpha antagonist (eg, phentolamine) or a vasodilator (eg, nitroprusside), however, would be reasonable therapy for a hypertensive crisis. Treatment with a benzodiazepine may be sufficient in the anxious or hallucinating patient with mild or absent sympathomimetic findings. Because chlorpromazine has been shown to potentiate both the psychic and autonomic effects of yohimbine,[11] phenothiazines should be avoided.

SUMMARY

The unfounded reputation and lay press promotion of yohimbine as an aphrodiasic, its stimulant and hallucinogenic effects, and its availability without prescription suggest the potential for widespread abuse. Physicians should consider the possibility of yohimbine poisoning in the differential diagnosis of patients presenting with anxiety, hallucinations, or dissociative reactions and findings of adrenergic hyperactivity.

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