CASE REPORT

Yohimbine Use in a Natural Setting: Effects on Posttraumatic Stress Disorder

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Background: *Numerous laboratory-based studies have shown that chronic posttraumatic stress disorder (PTSD) is associated with alterations in catecholamines. In a recent neuroendocrine challenge study, IV yohimbine caused exaggerated subjective, behavioral, cardiovascular and catecholamine responses among combat veterans with PTSD compared to healthy controls. Yohimbine is an alpha-2-adrenergic receptor antagonist that activates noradrenergic neurons.*

Methods: *This report describes the experience of 4 individuals with PTSD who took over-the-counter oral yohimbine that they had purchased from a health food store or pharmacy.*

Results: *All 4 subjects experienced a marked exacerbation of anxiety/panic and PTSD-specific symptoms immediately after ingesting yohimbine in a natural setting.*

Conclusions: *The response in these individuals closely resembled the response observed after IV yohimbine in combat veterans with PTSD. The present cases occurred in a natural setting and thus complement laboratory-based findings. The authors caution against the recreational or medical use of yohimbine in individuals who have PTSD.*
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Key Words: Posttraumatic stress disorder, naturalistic, yohimbine, norepinephrine, sensitization, flashback

Introduction

A large body of psychophysiologic, neuroendocrine, receptor binding and brain imaging data clearly has shown that chronic posttraumatic stress disorder (PTSD) is associated with alterations in catecholamine systems. Evidence for catecholamine dysregulation in PTSD includes exaggerated cardiac reactivity to auditory and visual reminders of trauma, elevated 24-hour urine epinephrine and norepinephrine excretion, decreased platelet alpha-2 adrenergic receptor number and exaggerated behavioral, cardiovascular and neuroendocrine responses to yohimbine hydrochloride (Charney et al 1993; Murburg 1994; Southwick et al 1995; Southwick et al 1993).

Yohimbine is an alpha-2-adrenergic receptor antagonist that activates noradrenergic neurons by blocking the alpha-2-adrenergic autoreceptor, thereby increasing the release of endogenous norepinephrine. In a recent neuroendocrine challenge study (Southwick et al 1993), IV yohimbine caused panic attacks in 70% and flashbacks in 40% of combat veterans with PTSD but had minimal effects in the control group. Subjects with PTSD also had significantly greater increases in heart rate, sitting systolic blood pressure and plasma MHPG, a breakdown product of norepinephrine. The data were consistent with the notion that traumatic stress can cause a compensatory increase in norepinephrine synthesis and subsequent release over time (Post 1992; Irwin et al 1984; Karmarcy et al 1984; Melia et al 1991). Sensitization of catecholamine systems may contribute to symptoms commonly associated with PTSD such as hypervigilance, irritability, insomnia, and exaggerated startle response (Charney et al 1993; Murburg 1994; Southwick et al 1995; Southwick et al 1993).

The present report describes the experience of four individuals with PTSD who took over-the-counter oral yohimbine that they purchased from a health food store or pharmacy. Yohimbine is typically marketed as an aphrodisiac, an energy aid, and as a treatment for male impotence. PTSD was caused by combat in two subjects and by civilian transportation accidents in the other two. These cases are presented now because they occurred in a natural setting and thus complement laboratory-based yohimbine findings and because they highlight the importance of informing physicians and patients about potential side effects of yohimbine in individuals who have PTSD.

Case Reports

Subject 1

RC is a 44-year-old Vietnam combat medic who was awarded bronze and silver stars for bravery. Before

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entering the military, RC was described as a well-adjusted, friendly adolescent with no known history of psychopathology. After returning from Vietnam, RC gradually developed severe PTSD with debilitating symptoms of hyperarousal and re-experiencing. RC first took yohimbine approximately 1 year before going to Vietnam. "It was a pleasant feeling. I had lots of energy. There wasn't the clouding that you get with alcohol. It was definitely an aphrodisiac."

Six years after Vietnam, RC again tried yohimbine expecting to recreate his earlier pleasant experience with the drug. Four friends, one a combat veteran, joined him. RC's three non-veteran friends reported an energized and sensual feeling. RC and his combat veteran friend both experienced a panic attack and flashback. "I felt like I was going crazy. I was sweating and shaking and my heart seemed like it was pounding outside of my chest. It seemed like I was losing my mind. At first I thought we had been poisoned, but I could see that three of my friends were fine. The whole thing was terrifying and seemed like it lasted for a long time. I kept thinking that my combat buddy was wounded. I kept thinking that I was a medic and that I had to save him. He was having a terrible time too."

Subject 2

CF is a 45-year-old Vietnam combat veteran who developed severe PTSD within several years of his return to the United States. Approximately 10 years after the war CF first purchased yohimbine from a health food store. In the patient's words, "At low doses yohimbine excited my nerve endings. It made me almost hyper, but that was good because I could face my environment. Before I took it, I was almost withdrawn and it helped me to come out and reconnect with the world and become more alert."

At high doses he reported, "My palms would sweat, my breathing would increase, my heart would race, and I would get a numb feeling at the top of my head. I would be scared to death. Sometimes I would intentionally cause flashbacks by taking a lot of yohimbine. I know that sounds strange."

Subject 3

RM is a 45-year-old Italian-Mexican American male who struck and killed a woman in her mid-sixties while operating a commuter train. Afterward he developed major depression and PTSD. RM was treated with psychotherapy, behavioral re-exposure and pharmacotherapy including a tricyclic antidepressant, propranolol and low-dose benzodiazepines. His symptoms decreased markedly. Five months after discharge from treatment he continued to suffer from mild to moderate symptoms of anxiety but no longer complained of PTSD-specific symptoms.

RM returned to treatment 18 months later after a sudden increase in PTSD symptoms that interfered with work. He was taking fluoxetine as prescribed by his family physician. Because fluoxetine seemed to cause partial impotence and decreased libido, the patient followed the advice of fellow workers and began to take over-the-counter yohimbine. Shortly thereafter he experienced a rapid return of his PTSD symptoms. Discontinuation of yohimbine, in addition to psychotherapy and continued fluoxetine, resulted in moderate therapeutic success.

Subject 4

HM is a 53-year-old Mexican-American male bus driver who developed PTSD after he witnessed and heard a pedestrian slip and fall against his bus with a loud "thumping and bumping" sound. He initially thought the pedestrian had been killed, though he was only slightly injured. His chief complaint was, "I can't get this thumping bumping noise out of my mind." His bus accident re-awakened memories of an accident in the military. While jumping with the Army's Airborne Rangers, he became entangled and nearly hanged in his parachute cord and recalls a thumping and bumping against the side of the fuselage. With the exception of periodic ruminations about a repeat accident, HM had a good response to fluoxetine, benzodiazepines and cognitive behavioral therapy. Of note, he also recently had been diagnosed with Type II diabetes and was taking an oral hypoglycemic agent.

Three months after the accident he reported a marked increase in fear, insomnia, and nightmares about hitting pedestrians with his bus. Shortly before this exacerbation of PTSD symptoms, the patient began to take over-the-counter yohimbine to treat recent onset impotence that he believed was related to oral hypoglycemics or fluoxetine. After discontinuing yohimbine his symptoms improved rapidly.

Discussion

These four cases add support to the findings of altered noradrenergic neuronal reactivity in combat veterans with PTSD. The response in these individuals closely resembles the response observed in a recent laboratory-based yohimbine investigation of Vietnam combat veterans with PTSD (Southwick et al 1993). The present cases occurred in a natural setting where at least 3 of 4 subjects had no prior knowledge of potential yohimbine-induced anxiogenic effects. In fact, Subject 1 expected a pleasant and sensual feeling rather than a panic attack and flashback based on his pre-military experience with yohimbine and Subjects 3 and 4 expected yohimbine to help with medication induced sexual dysfunction.

In Case 1, the three friends who had not served in the military, but who were similar to the patient in age, education and socioeconomic status, may be viewed loosely as a naturally occurring control group. Like subjects in the laboratory-based intravenous yohimbine control group, they did not have a panic attack or flashback. Further, the fact that yohimbine induced a panic attack and flashback only after and not before the war raises the possibility that the trauma of war may have sensitized noradrenergic neurons in an individual who did not exhibit pre-existing alpha-2 adrenergic receptor sensitivity.

Cases 3 and 4 suggest that yohimbine's capacity to temporarily exacerbate PTSD symptoms is not limited to victims of combat trauma but also may include victims of civilian trauma. In both cases yohimbine was taken to treat adverse effects on sexual function that may have been caused by medications prescribed to treat symptoms of PTSD. These cases point out the need to ask trauma victims about sexual dysfunction and to inform them about the potential negative effects of yohimbine. It also is important for physicians who prescribe yohimbine to be aware of potential anxiogenic effects in patients with PTSD or panic disorder (Charney et al 1987).

This report has a number of limitations. First, patient accounts are retrospective in nature and thus subject to possible inaccurate recall. This may be particularly relevant to Subject 1 where the time interval between pre and post military use of yohimbine was approximately 8 years. Second, the doses of yohimbine are not known. It is possible that Subject 1 took different doses of yohimbine before and after the war and that these differences explain his variable behavioral response to yohimbine. Third, the present report involved only 4 subjects. It is not clear whether the experiences of these patients can be generalized to other trauma patients.

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