Case Reports

Acute Hepatitis and Personality Change in a 31-Year-Old Man Taking Prohormone Supplement SUS500

Nathaniel Wingert, B.A.
Hamid Tavakoli, M.D.
Elizabeth Yoder, D.O.

Background: *For decades, anabolic-androgenic steroids have been abused to enhance muscle growth. The harm inflicted by these compounds is well documented.* **Objective:** *The authors investigated and report on a case in which a male patient self-prescribed some newer dietary supplements, about which less is known.* **Method:** *The authors report on a case of hepatitis and aggressive personality changes in a 31-year-old man taking purported prohormone agent SUS500 and other, newer supplements.* **Results:** *Diagnosis was based on history, mental status exam, and laboratory findings. With discontinuation of all supplements and supportive care, the patient's personality changes resolved, and normal liver function returned.* **Conclusion:** *The authors conclude that newer anabolic supplements may cause some of the same side effects as traditional steroid hormones.* (Psychosomatics 2010; 51:340–344)

The use of anabolic-androgenic steroids (AAS) to enhance athletic ability is no longer new. Competitive athletes, from former East German Olympians to current, high-profile American professional baseball players, have notoriously used steroids.[1] Yet we know the bigger problem has been the widespread use of AAS among the mainstream public. An estimated 1 million to 3 million Americans are thought to misuse AAS every year.[2,3] Thanks to diligent study and reporting by scientists and clinicians over recent decades, we now know much about the adverse side effects of misusing anabolic steroid hormones.

Among the known clinical manifestations of using anabolic-androgenic steroids are musculoskeletal, hepatic, infectious, dermatologic, endocrine, cardiovascular, and psychiatric complications.[4] Recent reviews in this journal and elsewhere describe the spectrum of psychiatric effects, including depression, mania, delirium, anxiety, and personality changes such as increased aggression (" 'roid rage").[5,6] With this increasing fund of knowledge on the pathological effects of androgenic hormones has come better testing, more stringent athletic monitoring, and more severe legal consequences. Under the Anabolic Steroid Control Act of 1990, anabolic steroids were officially declared Schedule III controlled substances.

In response to better enforcement, a new wave of compounds have reached the market and become popular. These include prohormones, amino acid/protein supplements, human growth hormone, insulin, insulin-like growth factor, human chorionic gonadotropin, and erythropoietin, to name just a few. Some of these compounds are obtainable by prescription only. Others on this list are available over the counter, or even online and in nutrition stores, legally and widely available for anyone to purchase. (See Table 1 for availability details.)

Classified officially as dietary supplements under the Dietary Supplement Health and Education Act of 1994

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From the Dept. of Psychiatry, Eastern Virginia Medical School; the Dept. of Psychiatry, Naval Medical Center, Portsmouth, VA. Send correspondence and reprint requests to Hamid Tavakoli, M.D., Dept. of Psychiatry, Naval Medical Center, Portsmouth, 620 John Paul Jones Circle, Portsmouth, VA 23708. e-mail: Hamid.Tavakoli@med.navy.mil

(DSHEA), many new compounds touted for muscle gain are not subject to the same level of regulation imposed by the FDA on pharmaceutical drugs. Compared with traditional anabolic-androgenic steroids, much less is known about many of these newer-generation supplements. One important question, for which there seems a relative paucity of information in the medical literature, is: Can some of these newer supplements lead to the same types of side effects as their AAS predecessors?

In this report, we document the case of a 31-year-old male body-builder who developed hepatitis and aggressive personality/behavior changes secondary to chronic ingestion of SUS500, a purported prohormone; Leukic, an amino acid-based supplement; and creatine, a high-energy, phosphate bond-containing amino acid.

Case Report

"Mr. R" was a 31-year-old, active-duty member of the United States Armed Forces, an African American man with no past medical history, who was admitted to a major military hospital for a 1-day history of acute-onset weakness, fatigue, and subjective inebriation. He first noted these symptoms after mowing his lawn earlier in the day. He subsequently tried to rest, but had difficulty getting up the stairs to go to bed. He described one similar episode 9 months earlier that was associated with fever, chills, weakness, fatigue, and elevated blood pressure. At that time, he was evaluated as an outpatient, with no lab work done and no conclusive diagnosis made. Mr. R managed to bring himself to an Emergency Department (ED) around midnight, with continued symptoms. He reported that on the way to the ED, he experienced chills, subjective fever, and non-radiating chest tightness making it difficult to breathe.

TABLE 1. Availability of Performance-Enhancing Substances

Amino acid/protein supplements[a]	Commercially available without prescription
Creatine	Commercially available without prescription
Erythropoietin	Prescription only
Human chorionic gonadotropin	Prescription only
Human growth hormone	Prescription only
Insulin	Prescription only
Insulin-like growth factor	Prescription only
Prohormones and anabolic steroids	
● Specifically listed under Anabolic Steroid Control Act of 2004	Prescription only (Schedule III Controlled Substance)
● Not specifically listed under Anabolic Steroid Control Act of 2004[b]	Commercially available without prescription

[a] Leukic, the tradename of a compound taken by our patient, is considered an amino acid supplement.

[b] SUS500, the tradename of a compound taken by our patient, is not specifically mentioned in the Anabolic Steroid Control Act of 2004, and therefore currently commercially available without prescription as a dietary supplement.

By the time of arrival to the ED, Mr. R reported that all of his symptoms had resolved. The Emergency Department team described an alert, oriented, and well-developed individual in no apparent distress. Evaluation at this time revealed no symptoms of elevated or depressed affect, no mood lability, and no irritability or aggression. Medical history was notable only for alcohol and tobacco use. He reported a smoking history of 1 pack of cigarettes per day for 12 years and typical alcohol consumption of 3 to 4 drinks most nights for the past 7 years. A physical exam was within normal limits.

The initial laboratory work-up included complete blood count, CMP, electrocardiogram, cardiac enzymes, chest x-ray, urinalysis, serum lipase, and influenza and rapid strep test. Results were significant for an AST of 1,628 IU/L and an ALT of 1,754 IU/L. Creatinine was mildly elevated, at 1.4. Additional testing revealed an elevated serum creatine kinase, at 693, and a gamma glutamyl transferase of 142. Clotting times were elevated, with PT: 16.0, APTT: 36.6, and INR: 1.3. Subsequent acetaminophen levels, hepatitis B and C serology, and a urine toxicology screen were negative. Blood alcohol levels were not obtained. At this point, Mr. R was admitted with a diagnosis of hepatitis of uncertain etiology and started on N-acetylcysteine, thiamine, folic acid, and a multivitamin.

A detailed history taken by the Internal Medicine admitting team eventually revealed the patient to be a body-builder taking multiple nutritional supplements. Although he denied taking steroid hormones, the patient did endorse use of SUS500 (a reported anabolic prohormone), Leukic (a reported anabolic supplement), and Creatine (an energy supplement) for the past year. Poison Control was contacted for recommendations. Although unfamiliar with these specific compounds, they recommended treating him as though he had acute steroid-hormone toxicity and protecting his liver with N-acetylcysteine. A serum testosterone level was not drawn.

During Hospital Day 1, the Dept. of Psychiatry was consulted out of concern for alcohol abuse, especially given Mr. R's active-duty status and potential for deploy-

ment. Mr. R denied symptoms of tolerance or withdrawal, as well as any legal, social, or occupational problems related to alcohol use. Further symptoms of alcohol dependence were absent. The CAGE screening was negative (0/4). His history revealed reports of "aggressive mood swings," with irritability, insomnia, and depressed mood experienced over the preceding 9 months. Other diagnostic criteria for major depression, including anhedonia, appetite change, psychomotor agitation or retardation, feelings of worthlessness or guilt, inability to concentrate, thoughts of death or suicide, and reduced energy, were denied.

Mr. R also denied any history of persistently elevated or expansive moods. Diagnostic criteria for mania, including distractibility, grandiosity, increased goal-directed activity, racing thoughts, pressured speech, and excessive pursuit of pleasurable activities, were denied. As reported by Mr. R, his symptoms of depressed mood, mood lability, irritability, aggression, and insomnia began when he started taking SUS500 about 9 months earlier and persisted with continued ingestion of SUS500. His sister and colleagues also independently corroborated perceived personality changes, noting increased irritability, anger, and aggression over the preceding months. Additional time-course data regarding ingestion of SUS500, Leukic, and Creatine were not obtained. Mr. R denied any psychiatric history and did not endorse symptoms of posttraumatic stress disorder, anxiety, or psychosis. Mental status exam revealed a large, well-developed man who was cooperative and appropriately groomed. Speech was spontaneous. He reported a "good" mood and demonstrated a mid-range, euthymic, and congruent affect. Further questioning revealed a goal-directed, linear, and logical thought-process, with no delusional thought content. Memory and cognition were intact. Judgment and insight were thought to be questionable because of his decision to chronically ingest untested substances. He denied any suicidal or homicidal ideation.

On Hospital Day 2, Mr. R's liver enzymes fell to AST: 762 IU/L, ALT: 1,338 IU/L, and GGT: 121 IU/L, and we determined that outpatient follow-up would be sufficient to ensure return of normal liver function. He was advised to stop drinking and cease all commercial nutritional supplements because of concern for liver function. He was also advised to quit smoking. Discharge diagnosis was medication-induced hepatitis and substance (anabolic supplement)-induced mood disorder (aggression and irritability), now resolved.

At 2 weeks post-hospital discharge, Mr. R reported to his outpatient primary-care provider for follow-up. Since the time of discharge, he had remained asymptomatic. Liver enzymes had further improved, with an AST of 31 IU/L, ALT of 79 IU/L, and GGT of 73 IU/L.

Discussion

Prohormone supplements, such as androstenedione, dehydroepiandrosterone, and androstenediol are precursors in the endogenous synthesis of testosterone. Advertisers have suggested that oral intake of testosterone precursors increase circulating testosterone levels and induce muscle gain. Contrary to these claims however, studies to-date have indicated that these compounds are ineffective at increasing either muscle mass or athletic performance.[7,8] Because no large-scale trials on the effects of prohormones have been conducted, safety information is limited. Research has shown ingestion of one prohormone to be associated with increased aggression and hypertrophy in the areas of the brain that regulate aggression in rats.[9] Under the Anabolic Steroid Control Act of 2004, many prohormones were officially added to the list of Schedule III controlled substances. Enacting this measure has explicitly outlawed possessing or selling known prohormone compounds, but appears to have left the door open for companies to market lesser-known or novel prohormones that are not yet federally banned.

SUS500 is a brand name for a product made by Genetic Edge Technologies (G.E.T.). This supplement is widely commercially available and marketed online as a legal steroid. The active ingredients are purported to be prohormones but do not appear on the list of banned compounds created by the Anabolic Steroid Control Act of 2004. The idea seems to be that by selling a precursor molecule that is later metabolized to an active steroid and does not yet appear on banned supplement lists, a company is able to offer the physiologic effects of steroids while escaping legal repercussions. The active ingredients include Estra-4,9-Diene-3,17-Dione, 13-Ethyl-3-Methoxy-Gona-2,5[10]-Diene-17-One, and 3,17-Keto-Etiochol-Triene. A PubMed search for the first compound, Estra-4,9-Diene-3,17-Dione, revealed just one article suggesting that the compound may act as a selective progesterone antagonist.[10] Further searches for information on these compounds, using PubMed, Medline, Cochrane, toxicology textbooks, a toxicologist consultant, and computerized pharmacologic-agent databases Micromedex, Natural Standard, International Bibliographic Information on Dietary Supplements (IBIDS), and others, revealed almost no information on these compounds. Suffice it to say, little concrete information was readily obtainable on pharmacologic mechanism

of action, proper dosing, side-effect profiles, human safety trials, or even animal safety. Interestingly, though, G.E.T. appears to have some idea of likely side effects. An internet-site advertisement proclaimed the product to include "estrogen-blocker and liver-support technology to ensure you get maximum results without side effects."[11]

Leukic (L-leucine-ketoisocaproic acid calcium) is the brand name for a supplement made by MuscleTech that contains an amino acid, l-leucine, and its keto-acid metabolite ketoisocaproate (KIC). Unlike the compounds in SUS500, the role of L-leucine and KIC in human metabolism has been studied in the clinical literature. At least one study has claimed that KIC is a factor in reducing protein catabolism, stimulating muscle synthesis, sparing glucose utilization, and increasing insulin release in rat muscle models.[12] We found small studies in which L-leucine and KIC were administered to human subjects without apparent adverse effects.[13,14] However, we found no adequately-sized trials on safety or efficacy of oral KIC or L-leucine supplementation in human subjects. Therefore, efficacy, side-effect profiles, and human safety are largely unknown.

Creatine is an amino acid synthesized naturally by the liver, kidneys, and pancreas. It is found in protein-containing foods such as meat and fish.[15] Exceptional athletes have admitted using creatine as a component of their nutritional regimen, and general use among the public has followed. Taken orally in its phosphorylated form, creatine supplements facilitate the resynthesis of stores of adenosine triphosphate (ATP) in muscle. Creatine has been reported to increase performance in short, high-intensity exercise.[16] Side effects of creatine supplementation include weight gain, thought to be secondary to water retention.[17,18] Creatine supplementation also increases serum creatinine, which is consistent with our own patient's mildly elevated levels. Although of theoretical concern, it is currently thought that creatine does not lead to long-term adverse effects on renal functioning.[19,20]

Given the assortment of supplements taken by our patient, it is difficult to know which compounds caused which of our patient's symptoms. SUS500, the prohormone compound taken by our patient, and Leukic, the amino acid-based supplement with purported anabolic pathway activity, do not have readily obtainable efficacy or safety data. Since a testosterone level was never drawn on our patient, we also do not know whether purported prohormone SUS500 increases serum testosterone. Creatine, the third compound Mr. R was taking, has been fairly well studied. Taken in moderation, this compound, tentatively, appears to be safe, although more trial data are needed. Given the popularity of newer-generation supplements and the corresponding dearth of concrete information on them, it is clear that we need to know more about these relatively novel compounds and their possible effects on humans.

This case report is designed to highlight potential adverse health effects of various untested muscle-building supplements. We began this case report wondering whether newer-generation, non-AAS compounds could cause harmful side effects similar to those long reported in anabolic-steroid users. Our patient's hepatitis and aggressive personality/behavioral changes suggest that the answer to this question is a tentative "yes." We also recommend maintaining a high index of suspicion for possible supplement-induced symptoms in all weight-lifters/body-builders, or other athletes, even if they deny steroid use. A better screening question than "Have you used illegal steroids?" might be "Are you taking any dietary supplements whatsoever?" The bottom line is that SUS500, Leukic, and other similar commercially available supplements are untested and not approved by the FDA. The safety of these agents is not known. Any patient using compounds such as SUS500 should be warned of the many possible adverse effects and advised to discontinue use of these compounds immediately.

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