Past Anabolic-Androgenic Steroid Use Among Men Admitted for Substance Abuse Treatment: An Underrecognized Problem?

Gen Kanayama, M.D., Ph.D.; Geoffrey H. Cohane, B.A.; Roger D. Weiss, M.D.; and Harrison G. Pope, Jr., M.D., M.P.H.

Background: Recent reports suggest that anabolic-androgenic steroids (AAS) may cause mood disorders or dependence syndromes and may help to introduce some individuals to opioid abuse. At present, however, little is known about prior AAS use among men entering inpatient substance abuse treatment.

Method: We assessed lifetime AAS use in 223 male substance abusers admitted to a substance abuse treatment unit primarily for treatment of alcohol, cocaine, and opioid dependence. Subjects reporting definite or possible AAS use were then asked to participate in a detailed semi-structured interview that covered demographics, drug use history, and symptoms experienced during AAS use and withdrawal, and whether AAS use had helped introduce the subject to other classes of drugs.

Results: Twenty-nine men (13%) reported prior AAS use, but this history was documented on physicians' admission evaluations in only 4 cases. Among 88 men listing opioids as their drug of choice, 22 (25%) acknowledged AAS use, versus only 7 (5%) of the other 135 men ($p < .001$). Twenty-four (83%) of the 29 AAS users were interviewed in detail. Seven (29%) of the men interviewed, all with opioid dependence, reported that they first learned about opioids from friends at the gym and subsequently first obtained opioids from the same person who had sold them AAS. Eighteen (75%) of the men interviewed reported that AAS were the first drugs that they had ever self-administered by injection, 4 (17%) reported severe aggressiveness or violence during AAS use, 1 (4%) attempted suicide during AAS withdrawal, and 5 (21%) described a history of AAS dependence.

Conclusion: Prior AAS use appears to be common but underrecognized among men entering inpatient substance abuse treatment, especially those with opioid dependence. AAS use may serve as a "gateway" to opioid abuse in some cases and may also cause morbidity in its own right.

(J Clin Psychiatry 2003;64:156–160)

Received March 18, 2002; accepted Aug. 8, 2002. From the Alcohol and Drug Abuse Research Center, McLean Hospital; and the Department of Psychiatry, Harvard Medical School, Belmont, Mass.

Supported in part by a grant from the Center for Education on Anabolic Steroid Effects, Atlanta, Ga. (Dr. Pope); grant K02-DA00326 from the National Institute on Drug Abuse, Bethesda, Md. (Dr. Weiss); and a grant from the Dr. Ralph and Marian C. Falk Medical Research Trust, Chicago, Ill. (Dr. Weiss).

In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Drs. Kanayama and Weiss and Mr. Cohane have no significant financial or other relationships relevant to the presentation to disclose other than the grant support described above; Dr. Pope is a member of the advisory board for the Center for Education on Anabolic Steroid Effects.

Corresponding author and reprints: Harrison G. Pope, Jr., M.D., McLean Hospital, 115 Mill St., Belmont, MA 02478 (e-mail: pope@mclean.harvard.edu).

The anabolic-androgenic steroids (AAS) are a family of drugs that includes the male hormone, testosterone, and numerous synthetic analogues of testosterone developed over the last 50 years.[1] Epidemiologic studies suggest that at least 1 million Americans have used these drugs illicitly to gain muscle or lose fat; the great majority are males in their teens or young adulthood.[1–3] Once used almost exclusively by athletes, AAS are increasingly used illicitly by individuals simply to improve personal appearance; thus, these drugs may pose a growing public health problem.[4] AAS may cause not only adverse medical effects,[1] but also psychiatric morbidity, including mania or hypomania,[5] withdrawal-associated major depression,[6] and dependence syndromes.[7]

Another risk, only recently noted in the literature, is that AAS use may help to introduce some individuals to opioids. For example, reports from the United Kingdom[8] and the United States[9] have described AAS users who were introduced at the gym to the opioid agonist-antagonist nalbuphine. Some developed dependence on this drug, and a few progressed to abuse of or dependence on classical opioid agonists, including heroin.[9] In a subsequent study of 227 men with opioid dependence admitted to a New Jersey treatment facility,[10] 21 (9%) were found to have a history of AAS use. Fourteen (67%) of these men reported that they were first introduced to opioids by fellow AAS-using bodybuilders, and 17 (81%) reported that they first purchased opioids from the same drug dealer who had

sold them AAS. Although one cannot conclude with certainty that AAS use per se led to opioid use in these cases, these and other observations in the study favor this interpretation.

The New Jersey study, however, appears to be the only recent investigation of AAS use among inpatient substance abusers. To augment these limited data, we assessed history of AAS use in 223 men admitted to a substance abuse treatment unit in the Boston, Mass., area. Most of these men were admitted for alcohol, cocaine, and opioid dependence. We hypothesized that past AAS use in these men might represent an underrecognized source of morbidity.

METHOD

We screened men admitted over a 1-year period to a general inpatient substance abuse treatment unit at McLean Hospital (Belmont, Mass.). This unit serves a population of patients with a primary DSM-IV diagnosis of substance dependence, many of whom have co-occurring psychiatric disorders. Patients are generally admitted for medical detoxification that cannot be accomplished on an outpatient basis either because of the severity of dependence or because of medical or psychiatric comorbidity. We did not screen women admitted to the unit, because AAS use is much less common in women than in men.[1,2] We first asked each man to specify his "drug of choice," defined as "the principal drug for which you are being treated here in the hospital." Men naming more than 1 drug of choice were classified by the first drug listed. We then asked subjects whether they had ever used performance-enhancing drugs such as AAS. Subjects reporting definite or possible AAS use were subsequently asked to participate in a detailed semistructured interview. This interview covered (1) basic sociodemographic information; (2) history of AAS use, including age at first use, drugs used, duration of use, and maximum weekly dose used, estimated by methods previously described[11]; (3) lifetime history of all other substance use syndromes; and (4) history of treatment for both substance use disorders and other psychiatric disorders, if any. With regard to AAS use, we also (5) asked subjects about any psychiatric symptoms experienced during AAS use and withdrawal, with attention to whether these symptoms had occurred exclusively in association with AAS use or had occurred at other times in the subject's life as well. Finally, we (6) asked questions regarding whether AAS use had helped to introduce the subject to other classes of drugs. In particular, we asked each subject (a) whether he first learned about other drugs through fellow AAS users, (b) whether he first purchased other drugs from the same person who sold him AAS, and (c) whether he had begun using the other drugs specifically to counteract adverse effects of AAS, such as irritability or mood changes. In addition to the interview, we also reviewed the physician's admission note in each subject's chart, with particular attention to whether AAS use had been noted. All subjects provided signed informed consent after the study procedures had been fully explained.

We tabulated the frequencies of various attributes among all subjects screened and among the subgroup reporting AAS use. Comparisons between groups were performed using 2-tailed t tests for continuous variables and 2-tailed Fisher exact test for categorical variables, with alpha set at .05.

RESULTS

Subjects Screened

We screened 223 (60.1%) of the 371 men admitted during the study period; among the 40% of men not screened, about 10% refused screening and 30% were discharged before they could be seen for screening. Hospital records showed little difference between the subjects screened and those who were missed in mean age (38.6 vs. 42.5 years), ethnic distribution (91.4% vs. 93.9% white), and proportion with a primary diagnosis of alcohol dependence (46% vs. 50%) or opioid dependence (39% vs. 36%). Of the 223 men screened, 29 (13%) reported past AAS use (Table 1). Only 4 (14%) of these 29 men's admission notes mentioned AAS, although each admission note included a section in which the physician specifically inquired about use of other drugs. The prevalence of AAS use was much higher among opioid users than among those in the other drug-of-choice categories ($p < .001$ for opioids vs. all other groups combined) (see Table 1). Moreover, among the 7 AAS users listing drugs of choice other than opioids, 4 (3 cocaine and 1 alcohol) displayed current opioid abuse or dependence as well.

Subjects Interviewed

We performed semistructured interviews of 24 (83%) of the men reporting AAS use at screening; the other 5 were discharged before they could be followed up. The mean ± SD age of those interviewed was 32.1 ± 8.2 years; 23 (96%) were white, and 1 (4%) was Hispanic. Eleven (46%) were graduates of 4-year colleges, and 10 others (42%) reported at least some college work. The men reported that they had first used AAS at a mean age of 22.2 ± 6.6 years; 9 (38%) had first tried AAS between the ages of 14 and 17 years. Their mean duration of reported AAS use was 16.1 ± 18.5 months (range, 1.5–70 months), and their estimated mean weekly dose of AAS was 1070 ± 1000 mg of testosterone equivalent per week (range, 150–4875 mg). Specifically, 11 (46%) of the subjects had used doses of at least 1000 mg per week; in previous field studies of AAS users, doses above this level have been reported to be associated with higher rates of AAS-associated psychopathology.[1,11]

Table 1. Demographic Characteristics and Anabolic-Androgenic Steroid (AAS) Use in 223 Men Admitted for Substance Dependence

	Drug of Choice				
Variable	Alcohol (N = 102)	Opioids (N = 88)	Cocaine (N = 23)	Other (N = 10)	Total (N = 223)
Age, mean (SD), y[a]	43.6 (9.2)	35.3 (10.6)	34.1 (7.0)	27.5 (12.4)	38.6 (10.8)
White, N (%)[b]	98 (96)	78 (89)	17 (74)	10 (100)	203 (91)
History of AAS use, N (%)[c]	4 (4)	22 (25)[d]	3 (13)	0 (0)	29 (13)[d]
Participated in a follow-up interview, N	2	19	3	0	24
Morbidity apparently due to AAS (among those interviewed), N[e]					
Psychiatric effects from AAS	0	4	1	0	5
AAS dependence	0	5	0	0	5
Introduced to opioids through AAS	0	6	1	0	7
Any of above 3 categories	0	8	2	0	10

[a]Alcohol vs. opioids, t = 5.78, df = 188, p < .001; alcohol vs. cocaine, t = 4.65, df = 123, p < .001; alcohol vs. other, t = 5.11, df = 110, p < .001; opioids vs. other, t = 2.17, df = 96, p = .03; all other differences not significant.
[b]Cocaine vs. alcohol, p = .003; all other differences not significant.
[c]AAS users did not differ significantly from nonusers in ethnic distribution (27 [93%] vs. 176 [92%] white; p = 1.0), but were significantly younger (mean ± SD age = 32.1 ± 7.6 vs. 39.8 ± 10.9 years; t = 3.66, df = 219, p < .001).
[d]Two additional opioid users, who reported possible but uncertain past AAS use, are omitted from these numbers.
[e]*Psychiatric effects* indicates hypomanic or depressive symptoms sufficient to interfere with social or occupational functioning, *introduced to opioids through AAS* indicates that the subject first learned about opioids from fellow AAS users and first purchased opioids from the same individual who had sold him AAS, and *AAS dependence* indicates AAS use meeting 3 or more of the DSM-IV criteria for substance dependence.

Psychiatric Effects of AAS Use or Withdrawal

Five (21%) of the 24 interviewed AAS users reported marked psychiatric effects (sufficient to interfere with social or occupational functioning) that appeared attributable to AAS use. While using AAS, 1 subject violently assaulted another driver in a roadside dispute, 1 was charged with 3 episodes of assault and battery, 1 repeatedly damaged property during episodes of irritability, and 1 became so irritable that his boss threatened to fire him. All of these subjects stated that they had not experienced comparable behavior at times before or after AAS use. A fifth subject attempted suicide during AAS withdrawal; he reported no other episodes of comparable depressive symptoms or suicide attempts at other times in his life. Four additional subjects described severe irritability or aggressiveness during AAS use, and 1 additional subject reported symptoms of major depressive disorder during AAS withdrawal, but the causal role of AAS in these latter cases was less clear, in that these individuals reported at least some comparable symptoms at times when they were not using AAS.

AAS Dependence

Five (21%) of the interviewed AAS users had a history of possible dependence on AAS. These individuals all reported use of AAS at higher doses and for longer periods than originally intended; persistent use despite adverse medical, psychiatric, and/or social consequences; tolerance; and prominent withdrawal effects. In these 5 individuals, the mean ± SD lifetime duration of AAS use was 43.8 ± 19.1 months (range, 18–70 months), significantly longer than the mean duration of 8.9 ± 9.5 months in the 19 subjects without a history of AAS dependence (t = 5.9, df = 22, p < .001).

AAS as an Introduction to Opioid Use

In 7 (29%) of the interviewed AAS users, all being treated for opioid dependence, AAS use appeared to play a role in introducing them to opioids (note that 1 of these 7 subjects identified cocaine as his drug of choice, but was also undergoing treatment for opioid dependence). All 7 of these subjects reported that they first learned about opioids from fellow AAS users in the gym, and all first purchased opioids from the same person who had sold them AAS. Two of the 7 subjects were first introduced to the opioid agonist-antagonist nalbuphine and then progressed to pure opioid agonists such as oxycodone or heroin—a sequence described in previous studies.[8,9] The other 5 subjects were introduced to pure opioid agonists directly. In a related observation, 22 (92%) of the 24 interviewed AAS users reported that they had self-administered AAS by injection; in 18 (82%) of these 22 individuals, AAS were the first illicit drugs that they had ever injected. These 18 subjects included all 7 of the men who appeared to have been introduced to opioids through AAS use; 3 of these 7 men became dependent on intravenous opioids, and 4 used primarily oral opioids.

Overall Morbidity From AAS

In all, 10 (42%) of the 24 interviewees reported at least 1 of the 3 forms of AAS-associated morbidity described in the above paragraphs (Table 1). Specifically, all 5 men with AAS dependence had also been introduced to opioids through AAS, and 2 of these 5 had additionally experienced serious AAS-associated psychiatric syndromes. Of the remaining 5 men, 3 reported only AAS-associated psychiatric syndromes, and 2 reported only being introduced to opioids through AAS.

DISCUSSION

Among men entering general inpatient substance abuse treatment, we found a 13% lifetime prevalence of AAS use; in the subgroup of opioid-dependent patients, the prevalence reached 25%. By contrast, a 1989–1990 survey of inpatient substance abuse treatment directors found AAS use among fewer than 1% of all admissions.[12] However, this earlier survey identified primarily cases in which AAS use was specifically noted as part of the clinical presentation, and, hence, it might be expected to yield lower prevalence estimates. In our study, semistructured interviews suggested that, in 10 (42%) of the 24 cases, AAS use was associated with (1) AAS-induced psychiatric syndromes, (2) AAS dependence, and/or (3) a progression to opioid dependence. Thus, it appears that clinicians should be alerted to seek a history of AAS use in individuals entering substance abuse treatment, especially opioid users.

Six (7%) of the 88 men listing opioids as their drug of choice, plus a seventh man admitted for both cocaine and opioid dependence, first learned of opioids from friends at the gym and first purchased opioids from the same person who had sold them AAS. These observations, while hardly conclusive, suggest that AAS use may have served as a "gateway" to opioid dependence for these individuals. These findings resemble those of the New Jersey study described above, in which 9% of all male patients with opioid dependence were apparently introduced to opioids through AAS use.[10] It should be noted, however, that the New Jersey study identified only opioid users for whom AAS had apparently served as a gateway drug; opioid users with only an incidental history of AAS use were not reported. By contrast, we screened all subjects for past AAS use, regardless of whether AAS might have contributed to their current substance use disorder. Probably as a result of our broader method of ascertainment, we identified 16 additional opioid users (18%) with past AAS use that was apparently incidental and unrelated to subsequent opioid use.

It is striking that AAS use appears to assort so strongly with opioid dependence in substance abusers; the gateway hypothesis described above can account for only a portion of this association. Another possible explanation is that AAS and opioids stimulate similar reward pathways in the brain[13,14] and that individuals who experience reinforcing effects from one of these classes of drugs obtain similar reinforcing effects from the other. However, animal studies remain inconsistent on this point.[15–18] An alternative possibility is that specific psychological attributes may predispose individuals both to AAS use and to opioid use. For example, body image disorders may prompt some men to use AAS,[1,3,7] and, interestingly, some patients with body dysmorphic disorder have commented that opioids were the only illicit drugs that relieved their symptoms (K. A. Phillips, M.D.; oral communication, July 2002). Also on an anecdotal level, several of our interviewees spontaneously commented that opioids gave them a sense of self-confidence similar to what they had previously experienced with AAS.

Although we screened only about 60% of men admitted to our substance abuse treatment unit during a year, this ratio seems unlikely to represent a serious limitation, since we found no major demographic differences between men who were screened and those who were not, as noted above. A more important limitation of our study is that men entering our unit may not be representative of men entering treatment elsewhere. For example, our subjects were mostly white and reported high levels of education. Also, since our inpatient unit treated primarily individuals with serious levels of drug dependence or concomitant medical and psychiatric problems, our subjects likely displayed greater overall morbidity than men with substance use disorders in the community as a whole.

Finally, the retrospective design of the study limits our ability to establish whether AAS played an etiologic role in all of the syndromes reported. Studies at other centers will be required to confirm our findings that AAS use may be underrecognized in male substance abusers and may represent both a risk factor for opioid dependence and a cause of psychiatric morbidity in its own right.

Drug names: nalbuphine (Nubain and others), oxycodone (OxyContin, Percocet, and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

REFERENCES

1. Pope HG Jr, Brower KJ. Anabolic-androgenic steroid abuse. In: Sadock BJ, Sadock VA, eds. Comprehensive Textbook of Psychiatry/VII. Philadelphia, Pa: Lippincott Williams & Wilkins; 2000:1085–1095
2. Yesalis CE, Kennedy NJ, Kopstein AN, et al. Anabolic-androgenic steroid use in the United States. JAMA 1993;270:1217–1221
3. Pope HG, Phillips KA, Olivardia R. The Adonis Complex: How to Identify, Treat, and Prevent Body Obsession in Men and Boys. New York, NY: Simon & Schuster; 2002
4. Kanayama G, Pope HG Jr, Hudson JI. "Body image" drugs: a growing psychosomatic problem. Psychother Psychosom 2001;70:61–65
5. Su T-P, Pagliaro M, Schmidt PJ, et al. Neuropsychiatric effects of anabolic steroids in male normal volunteers. JAMA 1993;269:2760–2764
6. Malone DA Jr, Dimeff R, Lombardo JA, et al. Psychiatric effects and psychoactive substance use in anabolic-androgenic steroid users. Clin J Sports Med 1995;5:25–31
7. Brower KJ, Blow FC, Beresford TP, et al. Anabolic-androgenic steroid dependence. J Clin Psychiatry 1989;50:31–33
8. McBride AJ, Williamson K, Petersen T. Three cases of nalbuphine hydrochloride dependence associated with anabolic steroid abuse. Br J Sports Med 1996;30:69–70
9. Wines JD, Gruber AJ, Pope HG, et al. Nalbuphine hydrochloride dependence in anabolic steroid users. Am J Addict 1999;8:161–164
10. Arvary D, Pope HG. Anabolic-androgenic steroids as a gateway to opioid dependence [letter]. N Engl J Med 2000;342:1532
11. Pope HG Jr, Katz DL. Psychiatric and medical effects of anabolic-

androgenic steroid use. Arch Gen Psychiatry 1994;51:375–382
12. Clancy GP, Yates WR. Anabolic steroid use among substance abusers in treatment. J Clin Psychiatry 1992;53:97–100
13. Tennant F, Black DL, Voy RO. Anabolic steroid dependence with opioid-type features [letter]. N Engl J Med 1988;319:578
14. Kashkin KB, Kleber HD. Hooked on hormones? an anabolic steroid addiction hypothesis. JAMA 1989;262:3166–3170
15. Menard CS, Hebert TJ, Dohanich GP, et al. Androgenic-anabolic steroids modify β-endorphin immunoreactivity in the rat brain. Brain Res 1995;669:255–262
16. Johansson P, Ray A, Zhou Q, et al. Anabolic androgenic steroids increase beta-endorphin levels in the ventral tegmental area in the male rat brain. Neurosci Res 1997;27:185–189
17. Harlan RE, Brown HE, Lynch CS, et al. Androgenic-anabolic steroids blunt morphine-induced c-*fos* expression in the rat striatum: possible role of β-endorphin. Brain Res 2000;853:99–104
18. Negus SS, Pope HG Jr, Kanayama G, et al. Lack of evidence of opioid tolerance or dependence in Rhesus monkeys following high-dose anabolic-androgenic steroid administration. Psychoneuroendocrinology 2001;26:789–796

For the CME Posttest for this article, see pages 223–224.