

Gynecomastia and Cannabis Smoking

A Nonassociation among US Army Soldiers

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An anecdotal report of gynecomastia in chronic cannabis smokers [1] stimulated research into the effect of cannabis on male hormones [2,3]. A causal association between cannabis and gynecomastia was hypothesized based on the structural similarity of tetrahydrocannabinol (THC) and estradiol. Moreover, tetrahydrocannabinol was shown to directly stimulate development in rat breast tissue [4].

Although laboratory investigations on human subjects provided conflicting results regarding the effects of cannabis use on testosterone levels [2,3], one study failed to demonstrate any influence of intensive cannabis use on prolactin levels [2]. The present report is a case-control study of gynecomastia in a military population—US Army soldiers in Nuremberg, Germany—where the incidence of cannabis use was nearly 50 per cent [5,6].

Material and Methods

Eleven patients diagnosed with idiopathic gynecomastia requiring mastoplasty at the US Army Hospital Nuremberg (USAHN) between December 1971 and May 1974 were studied. One control was chosen for each patient and matched for age, race, rank, duration in Europe (within 2 months), and unit of assignment. We chose these matching criteria because previous studies of drug use among European army personnel had shown that young, white, low ranking soldiers in Europe for less than one year are more likely to be drug users than their average army counterparts [5,6].

We questioned patients one to six months after their operation about pre- and postoperative drug use and about other correlates of gynecomastia. Interviews were conducted in a confidential manner at the patients' units of assignment after they had been discharged from the hospital. The matched controls were chosen during our visit

to the patients' units and were interviewed in a similar confidential setting. Responses for both patients and controls were validated by checking each individual's record regarding drug arrests, urine testing, and other drug-related indicators [7].

Differences between patient and control responses were tested for significance using the standard matched-pair analysis and the marginal chi-square test [8]. Standard laboratory tests, including liver function and hepatitis B surface antigen by counter electrophoresis, were performed for all patients. No laboratory tests were performed for controls. No facilities for testing for estrogen, testosterone, leutinizing hormone, follicle-stimulating hormone, or prolactin were available at USAHN.

Results

Patients with gynecomastia had a median age of twenty years, median rank of E-3 (PFC), and an average duration in Europe of fourteen months prior to their operation. (Table I.) Six of the eleven patients were white. The causes of their gynecomastia were undetermined. They had no history of hepatitis or symptoms of adrenal disorders, and no galactorrhea or mastodynia. Three patients had fathered children, and three related recent decreases in libido. No exogenous hormones, digitalis, or phenothiazines were being taken. One patient admitted to using intravenous amphetamines on a monthly basis, but there was no admitted methadone or heroin use among the group. There had been no drug arrests or positive urine samples for any of the patients, including the individual who used amphetamines. Physical examination revealed no testicular or liver abnormalities, and liver function tests were within normal limits. Hepatitis B surface antigen determinations were negative.

Controls had similar medical histories. One individual had a previous history of hepatitis prior to entering the army and two others had documented histories of alcohol-related arrests. No control subject had any physical evidence of gynecomastia or admitted to any illicit drug use other than cannabis.

From the US Army Hospital, Nuremberg, Germany. The opinions or assertions contained herein are the private views of the authors, and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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TABLE I Data on 11 Patients with Idiopathic Gynecomastia

Case	Age (yr)	Rank	Duration of Symptoms	Drug Use during 6 Months Before Surgery		Miscellaneous
				Oral Cannabis	Parenteral	
1	18	E-2	2 mo	none	none	
2	18	E-3	1 mo	3/wk	none	
3	18	E-2	1 mo	none	none	
4	19	E-3	3 wk	1/wk	none	
5	19	E-3	3 mo	2/wk	none	
6	20	E-3	1 mo	none	IV amphetamines 1/mo	drug urines negative, decreasing libido
7	20	E-4	2 mo	none	none	
8	20	E-3	2 wk	1/wk	none	1 child at age 18 years
9	21	E-4	3 wk	none	none	
10	26	E-5	1 wk	none	none	2 children, decreasing libido
11	32	E-6	1 mo	1/wk	none	3 children, decreasing libido

TABLE II Characteristics of Gynecomastia Patients and Matched Controls

Characteristic	Cases (n = 11)	Controls (n = 11)
Cannabis		
Within previous 6 mo	45%	55%
Frequency of use (per week among users)	1.6 times	1.3 times
Duration of use (median)	25 mo	29 mo
Noncannabis drug use	9%	0%

Regarding cannabis exposure, gynecomastia patients were slightly *less* likely than controls to have had a history of cannabis use. (Table II.) Those patients who admitted using cannabis had a higher average frequency but a shorter median duration of use. Differences were not statistically significant.

Comments

In our study, no association was found between idiopathic gynecomastia and cannabis use. Compared with matched controls, patients were not significantly different in either cannabis use or frequency of cannabis exposure.

The small number of patients in our study limited its statistical power; it would have required a risk ratio of 4.5 to achieve statistical significance. Nevertheless, we observed no tendency for the patients to use cannabis to a greater extent than the controls. If a causal relationship existed and the number of patients studied were the only limiting factor, we might have expected to find *some* increased cannabis use among gynecomastia patients; such was not the case.

The possibility of ascertainment bias cannot be excluded. Gynecomastia patients may have denied their use of cannabis to a greater degree than con-

trols. Patients were interviewed one to six months after their operation about drug behavior prior to surgery, whereas controls were queried regarding their drug use at the time of interview. An element of recall bias could have been operative. However, both groups admitted to illicit drug use in percentages similar to other surveys of drug use among US Army soldiers in Europe [5,6].

Confounding may have existed had exposure to other noncannabis drugs known to have centrally mediated endocrine effects been differentially admitted to by either patients or controls. However, the validation procedure which cross-checked drug use indicators with the interview response was the same for both patients and controls and produced no information not admitted to during the interviews.

The possibility for selection bias may exist if soldiers with gynecomastia who were using cannabis were less likely to solicit medical advice regarding their symptoms due to fear of discovery and eventual prosecution for illicit drug use. However, symptoms of gynecomastia would be difficult to hide in a military barracks situation, thereby reducing the likelihood of selective presentation.

The absence of any laboratory data on neuroendocrine or sex hormone levels in our study weakens our conclusion. Nevertheless, our epidemiologic findings are in agreement with the laboratory study showing cannabis use was not associated with increased prolactin levels [2]. Without an elevated prolactin level, the alleged association between cannabis and gynecomastia would not be related to a centrally mediated effect, but rather a direct effect of tetrahydrocannabinol on the male breast tissue. However, as noted in our results, we found no such association.

In summary, our epidemiologic evidence does not support the relationship between chronic cannabis use and gynecomastia. These findings do contradict

a previous anecdotal report, but are consistent with other subsequent laboratory investigations.

Summary

Eleven patients diagnosed with idiopathic gynecomastia requiring mammoplasty were compared with matched controls to determine if there was an association between cannabis use and gynecomastia. Patients with gynecomastia were not significantly different from controls regarding their history of cannabis use. For those who admitted using cannabis, patients had a higher average frequency but a shorter median duration of use than controls; differences were not statistically significant. Our epidemiologic evidence does not support the previously reported relationship between chronic cannabis use and gynecomastia.

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