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## BRIEF REPORT

# FLUOXETINE VERSUS PLACEBO FOR THE MARIJUANA USE OF DEPRESSED ALCOHOLICS

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**Abstract —** The aim of this analysis was to evaluate the efficacy of the SSRI antidepressant fluoxetine versus placebo for the marijuana use of depressed alcoholics. There are no previous reports involving and SSRI antidepressant for marijuana abuse. This analysis involved a subsample of 22 depressed alcoholic marijuana users out of a total of 51 depressed alcoholics. The entire sample was involved in a 12-week double-blind, placebo-controlled study evaluating the efficacy of fluoxetine versus placebo in depressed alcoholics. During the course of the trial, the cumulative number of marijuana cigarettes used was almost 20 times as high in the placebo group as in the fluoxetine group. Also, the number of days of marijuana use during the study was five times higher in the placebo group than in the fluoxetine group. These data suggest efficacy for fluoxetine in decreasing marijuana use of depressed alcoholics. © 1998 Elsevier Science Ltd

The National Comorbidity Survey has recently confirmed that marijuana is the most commonly used illicit drug in the United States (Anthony, Warner, & Kessler, 1994). Also, the Epidemiologic Catchment Area (ECA) study has demonstrated that marijuana abuse is significantly associated with affective disorders (Regier et al., 1990). Indeed, that study demonstrated an odds ratio (OR) of 3.8 for marijuana abuse and any affective disorder, which is twice that between alcohol abuse and any affective disorder (1.9). In addition, marijuana abuse is strongly associated with alcoholism, with an OR of 6.0 being noted between these disorders in the ECA study (Helzer & Pryzbeck, 1988).

Despite the prevalence of marijuana abuse and associated disorders, pharmacotherapy studies involving marijuana abuse are scarce. To date, no studies have evaluated the efficacy of any of the SSRI antidepressants in pure marijuana abusers or in patients with marijuana in combination with other comorbid disorders. Our own work has recently demonstrated efficacy for the SSRI antidepressant fluoxetine for treating both the alcohol use and the depressive symptoms of a sample of depressed alcoholics (Cornelius et al., 1997). However, in the earlier analysis, we did not focus our analyses on the 43% of those depressed alcoholics who also abused marijuana, so no conclusions could be made concerning the efficacy of fluoxetine for the marijuana abuse of depressed alcoholics. In this article we report findings from a secondary data analysis involving the marijuana abusers in that first double-blind placebo-controlled study of

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an SSRI antidepressant (fluoxetine) in depressed alcoholics. We hypothesized that fluoxetine would demonstrate efficacy versus placebo in decreasing the marijuana use of depressed alcoholics.

## METHODS

All patients were recruited from consecutive admissions on the inpatient services of the hospital. Upon admission to the hospital, all patients received a thorough medical and psychiatric evaluation by a psychiatrist to screen for these comorbid diagnoses, utilizing *DSM-III-R* (American Psychiatric Association, 1987) criteria. Marijuana abuse was also diagnosed utilizing *DSM-III-R* criteria, although this diagnosis was not required to participate in the study. The patients described in the current analyses included the 22 depressed alcoholics who were also marijuana abusers, out of a total sample of 51 depressed alcoholics. Following a 2- to 3-day detoxification with minor tranquilizers and a subsequent 1-week washout period, the continued presence of the comorbid diagnoses of major depression and alcohol dependence was confirmed utilizing the Structured Clinical Interview for *DSM-III-R* (SCID; Spitzer, Williams, Gibbon, & First, 1988).

After giving written informed consent, patients were randomly assigned to receive either fluoxetine or placebo, both of which were administered in identical-appearing capsules. This randomized allocation was stratified by gender and race to ensure an equal distribution of these factors across the two treatment groups. Other psychoactive medications were not permitted during the course of the double-blind treatment study. All patients were initially started on one capsule (20 mg fluoxetine or placebo), which could be increased to two capsules after 2 weeks if substantial residual depressive symptoms persisted (which was rare). All patients also received "usual care" for dual-diagnosis patients in the outpatient clinic, consisting of weekly supportive psychotherapy sessions and weekly meetings with an attending psychiatrist with expertise in treating dual-disorder patients. Weekly ratings of symptoms were performed by an attending psychiatrist for 12 weeks. The first two ratings were performed while the patient was still in the hospital, and the remaining weekly rating sessions were conducted on an outpatient basis. Outcome measures were compared by analysis of covariance.

## RESULTS

A total of 51 depressed alcoholics were recruited. Additional methodology information, descriptive data, and treatment outcome data concerning these 51 patients have already been published (Cornelius et al., 1997), though those previous data did not address marijuana use. The findings described in the present study are based on a secondary analysis involving this subgroup of 22 depressed alcoholic marijuana users. This subsample of marijuana users was coincidentally evenly distributed between the fluoxetine group ($n = 11$) and the placebo group ($n = 11$). The mean age of the depressed alcoholic marijuana users in this study was 30.8 ± 8.2 years. Thirteen of the patients (59.1%) were African-American; 9 (40.9%) were Caucasian. Half of the patients were female and half were male.

In the 90 days prior to admission, there was no significant difference between groups in the number of days of marijuana use [$\overline{X}$ (Fluoxetine group) = 26.1; $\overline{X}$ (Placebo group) = 27.1, *ns*]. During the week before hospitalization, the mean marijuana use was 5.5 ± 12.8 marijuana cigarettes per day, which did not differ significantly be-

tween treatment groups. The mean number of drinks in the week prior to hospitalization was 54.7 ± 52.7, indicating heavy recent drinking. The mean HAM-D-24 score at baseline was 19.4 ± 8.3, while the mean BDI score at baseline was 16.7 ± 11.4. Thus, following detoxification and a 1-week washout, the patients continued to demonstrate a moderate level of depressive symptoms. The mean Global Assessment Scale score at baseline was 52.1 ± 8.5, which is in the moderately severe range.

During the course of the study, marijuana use decreased in the fluoxetine group and increased in the placebo group. There was a significant group-time effect on marijuana use shown on repeated-measures ANOVA ($F = 3.61$; $df = 2, 19$; $p = .036$). The cumulative number of marijuana cigarettes used during the course of the study was almost 20 times as high in the placebo group as in the fluoxetine group (61.3 vs. 3.3, respectively). Also, the number of days of marijuana use during the study was five times higher in the placebo group than the fluoxetine group ($x = 20.4$ vs. $x = 4.5$ days; $F = 3.9$; $df = 1$; $p = .06$).

During the course of the study, the fluoxetine group demonstrated a significantly greater improvement in depressive symptoms on the HAM-D-24 than the placebo group ($\Delta = -5.6$ vs. $\Delta = -0.9$, respectively, $F = 7.4$; $df = 1,21$; $p = .014$). The fluoxetine group also showed a trend toward a greater improvement than the placebo group on the BDI ($\Delta = -8.5$ vs. $\Delta = -1.5$, respectively, $F = 3.9$, $df = 1,21$; $p = .062$). The fluoxetine group demonstrated a significantly greater improvement than the placebo group on the Global Assessment Scale ($\Delta = 11.9$ vs. $\Delta = 4.6$; $F = 7.1$; $df = 1,21$; $p = 0.015$). Finally, the fluoxetine group demonstrated a significantly greater improvement than the placebo group in drinking (number of drinks per week) ($F = 4.6$, $df = 1,20$; $p = .045$).

## DISCUSSION

This report provides preliminary data regarding the potential benefit of an SSRI antidepressant in the treatment of the marijuana abuse of depressed alcoholics. To our knowledge, this is the first study to evaluate the efficacy of any SSRI antidepressant for the marijuana abuse of any clinical sample, regardless of the presence or absence of any comorbid disorder.

Our findings suggest efficacy for fluoxetine in decreasing the marijuana consumption of depressed alcoholics, as well as for decreasing the depressive symptoms and drinking of these patients. These findings extend our previous findings, which demonstrated efficacy for fluoxetine in treating alcohol use and depressive symptoms of depressed alcoholics (Cornelius et al., 1997).

The pharmacology of the effect on marijuana usage demonstrated by fluoxetine in this study is unclear. This effect may result at least in part from its antidepressant effect. However, the antidepressant effect of fluoxetine in depressed alcoholics is modest in magnitude (Cornelius et al., 1997), whereas the antimarijuana effect demonstrated in the current report is robust. These findings suggest that the antimarijuana effect of fluoxetine may not be entirely due to its antidepressant effect. Further studies are warranted to clarify the nature of the antimarijuana effect of fluoxetine. Additional studies are also warranted to clarify the relationship between depression and marijuana use as some (Gruber, Pope, & Brown, 1996) have suggested that many patients may use marijuana to "self-treat" depressive symptoms. Finally, more studies are warranted to clarify the nature of the "amotivational state" of marijuana smokers, which some have suggested is a symptom of depression (Kupfer, Detre, Koral, & Fajans, 1973).

Our study is limited by its modest sample size and by the fact that marijuana use was not the original primary outcome variable of this study. Also, it is unclear whether the results of this study extend to populations that are not depressed and to alcoholics. Large, multisite trials of selective serotonergic medications are warranted to assess the efficacy of these agents in comorbid populations.

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