Cannabis in Acute Migraine Treatment Project

Ethan Russo, M.D., Neurologist,
University of Montana
Jeannine Mielke,
University of Montana, Dept. of Psychology
Laura Taylor Painter,
Stuart Hall, Ph.D.,
Brian Steele, Ph.D.,
University of Montana, Dept. of Mathematics

THIS GROUP of researchers, with the aid of a $3,500 grant from MAPS, has submitted a research proposal to the National Institutes of Health (NIH). The study was approved by the St. Patrick Hospital/Community Medical Center Joint Investigational Review Board, whose ruling was also accepted by the IRB of the University of Montana.

Rationale

Cannabis, or marijuana, has been used for centuries for both symptomatic and prophylactic treatment of migraine. It was part of the Western pharmacopoeia for this indication even into the mid-twentieth century. Current anecdotal studies continue to refer to its efficacy for this malady, while biochemical studies of THC and anandamide have provided a scientific basis for such treatment.

Design

Thirty patients meeting *International Headache* Society (IHS) criteria of acute migraine with or without aura, and in whom treatment with subcutaneous sumatriptan has been ineffective or poorly tolerated, will be recruited. Exclusion criteria will include concomitant use of MAO inhibitor drugs, pregnancy, cardiac conditions, history of drug or

Abrams protocol submitted anew

Donald Abrams, M.D.
UC San Francisco

BELOW IS A SUMMARY of the protocol, "Short-term Effects of Cannabinoids in HIV Patients" which was submitted by Dr. Donald Abrams, et al., UC-San Francisco, to the National Institutes of Health (NIH) by a May 1, 1997 grant deadline. If accepted by the NIH, this study would cost nearly a million dollars and would take three years to complete. MAPS donated $5,000 for the preparation of this grant application. NIH's decision regarding this application will be announced before the end of September, 1997.

Summary

Our primary aim is to determine the safety/toxicity profile of cannabinoids in persons with HIV infection. We propose to do this by conducting a randomized, prospective study whose primary goal is to determine the short-term effects of smoked marijuana on the pharmacokinetics of indinavir, the immune system and the level of HIV-1 viral load in persons with HIV-1 infection. The study will be composed of three successive phases. The first phase will be a 4-day lead-in period in which baseline measurements are obtained. This will be followed immediately by a 21-day intervention phase in which subjects receive either marijuana cigarettes (Group A), dronabinol capsules (Group B), or placebo capsules

analgesic dependency.

After suitable informed consent, study patients will be randomized to receive study medications consisting of meperidine 1 mg./kg. I.M. along with hydroxyzine 50 mg. as an anti-emetic, or Marinol (dronabinol, synthetic THC) 10 mg. p.o., or an oral placebo capsule (Vitamin E), or alternatively, one or more inhalations of pre-sterilized, pyrolysed Cannabis, employing marijuana cigarettes with a standardized 4% THC content. The pyrolysed Cannabis dose will be titrated to the patients' responses. All patents will be monitored for one hour, at which time a preliminary questionnaire regarding symptom relief, and a Folstein Mini-Mental State Examination will be performed. Blood samples for THC will be drawn at one and two hours in the dronabinol and placebo capsule groups and, and at ten minutes and one hour in the marijuana-treated patients. Folstein tests will be repeated at the two-hour mark. Patients will then be allowed to return home, with a designated driver, or via arranged transportation.

All patients will subsequently complete questionnaires at the four-hour, and twenty-four hour marks employing visual analog scales to determine efficacy of their treatment with respect to pain levels, nausea and photophobia, and their perceived ability to engage in work or study activities.

The proposed budget for this study is $145,500. After the review by a NIDA study section, the results of which will be known in November 1997, there are three possible outcomes. The study may be rejected outright, approved but not funded, or approved and funded. Should it be accepted, but not funded, the possibility remains that it could be completed through private funding sources. •

Questions may be directed to:
Ethan Russo, M.D.
Dept. of Neurosciences
Western Montana Clinic
515 West Front St.
Missoula, MT 59807-7609
E-mail: ptm5739@montana.com

MAPS donated $3,500 for the preparation of Dr. Russo's application to the NIH to study the effects of cannabis on migraine.

(Group C). Subjects in Group A will smoke one 4% THC-content marijuana cigarette three times daily, one hour prior to each meal. Group B and C subjects will receive dronabinol 2.5 mg or placebo three times daily, one hour prior to meals. In the last phase, subjects will be evaluated as out-patients (with no intervention) on days 28, 35 and 32. Subjects will be hospitalized in the General Clinical Research Center (GCRC) at San Francisco General Hospital for the first two phases of the trial (25 days) because, at present, legal use of smoked marijuana is restricted to medically supervised settings. The inpatient setting also permits us to measure plasma THC levels as a means to assess the total dose delivered, and to rigorously assess the safety parameters and measures of possible efficacy, including appetite, food intake, body composition and weight. Eligible subjects will be currently receiving indinavir and will be experienced marijuana users. The primary outcomes are change from baseline in (1) HIV-1 viral load and (2) indinavir concentration (area under the curve). Because both indinavir and dronabinol are metabolized in the liver, interactions between these treatments could alter the concentration of indinavir, thus increasing its toxicity or decreasing its efficacy. In turn, lower indinavir concentration could result in an increase in viral load. We include Control Group B (dronabinol capsules) in order to simultaneously evaluate these outcomes in subjects treated according to the current standard of care. We include Control Group C (placebo capsules) to establish baseline values under our experimental conditions. We will also summarize the short-term effects of smoked marijuana on variables associated with HIV-1 wasting syndrome by measuring changes over 21 days of use in endocrine function, appetite, energy intake, body composition and weight. If the current study demonstrates that smoked marijuana does not have the serious short-term side effects studied here, we would next research safety and efficacy of the chronic use of marijuana for HIV-associated anorexia and weight loss. These data will help to identify the most powerful measures to assess efficacy and provide estimates of effect size and variance. •

Questions may be directed to:
Donald Abrams, M.D.
Community Consortium
3180 18th St., Suite 210
San Francisco, CA 94110

MAPS donated $5,000 for the preparation of Dr. Abram's application to the NIH to study the effects of cannabis on persons with HIV infection.