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TOLERABILITY STUDY OF A DEPOT FORM OF NALTREXONE SUBSTANCE ABUSERS

T. N. Alim, B. Tai, C. N. Chiang, T. Green, R. B. Rosse, T. Lindquist, and S. I. Deutsch

INTRODUCTION: Oral naltrexone has been associated with a high early dropout rate. A injectable depot form of naltrexone could improve compliance in otherwise poorly motivated opiate addicts. A previous sustained release preparation of naltrexone using 1.5 mm diameter spheres showed opiate receptor blockade but some subjects developed tissue inflammation. In the current study, we evaluate the safety and tolerability of a depot form of naltrexone with smaller microspheres (105-150 μm). SUBJECTS: Eight cocaine dependent males (34.1 years of age, range = 23-45) with no evidence of opiate dependence and in good physical health were subjects in the study. One subject on the high dose was excluded due to adverse effect of the morphine challenge. DESIGN: The study was a double-blind, placebo-controlled two dose inpatient/outpatient study. Subjects were evaluated for 64 days. LOW DOSE PHASE (n=4, 3 drug, 1 placebo): Subjects received 1.2 cc (103 mg) of naltrexone preparation or placebo subcutaneously in triceps of each arm (one arm received placebo). When subjects did not experience severe side effects to this low dose after 64 days, the high dose phase was conducted. HIGH DOSE PHASE (n=4, 3 drug, 1 placebo): Subjects received 2.4 cc (206 mg) of naltrexone preparation or placebo in a similar fashion to the low dose group. Plasma naltrexone levels were obtained during both phases. RESULTS: Subjects generally reported mild injection site pain; erythema was observed in most subjects, but was not severe and subsided over the course of the study. Induration without pain or discomfort was the most persistent side effect. Blood chemistries and CBC did not change significantly over the course of the study. Morphine challenge: Subjects in the high dose group were challenged with 10 mg IV morphine on days 8, 15, 22, and 29 of the inpatient stay. Opiate receptor blockade was observed although physiologic and subjective responses were variable. CONCLUSIONS: The depot formulation of naltrexone used in this study appeared well-tolerated and resulted in plasma levels of 1 ng/ml or greater for more than three weeks. Higher doses of opiate agonists may better assess efficacy of this depot formulation of naltrexone. Future studies to assess the acceptability, tolerance, and efficacy of depot naltrexone in outpatient detoxified opiate addicts appear indicated.

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AFFILIATION:

National Institute on Drug Abuse and the Department of Veteran's Affairs, Rockville, MD