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Naltrexone hydrochloride (Trexan) is an opioid antagonist, devoid of agonist activity, indicated in the maintenance of an opioid-free state in detoxified formerly opioid-dependent individuals. Typically, individuals are dosed with 50-150 mg of oral naltrexone every 24-72 hours. A major constraint on its utility as a treatment modality has been the lack of acceptance by clients, due in part to the frequency of dosing and incidence of adverse side effects.

The development of a depot formulation providing long-term opioid receptor blockade via sustained release of low levels of naltrexone may avoid these problems and thus improve treatment compliance. The purpose of this study was to evaluate the safety, pharmacokinetic, and pharmacodynamic profile of a newly developed form of depot naltrexone.

Four healthy nonsmokers, who reported no history of drug and alcohol dependence, participated in a placebo-controlled, double-blind, outpatient trial. On day one, subjects received two s.c. injections simultaneously, one in each upper arm (triceps area). Injections contained either naltrexone (52 mg) or placebo microcapsules. An assessment battery, consisting of dermatological, physiologic, subjective, and performance measures and blood samples for hematology, chemistry, and naltrexone concentration, was completed at pre-injection baseline and repeated at 4 and 8 hours postdrug and on days 2, 3, 5, 8, 11, 15, 22, 29, 36, 50, and 64.

Results indicated no tissue irritation or infection at the injection sites, and no adverse physical signs and symptoms. Laboratory results were normal. Mean maximal plasma naltrexone concentration of 0.93 ng/ml was observed at 24 hours post-naltrexone. Plasma levels declined to about 0.4 ng/ml at four days post-naltrexone and remained relatively stable through day 21.

Because the data suggest that this low dose (52 mg) of depot naltrexone is safe, testing will be conducted with higher doses to achieve a sustained naltrexone plasma concentration of 1-2 ng/ml.

AFFILIATIONS

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