

Induction of withdrawal-like symptoms in a small randomized, controlled trial of opioid blockade in frequent tanners

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Frequent tanning has reinforcing properties. We tested whether opioid antagonism blocks potential reinforcing effect of indoor tanning in 8 frequent tanners and 8 infrequent tanner control subjects. Opioid blockade reduced ultraviolet preference in frequent tanners. Four of 8 frequent tanners, but no infrequent tanners, exhibited withdrawal-like symptoms with naltrexone administration. A limitation of this study is its small size. (J Am Acad Dermatol 2006;54:709-11.)

When given a blinded choice between ultraviolet (UV)- and non-UV-emitting tanning beds, frequent tanners overwhelmingly prefer UV-emitting beds.¹ A questionnaire testing *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition's* addiction criteria suggests that frequent tanning has features of an addictive behavior.² Induction of cutaneous endorphins by UV light occurs in vitro and could play a role in driving UV exposure behavior.³ If cutaneous endorphins are involved in a reinforcing effect of UV exposure, then endorphin blockade would be expected to block the effect.¹

An open trial using 50 mg of the opioid antagonist naltrexone was performed to test whether endorphin blockade reduces the reinforcing effect of UV in frequent tanners. The study was stopped when 2 of 3 frequent tanners developed symptoms consistent with physiological withdrawal (eg, nausea,

jitteriness, shaking).⁴ This finding is unexpected but is consistent with the hypothesis that frequent tanning is driven by an opioid-dependent mechanism. The possibility that the withdrawal-like symptoms were simply nonspecific nausea related to naltrexone administration seems unlikely because naltrexone is generally well tolerated in non-opioid-dependent individuals.^{5,6} We performed a randomized, controlled trial of naltrexone exposure in frequent and infrequent tanners to test whether opioid blockade abrogates frequent tanners' preference for UV versus non-UV stimuli and to determine if opioid blockade induces withdrawal symptoms in frequent tanners.

METHODS

Eight frequent tanners and 8 infrequent tanners between the ages of 18 and 34 years were recruited. Frequent tanning was defined as tanning 8–15 times a month, more than is required to maintain a tan. Infrequent tanners were defined as having used tanning beds previously, but no more than 12 times in any given year. We included infrequent tanners rather than non-tanners so as not to expose indoor tanning-naïve individuals to conditions that we felt could potentially have addictive properties. The study was approved by the Institutional Review Board. Minimal erythema dose (MED) phototesting was performed to ensure that the amount of UV light exposure delivered in this study did not cause sunburn. We excluded individuals with Fitzpatrick skin type I to reduce potential side effects.

We performed a double-blind, placebo-controlled trial of UV and non-UV exposure in conjunction with placebo-controlled administration of an escalating

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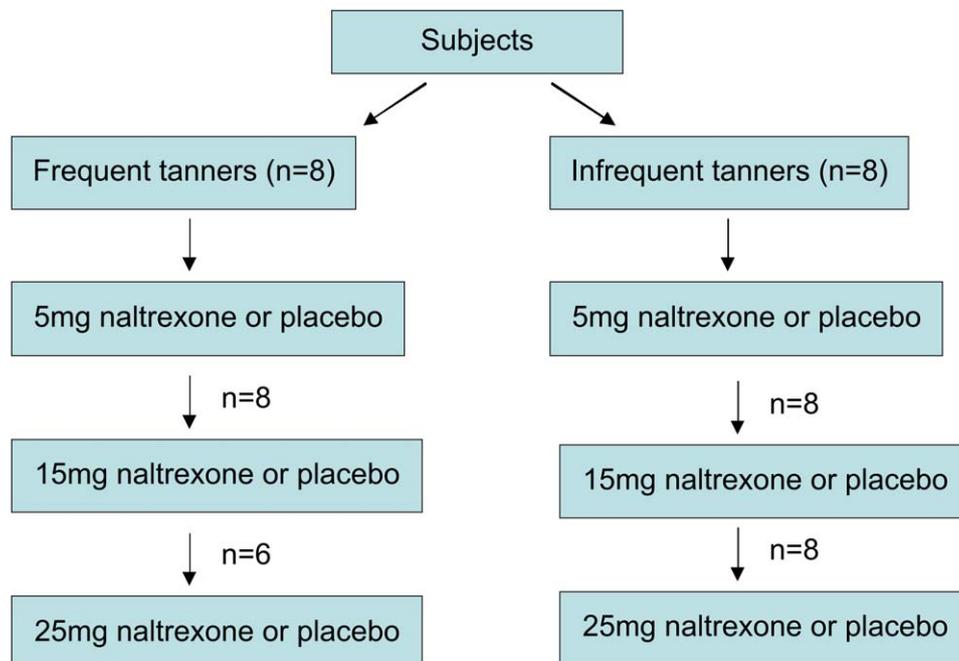


Fig 1. Flow diagram of patient allocation. Eight frequent tanners and 8 infrequent tanners were given escalating doses of naltrexone. At each dose level, subjects were randomized to receive either naltrexone or placebo; they were then given the other at the next visit. All 8 infrequent tanners completed the trial without adverse events. Two frequent tanners discontinued the study due to adverse events at the 15 mg naltrexone dose, and 2 others had adverse events associated with administration of 15 mg of naltrexone but continued in the study.

dose of naltrexone (Fig 1). Naltrexone is a relatively pure narcotic antagonist that effectively blocks both central and peripheral opioid receptors. This blockade results in withdrawal symptoms in opioid-dependent individuals, but is generally well tolerated in non-opioid-dependent people. Only 5% or fewer of normal, healthy individuals report adverse effects when given naltrexone.^{5,6} Block randomization was used.

Subjects agreed to not tan in UV beds or to tan outdoors for the duration of the study (2 weeks). We queried additional exposure to natural sunlight and treated it as a covariate in our analyses. Participants were given either placebo or naltrexone and, after a 1-hour rest period, were exposed in both UV and non-UV tanning beds in random order. Frequent tanners were exposed to the UV bed for a period up to 10 minutes on each visit, and the infrequent tanners were exposed to the UV bed for a period of time that was based on the results of previous MED phototesting. After completing each session, participants completed a survey which indicated their preference for a particular tanning bed. A 9-point rating scale that compared the two beds directly was used to assess the tanning bed preference (1 = greatly preferred first bed; 5 = no prefer-

ence; 9 = greatly preferred second bed). Participant responses were analyzed using SAS version 8 (SAS Institute, Cary, NC). Adverse events, when they occurred, were recorded following each tanning session. Because of the small size of this study, significance testing was not conducted.

RESULTS

With placebo and with a 5-mg dose of naltrexone, frequent tanners preferred the UV stimulus; however, frequent tanners showed a reduced preference for UV exposure with naltrexone doses of 15 and 25 mg (Fig 2). Placebo-treated infrequent tanners exhibited less preference for the UV stimulus as compared with frequent tanners (Fig 2).

There were no adverse events reported by either frequent or infrequent tanners with exposure to placebo, and there were no reported adverse events among the infrequent tanners at any administered naltrexone dose. The frequent tanners did not experience any adverse side effects with a 5-mg dose of naltrexone. However, at a naltrexone dose of 15 mg, 4 of the 8 frequent tanners reported adverse events (nausea and/or jitteriness), causing 2 of these 4 patients to remove themselves from the study. There

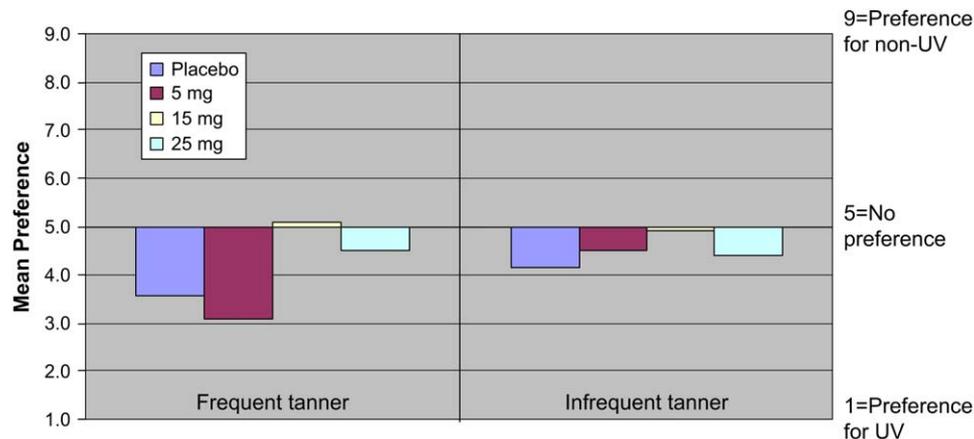


Fig 2. Preference for UV vs non-UV exposure in frequent and infrequent tanners given placebo or increasing doses of naltrexone. Mean preference scores less than 5 indicate preference for UV. With placebo and with 5 mg naltrexone, frequent tanners preferred the UV stimulus; however, frequent tanners showed a reduced preference for UV exposure with naltrexone doses of 15 and 25 mg.

were no adverse events reported in any of the remaining participants at a dose of 25 mg of naltrexone.

DISCUSSION

Some people will go to a tanning bed for just a few visits to obtain a tan before an event, while others may tan intermittently in order to maintain a tan. There are other individuals—whom we define as frequent tanners—who tan several times a week, more than is required to maintain a tan. It has been suggested that tanning is an obsession for frequent tanners (BBC, “Young ‘tanorexics’ risking cancer”; broadcast May 24, 2005). These individuals may be at greatest risk of adverse effects of UV.

The character of the adverse events observed in frequent tanner participants is consistent with symptoms of opiate withdrawal induced by the opioid blockade. We recognize that this was only a small study and that a larger study confirming these findings would be valuable. Nevertheless, the finding that 4 of 8 frequent tanners developed withdrawal-like symptoms with an opioid antagonist—while such symptoms were not observed with placebo or with infrequent tanners receiving naltrexone—lends support to the hypothesis that the reinforcing effects of UV exposure may be at least in part mediated by opioids. Further study confirming a high prevalence

of withdrawal symptoms among frequent tanners treated with opioid blockade would further support that UV exposure may have an addictive quality in frequent tanners.

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