

[Stabilization of remission in patients with opioid dependence with naltrexone implant: a pharmacogenetic approach].

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AIM:

To evaluate the effect of opioid receptor genes and dopamine system genes polymorphisms on treatment outcomes of opioid dependence with implantable and oral naltrexone.

MATERIAL AND METHODS:

Authors carried out a randomized double-blind, double-dummy, placebo-controlled clinical trial. Three hundred and six patients with opioid dependence were randomized into 3 equal treatment groups. The first group received implantation of 1000 mg naltrexone every 2 months during 6 months + oral naltrexone placebo; the second group - placebo implant every 2 months + oral naltrexone (50mg/day) and the third group - placebo implant + oral naltrexone placebo. It was genotyped polymorphisms in the following genes: mu-opioid receptor (OPRM1), kappa-opioid receptor (OPRK1), catechol-O-methyltransferase (COMT), dopamine receptors types 2 (DRD2) and 4 (DRD4), dopamine-beta-hydroxylase, and dopamine transporter (DAT1).

RESULTS:

Regardless of treatment several polymorphisms of these genes were associated with high risk of relapse: an allele L (2R) DRD4 120bp ($p=0.05$; OR (95% CI)=3.3(1.1-10.1)); an allele C DRD2 NcoI ($p=0,051$; OR (95% CI)=2,86 (1,09-7,52)); the genotype 9.9 DAT VNTR 40bp ($p=0,04$; OR (95% CI)=1,4 (1,3-1,5)); on the contrary, (CC+CT)-(TT) variants of OPRK1-DRD2NcoI increased a chance to complete treatment program ($p=0,004$; OR (95% CI)=7.4 (1.8-30.4)), Kaplan-Meier survival analysis ($p=0,016$). The probability of completing treatment program by the carriers of these variants was higher in the oral naltrexone group ($p=0.016$), lower in the double placebo group ($p=0.015$), but did not influence on treatment outcomes in the naltrexone-implant group.

CONCLUSION:

Naltrexone-implant is a highly effective medication for treatment of opioid dependence and its effectiveness exceeds that of oral naltrexone and placebo. The study has shown the joint influence of opioid receptor genes and genes of dopaminergic system on treatment outcomes of opioid dependence. Genetic analysis is useful for determining potential responders to naltrexone treatment of opioid dependence.