Different drug formulations of opiate antagonist naltrexone (oral, implantable and injectable) are widely used for treatment of opiate dependence in Russian Federation.

The main problem of naltrexone therapy is low level of compliance.

Pharmacogenetic approach to the naltrexone treatment has great potential for improving treatment outcomes by determination of responders and non-responders to pharmacotherapy.

Study was aimed to assess the effectiveness of oral and implantable naltrexone on the treatment outcomes of opioid dependence versus placebo with inclusion of genetic covariates (genes of mu- and kappa-opioid receptors, dopamine receptors, O2-polymerase, transmembrane dopamine transporter and catechol-ortho-methyltransferase).

Introduction

Materials and Methods

- It was the double blind double dummy study.
- 506 opioid addicts after detoxification have been randomly assigned to one of the 3 groups (102 patients in each group).
- It was the double blind double dummy study.
- Every patient received the naloxone challenge test, after which they received placebo implantable and surgical naltrexone implantation.
- Among homozygote T&T of DRD2Ncol (blue line) had a higher chance to complete treatment program compared to homozygote C&C and heterozygote C&T of DRD2Ncol (p=0.01; Log-rank criterion).

Results

Kaplan-Meier Survival Functions: Drop out

The retention in treatment program according Kaplan-Meier survival analysis was significantly higher in naltrexone implant group (p<0.01).

Conclusions

- Naltrexone implant is the effective for opiate dependence therapy, superior in effectiveness then oral naltrexone and placebo-implant.
- The genetic carrier of AAAGTT or AGAGTT alleles of OPRM13 genes, OPRK1 and COMT, and also CCAGTT or CTAGTT alleles OPRM11 genes, OPRK1 and COMT have better effectiveness of any therapy.
- Combination of genetic analysis of dopamine and opiate receptors system may be useful to define responders to opiate dependence of any therapy and therapy by naltrexone.

**Effectiveness of the treatment regardless any therapy**

<table>
<thead>
<tr>
<th>Group</th>
<th>NI+ON</th>
<th>NI+OP</th>
<th>PI+ON</th>
<th>PI+OP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>28.05±4.0</td>
<td>27.30±1.9</td>
<td>28.70±4.5</td>
<td>28.05±4.0</td>
</tr>
<tr>
<td>Median</td>
<td>28.05</td>
<td>27.30</td>
<td>28.70</td>
<td>28.05</td>
</tr>
</tbody>
</table>

**Effect of combination of alleles of the other two genes on the treatment program completion**

Kaplan-Meier survival functions (NI+ON group)

- Among homozygote CC and heterozygote CT of OPR1: homozygote TT of DRD2Ncol (blue line) had a higher chance to complete treatment program compared to homozygote CC and heterozygote CT of DRD2Ncol (p=0.01; Log-rank criterion).

Kaplan-Meier survival functions ON+PI group

- Among homozygote CC and heterozygote CT of OPR1, homozygote TT of DRD2Ncol (blue line) had a higher chance to complete treatment program compared to homozygote CT and heterozygote CT of DRD2Ncol (p=0.01; Log-rank criterion).

**Kaplan-Meier survival functions**

- Combination of OPRK1 & DRD2Ncol in the ON+PI group
- Combination of the OPRK1 & DRD2Ncol in the OP+PI group

<table>
<thead>
<tr>
<th>Group</th>
<th>DRD2Ncol</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT &amp; TC</td>
<td>Higher</td>
</tr>
<tr>
<td>CC &amp; CT</td>
<td>Higher</td>
</tr>
<tr>
<td>TT &amp; CT</td>
<td>Higher</td>
</tr>
<tr>
<td>CC &amp; TC</td>
<td>Higher</td>
</tr>
</tbody>
</table>

**Kaplan-Meier survival functions ON+PI group**

- Among homozygote CC and heterozygote CT of OPR1, homozygote TT of DRD2Ncol (blue line) had a higher chance to complete treatment program compared to heterozygote CT and homozygote CT of DRD2Ncol (p=0.01; Log-rank criterion).