The effectiveness of clozapine in reducing medical costs associated with treatment-resistant schizophrenia in Japanese patients

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Abstract

Objective: Treatment-resistant schizophrenia is costly. This study evaluated treatment-cost changes following prescription of clozapine in Japanese patients with treatment-resistant schizophrenia.

Methods: Thirty-six patients were recruited; five were subsequently excluded because clozapine was discontinued due to side effects. Medical costs (Japanese yen: JPY) of hospital stay and outpatient treatment were investigated separately, and the total medical cost calculated as their sum. Treatment was assessed at 6-month intervals, based on the month in which clozapine therapy began. The 6-month period after starting clozapine therapy was defined as "0," the prior 6-month period as "-0.5 years," and the subsequent 6-months as "0.5 years." Per-capita 6-month mean costs were calculated.

Results: Mean costs of hospital stay were JPY 253,306 at -2.5 years, JPY 312,093 at -2 years, JPY 418,900 at -1.5 years, JPY 442,247 at -1 year, JPY 450,538 at -0.5 years, JPY 507,850 at 0 years, JPY 273,679 at 0.5 years, JPY 374,665 at 1 year, and JPY 267,414 at 1.5 years. Mean costs for outpatient treatment were JPY 9,807 at -2.5 years, JPY 10,398 at -2 years, JPY 17,807 at -1.5 years, JPY 23,190 at -1 year, JPY 20,815 at -0.5 years, JPY 42,666 at 0 years, JPY 58,496 at 0.5 years, JPY 60,617 at 1 year, and JPY 62,001 at 1.5 years. Mean total costs were JPY 36,438 at -2.5 years, JPY 41,028 at -2 years, JPY 96,831 at -1.5 years, JPY 144,495 at -1 year, JPY 281,177 at -0.5 years, JPY 477,452 at 0 years, JPY 120,352 at 0.5 years, JPY 74,648 at 1 year, and JPY 72,999 at 1.5 years.

Conclusion: Costs of hospital stay and total costs gradually increased before starting clozapine therapy and peaked when clozapine therapy began. Subsequently, outpatient costs slightly increased, but total costs decreased notably. Clozapine therapy is effective in reducing medical costs.

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DRD2, 5-HT1A, and 5-HT2A gene polymorphisms and clinical factors modulate aripiprazole efficacy in different symptom dimensions of schizophrenia

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Abstract

Objectives: Aripiprazole acts as a partial agonist at dopamine D2 and serotonin 1A (DRD2, and 5-HT1A) receptors, and as an antagonist at serotonin 2A (5-HT2A) receptors. The current study aims to examine the possible association between genetic variants (DRD2/ANKK1 Taq1A (rs1800497), 5-HT1A C-1019G (rs6295), and 5-HT2A T102C (rs6313) polymorphisms) and clinical factors on the therapeutic response to aripiprazole in Han Chinese hospitalized patients with acutely exacerbated schizophrenia.

Methods: After hospitalization, the patients (n=128) were given a 4-week course of aripiprazole. Patients were genotyped for
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The association between serotonin receptor gene polymorphisms and hyperprolactinemia in antipsychotic drug-treated schizophrenic patients

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Abstract

Hyperprolactinemia (HPRL) is a common side effects of antipsychotic drugs. It is primarily attributed to blockade of DRD2 within the pituitary gland. Although dopamine is considered the primary prolactin (PRL) release inhibiting factor, the activity of PRL producing lactotrophs is also regulated by the secregogues: thyrotrophin releasing hormone, vasoactive intestinal polypeptide and serotonin (5-HT).

The aim of our study was to investigate the association between 5-HT receptor variants and hyperprolactinemia in antipsychotic drug treated patients with schizophrenia.

The study group included 446 Caucasian persons (M 221/F 225) with a clinical diagnosis of schizophrenia, who were treated with classical and/or atypical antipsychotic drugs. Prolactin level was determined with ELISA method. The upper limits for normal PRL concentration were set at ≤20 ng/ml for men and ≤25 ng/ml for women. We selected a subset of 29 SNPs, that would accurately represent the majority of SNPs for the following serotonin receptors genes: HTR1A, HTR1B, HTR2A, HTR2C, HTR3A, HTR3B, HTR6. DNA extraction and genotyping were conducted according to standard protocols and blind to the clinical status of the subjects. The software “R” and SPSS were used for statistical analysis.

None of the studied autosomal markers was found to be associated with HPRL. However, a statistically significant association was established between various HTR2C polymorphisms and HPRL. As a result of the analysis of association between HPRL and haplotypes of X-chromosome SNPs, the most statistically significant association was found for a combination of the rs569959*G and rs17326429*A alleles.

It is unlike, that our results are invalidated by the binding potential of the antipsychotic drug used by the patients. We found no clear evidence that the studied HTR2C variants correspond to lack of constitutive activity of this receptor.

This abstract is supported by the Russian Scientific Fund (project no. 14-35-00023)

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Association of DNA Methylation of Taq1A in the DRD2 with Response to Aripiprazole in acute schizophrenia

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Abstract

Background: Epigenetic modification including DNA methylation may have effects on response to antipsychotics in schizophrenia. The Taq1A is located 10kb downstream of DRD2, and causes an amino substitution within the 11th ankyrin repeat of ankyrin repeat and kinase domain containing 1 (ANKK1). We investigated the effects of the DNA methylation of Taq1A in DRD2 on the response to aripiprazole and plasma levels of homovanillic acid (HVA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) in antipsychotic-free acute schizophrenic patients.

Methods: Subjects were 34 Japanese patients with schizophrenia, and were treated with aripiprazole for 6 weeks. The Positive and Negative Syndrome Scale (PANSS) was used for assessment of clinical symptoms. Plasma levels of HVA and MHPG were measured using high-performance liquid chromatography before and after the treatment. The DNA methylation levels of all CpG sites ranging from -162 C to +260 C of 5’ region of ANKK1 gene were determined by sequencing using next-generation sequencer. This study was approved by the ethics committee of Fukushima Medical University, and the patients consented to participate after having been informed of the purpose of the study.

Results: Aripiprazole decreased PANSS scores after the 6 weeks. The Positive and Negative Syndrome Scale (PANSS) was used for assessment of clinical symptoms. Plasma levels of HVA and MHPG were measured using high-performance liquid chromatography before and after the treatment. The DNA methylation levels of all CpG sites ranging from -162 C to +260 C of 5’ region of ANKK1 gene were determined by sequencing using next-generation sequencer. This study was approved by the ethics committee of Fukushima Medical University, and the patients consented to participate after having been informed of the purpose of the study.

Conclusion: This is the first study of the association between the DNA methylation of Taq1A in DRD2 and the response to aripiprazole, suggesting that methylation of Taq1A at specific sites may have effects on the response to antipsychotics. Because of the small sample size, further studies are needed to confirm these results.

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Transition into overt psychosis in individuals at ultra-high risk for psychosis: possible roles of multidimensional schizotypy and basic symptoms

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