

統合失調症維持期治療において65%以上の持続的なドパミンD₂受容体遮断は必要か？:単盲検無作為化比較試験

Challenging the need for sustained blockade of dopamine D₂ receptor estimated from antipsychotic plasma levels in the maintenance treatment of schizophrenia: A single-blind, randomized, controlled study

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[Schizophrenia Research 2015. 164. 1-3. 149-154]

OBJECTIVE: Blockade of dopamine D₂ receptors with antipsychotics above 65% is associated with optimal chance of clinical response although recent data suggest a lower threshold for the maintenance treatment of schizophrenia. The objective of this study was to prospectively examine whether such continuous high blockade would be necessary for maintenance treatment. METHOD: In this single-blind, 52-week, randomized controlled trial, clinically stable patients with schizophrenia receiving risperidone or olanzapine were randomly assigned to the continuous D₂ blockade (i.e. an estimated trough D₂ blockade of > 65%) or non-continuous blockade group (i.e. an estimated peak level of > 65% with an estimated trough level of < 65%). Oral doses corresponding to the assigned blockade levels were estimated from random plasma drug concentrations, using the models we developed; antipsychotic doses were then adjusted accordingly. Psychopathology and side effects were assessed at baseline and one year with the Positive and Negative Syndrome Scale (PANSS), Simpson-Angus Scale (SAS), and Abnormal Involuntary Movement Scale (AIMS). The study was approved by the institutional review board at each participating site, and prior to study entry subjects provided written informed consent after receiving detailed information about the protocol. RESULTS: Sixty-eight subjects (34 in each group) were enrolled. Twenty-six (76.5%) and thirty-one (91.2%) subjects completed the study in the continuous and non-continuous blockade groups, respectively, without any significant group difference. A survival analysis also failed to show any significant difference in the completion rates between the two groups. No significant differences were found on any of the assessment scales between the two groups. The degree of dosage change was small in both groups. CONCLUSION: The findings from this pilot study suggest that sustained dopamine D₂ receptor blockade above 65% may not be necessary in the maintenance treatment of schizophrenia. Going forward, these preliminary findings must be confirmed in future studies using actual measurement of dopamine D₂ receptor occupancy levels with brain imaging. Moreover, they have to be confirmed through double-blind, larger scale trials with longer follow-up periods.