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EXPERT REVIEW SUPPLEMENT

PRACTICAL DOSING STRATEGIES IN THE TREATMENT OF SCHIZOPHRENIA

AUTHORS

Delbert Robinson, MD
Christoph U. Correll, MD
John M. Kane, MD

CME COURSE DIRECTOR

James C.-Y. Chou, MD

ABSTRACT

Patients with first-episode (FE) schizophrenia have an 81.9% chance of relapse within five years of initial episode, and only 13.7% of FE patients experience ≥2 years of sustained recovery. Medication non-adherence is the greatest predictor of relapse. Approximately 40% of FE patients are non-adherent, and ~60% have intermittent periods of non-adherence. Antipsychotic switching/augmentation strategies may be required in order to stabilize patients and prepare them for a maintenance regimen. To achieve the desired 60% to 80% striatal dopamine blockade and avoid EPS/akathisia, careful consideration must be given to many practical intra-individual and inter-individual variations relating to drug absorption and metabolism. It is especially important to account for the receptor profiles of the pre- and post-switch antipsychotics. Quantitative assessments are very helpful in determining baseline severity and worsening/improvement. Second-generation antipsychotics have demonstrated better rates of adherence in schizophrenia compared to first-generation antipsychotics, although a long-acting injectable medication may be necessary in cases of chronic non-adherence.

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Statement of Need and Purpose

Patients with first-episode schizophrenia generally show high positive symptom improvement with antipsychotic treatment. First-episode patients often respond to a lower medication dose than is required for response in patients with multi-episodes of schizophrenia. Importantly, however, first-episode patients are also more likely than multi-episode patients to experience adverse events. Clinicians treating early-phase patients must be particularly vigilant about assessing for potential side effects.

The goal of antipsychotic dosing is to achieve sufficient dopamine blockage in areas where dopamine excess can lead to psychosis, mania, or aggression. There is, however, considerable intra-individual variability in achieving the desired 60% to 80% striatal dopamine blockade. Careful and knowledgeable evaluation of these variations can help physicians find the optimal antipsychotic dose that leads to sufficient efficacy, without reaching the threshold of extrapyramidal symptoms or akathisia.

Medication non-adherence is one of the major reasons for the significant rates of relapse and re-hospitalization in schizophrenia. Adherence must be assessed and blood levels should be done (if feasible) to ensure that patients have an adequate amount of medication in their system. It is strongly recommended that treatment decisions in schizophrenia be measurement-based so that the clinicians are using quantitative assessment to help guide their decision-making process.

Learning Objectives

At the completion of this activity, participants should be better able to:

- Interpret clinical evidence regarding the dosage, efficacy, and safety profiles of pharmacotherapeutic agents to treat first-episode schizophrenia
- Formulate dosing strategies to achieve optimal antipsychotic efficacy with minimal adverse events
- Discuss the timeframe associated with the onset of action for antipsychotics

Target Audience

This activity is designed to meet the educational needs of psychiatrists.

Faculty Affiliations and Disclosures

Delbert Robinson, MD, is professor of psychiatry and behavioral sciences, Albert Einstein College of Medicine. Dr. Robinson has, within the past one year, received grant support from the National Institute of Mental Health (MH 60004); Bristol-Myers Squibb and Janssen provide medication supplies for Dr. Robinson's research.

Christoph U. Correll, MD, is medical director of the Recognition and Prevention Program, The Zucker Hillside Hospital; and is associate professor of psychiatry at the Albert Einstein College of Medicine. Dr. Correll, has, within the past one year, served as a consultant to and/or is on the advisory board of Actelion, AstraZeneca, Bristol-Myers Squibb, Cephalon, Eli Lilly, GlaxoSmithKline, Janssen, Lundbeck, Medicure, Otsuka, Pfizer, Schering-Plough, Supernus, Takeda, and Vanda; and received grant support from the American Academy of Child and Adolescent Psychiatry, the Feinstein Institute for Medical Research, the National Alliance for Research on Schizophrenia and Depression, and the NIMH. This presentation includes discussion of off-label or investigational use of antipsychotic agents.

John M. Kane, MD is chairman of the department of psychiatry at The Zucker Hillside Hospital; and is professor of psychiatry, neurology and neuroscience at The Albert Einstein College. Dr. Kane has, within the past one year, served as a consultant to/received speaking honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen, and Novartis; has served on the advisory board of AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen, and Novartis; and received honoraria from Eli Lilly and Janssen.

CME Course Director **James C.-Y. Chou, MD**, is associate professor of psychiatry at Mount Sinai School of Medicine. Dr. Chou has received honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Merck, Novartis, and Pfizer.

Eran Chemerinski, MD, is assistant professor of psychiatry at the Mount Sinai School of Medicine. Dr. Chemerinski reports no affiliations with, or financial interests in, any organization that may pose a conflict of interest.

Activity Review Information

The activity content has been peer reviewed and approved by Eran Chemerinski, MD.

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To Receive Credit for this Activity

Read this Expert Review Supplement, reflect on the information presented, and complete the CME posttest and evaluation on pages 18 and 19. To obtain credit, you should score 70% or better. Early submission of this posttest is encouraged. Please submit this posttest by April 1, 2012 to be eligible for credit.

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