Recent Advances in the Clinical Use of Atypical Antipsychotics

By Jeffrey A. Lieberman, MD

It is well accepted that patients with schizophrenia and affective disorders are at higher risk of medical morbidity and mortality compared with individuals in the general population. They exhibit elevated rates of comorbid medical conditions, such as cardiovascular disease, infectious diseases, non-insulin-dependent diabetes mellitus, respiratory disease, and other illnesses. Mortality rates among individuals with schizophrenia are ~1.6–3.0 times higher than expected. Life expectancy is 20% shorter for them when compared to the general population, or 61 years versus 76 years, respectively. Medical diseases are generally under-treated and, when combined with poverty, limited awareness and understanding as well as lack of access to medical care are part of their reality. The severity of functional deficit in schizophrenia and associated disorders is underscored by the statistics that only 10% of schizophrenic patients work full time, 33% work part time, and fewer than 10% of male patients with schizophrenia are married.

Antipsychotic drugs have been available for more than 50 years. Their principal pharmacologic property and probable mechanism of action is dopamine-2 receptor (D₂) antagonism. Clozapine introduced the first second-generation or atypical antipsychotic agents as pharmacologically distinct for its relatively low affinity for the D₂ receptor and high affinity for other neuroreceptors, particularly the serotonin 2A receptor. Clozapine was followed by other atypicals: risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole, which have become first-line treatments for schizophrenia.

The promise of these newer antipsychotics was increased efficacy, improved efficacy for negative symptoms, fewer side effects, and better long-term outcomes for patients with schizophrenia. The reduction of side effects is true for extrapyramidal symptoms and prolactin, but atypical antipsychotics come with their own burden of side effects—weight gain and altered glucose and lipid metabolism with certain atypicals. Clinicians should be aware of the potential for drug-induced increases in adiposity as a major risk factor for the development of metabolic and cardiovascular complications during antipsychotic treatment.

The articles in this academic supplement are based on proceedings from the symposium “Recent Advances in the Clinical Use of Atypical Antipsychotics,” presented at the 24th Congress of the Collegium Internationale Neuropsychopharmacologicum held June 20–24, 2004, in Paris, France. The articles are intended to help physicians recognize the similarities and differences in the mechanism of action of the antipsychotic drugs, to understand appropriate dosing that is necessary for optimal benefits, to demonstrate the benefits of atypical antipsychotics on the symptoms of psychotic and nonpsychotic disorders, to assess clinical and tolerability issues in guiding selection and implementation of treatment, and to suggest strategies on how these treatments can be applied to produce the best outcomes.

In the first article, Fernando Cañas, MD, discusses the mechanism of action of atypical antipsychotics. Receptor occupancy has been shown to be a function of antipsychotic dose, and the precise nature of the relationship between clinical utility and receptor occupancy is beginning to emerge.

The second and final article of this supplement, by John W. Newcomer, MD, reviews the evolution of antipsychotic treatment from conventional to atypical agents, which has resulted in safer overall treatment of schizophrenia.

REFERENCES

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Disclosure: Dr. Lieberman is a consultant to AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Novartis, and Pfizer; is on the advisory boards of AstraZeneca, Bristol-Myers Squibb, Eli Lilly, and Pfizer; and receives grant/research support from AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, and Pfizer.

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