Introduction

Treatment-Resistant Schizophrenia and Beyond: Current Concepts and Future Prospects

The publication of the U.S. Clozaril Multicenter Trial more than a decade ago led to the worldwide use of clozapine (Clozaril, Leponex) for treatment-resistant schizophrenia.[1] Despite the subsequent introduction of other atypical antipsychotics, clozapine remains the "gold standard" for treatment of this patient population, with superior efficacy compared with conventional antipsychotics. Indeed, it is the only drug with proven efficacy in treatment-resistant schizophrenia.

Over the past decade, the definition of treatment-resistant schizophrenia has evolved to include a wider range of outcome measures. It is important to remember that treatment-resistant schizophrenia includes not only those patients who are unresponsive to conventional therapy, but also those unable to tolerate treatment. In the United States, patients "who fail to respond adequately to standard antipsychotic drug treatment" are considered as suitable for treatment with clozapine, leading to its use in a wider range of patients.

Although approximately 70% of patients respond to antipsychotic treatment with remission of positive symptoms, the majority of these patients will have further episodes of illness and subsequently develop treatment resistance.[2] Furthermore, the remaining 30% of patients are treatment-resistant at first onset. Early identification of these patients is vital. The recent guidelines of the American Psychiatric Association suggest that clozapine should be considered when patients have failed to respond to adequate trials (4–6 weeks at an adequate dose) of at least one antipsychotic medication.[3] The prompt identification of those patients who remain symptomatic or intolerant at the end of a first or second course of treatment will enable them to gain greater benefit from treatment with clozapine.

Clozapine has been used successfully to treat hundreds of thousands of patients with schizophrenia and other forms of psychosis who could not have been treated with conventional therapies. The ability of clozapine to achieve extraordinary resolution of function in even the most refractory of schizophrenic patients has changed the conception of schizophrenia. Clozapine also has a remarkably low propensity to cause tardive dyskinesia compared with conventional antipsychotics, improves negative symptoms, and is the first antipsychotic shown to improve significant aspects of cognitive function. In addition, clozapine treatment is associated with an 80% to 85% reduction in suicide in treatment-resistant patients,[4] accompanied by a decrease in depression and psychopathology and reduced aggressive behavior.

The evolving definition of treatment resistance, the current status of treatment, the place of clozapine in the treatment of schizophrenia, and its optimal use were the topics of a 2-day meeting chaired by Professors Herbert Y. Meltzer and Hanns Hippius. This supplement includes reviews of the presentations by the attending field of eminent experts.

REFERENCES

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