Cochrane Briefs

Clozapine vs. Other Atypical Antipsychotics for Schizophrenia

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Clinical Question

Compared with other atypical antipsychotic medications, what are the effects of clozapine (Clozaril) in patients with schizophrenia and schizophrenia-like psychoses?

Evidence-Based Answer

Although further trials are needed, there is some evidence that clozapine is slightly more effective than risperidone (Risperdal). Fewer participants taking clozapine dropped out of studies because of lack of effectiveness compared with those taking risperidone (number needed to treat = 11; 95% confidence interval [CI], 7 to 21). However, adverse effects led to a higher attrition rate in patients taking clozapine than those taking olanzapine (Zyprexa; number needed to harm = 25; 95% CI, 15 to 73) and risperidone (number needed to harm = 16; 95% CI, 9 to 59). Clozapine is associated with more sedation and hypersalivation than olanzapine, quetiapine (Seroquel), and risperidone; more seizures than olanzapine and risperidone; and more weight gain than risperidone. (Strength of Recommendation = B, based on inconsistent or limited-quality patient-oriented evidence)

Practice Pointers

Clozapine was developed as an alternative to chlorpromazine and haloperidol for the treatment of schizophrenia, in part because the older antipsychotics cause movement disorders. Although it is effective for refractory symptoms, clozapine is associated with fatal agranulocytosis, seizures, myocarditis, orthostatic hypotension, and respiratory and cardiac arrest. Blood counts must be carefully monitored during and after treatment. Other atypical antipsychotics have subsequently been developed, such as aripiprazole (Abilify), olanzapine, quetiapine, risperidone, and ziprasidone (Geodon).

In this Cochrane review, the authors compared single- and double-blind trials of clozapine versus other atypical antipsychotics; 27 studies with a total of 3,099 participants fulfilled their review criteria. Many of the studies included participants who had been unsuccessfully treated with other medications. Most of the studies compared clozapine with olanzapine, risperidone, and quetiapine.

Overall, the attrition rate in the studies was high (30.1 percent), requiring caution in the interpretation of the results. The attrition rate due to adverse effects was higher for clozapine than for olanzapine or risperidone, but fewer patients taking clozapine left the study because of ineffectiveness versus those taking risperidone. Clozapine was not more effective at improving general mental state than olanzapine, quetiapine, risperidone, or ziprasidone. There was no difference in symptoms of schizophrenia, but there were fewer movement disorders with clozapine than with risperidone (number needed to treat = 7; 95% CI, 5 to 15). Patients taking clozapine had more blood dyscrasias, hypersalivation, seizures, and sedation than those taking olanzapine, risperidone, or quetiapine. Compared with those taking risperidone, the

clozapine groups showed fewer extrapyramidal adverse effects but had an important weight gain not seen with risperidone.

The National Institute for Health and Clinical Excellence in the United Kingdom recommends clozapine for persons with schizophrenia who have not responded to two other antipsychotic medications, including another atypical antipsychotic.[1] The American Psychiatric Association has not issued a guideline on schizophrenia since April 2004.[2]

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SOURCE

Asenjo Lobos C, Komossa K, Rummel-Kluge C, et al. Clozapine versus other atypical antipsychotics for schizophrenia. *Cochrane Database Syst Rev*. 2010;(11):CD006633.

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