Schizophrenia: risperidone and olanzapine increase time to discontinuation compared with quetiapine and ziprasidone


Q What are the effects of risperidone, olanzapine, quetiapine, and ziprasidone on time to discontinuation in people who have discontinued another atypical antipsychotic?

CONCLUSIONS

Risperidone and olanzapine increase time to treatment discontinuation compared with quetiapine and ziprasidone in people with schizophrenia who have previously discontinued taking another atypical antipsychotic.

Commentary

F ifty years of antipsychotic drug treatment of people with schizophrenia have not provided sufficient data for evidence-based approaches to the challenges clinicians face everyday. Which drug is best for this patient, and at what dose? Should the dose be changed and, if so, in which direction? Should a switch to another drug be effected and, if so, to which one? Other than the modest superiority of clozapine in treatment resistant patients and the clarification of the optimal dose range with risperidone, clinical trials have not provided this vital information. Research to gain regulatory approval does not address these practical questions, and post-marketing research provides much data of the “our drug is better” variety, giving the clinician little help with these key decisions.

In this regard the CUTLASS and CATIE clinical trials are welcome. Dealing with patients representative of common practice and asking clinically relevant questions, these trials have supported clozapine superiority while finding little or no evidence for differential efficacy and modest evidence for differential effectiveness among first and second generation antipsychotic (SGA) drugs. The current report by Stroup et al addresses switching between SGA drugs. Results support the feasibility of switching, but benefit is modest. Time remaining on drug favours olanzapine and risperidone over ziprasidone and quetiapine, but the latter two drugs may have been dosed too low—the problem of coming to market without determining optimal dose. The time remaining on olanzapine will be sharply reduced by increased awareness of the robust adverse effects on metabolism.

These new data are important, but do they guide evidence-based practice? The clinical trial creates a horse race. A clear winner on a key variable has implications for the individual patient. But when efficacy and effectiveness differences are modest and risk is not calculated, little guidance for clinical decisions is forthcoming. In this instance, note that all antipsychotic drugs impede dopamine signalling and have similar efficacy except for clozapine. Attention then turns to adverse effects and cost where there are substantial differences. The doctor treats an individual (not a cohort), so the task is to find the optimal risk/benefit ratio for each individual patient. It is here that general knowledge and clinical judgement are critical: dyskinesia—switch to a drug benign for TD; sexual side effects—select a compound which does not elevate prolactin; risk for cardiovascular disease and diabetes—select a compound to minimise adverse metabolic effects (and institute treatment aimed at lifestyle change).

In short, there are minimal therapeutic differences between the dopamine antagonists and, substantial differences in adverse effect profiles. Doctors use this knowledge for clinical reasoning with individual patients, with little specific guidance from clinical trials.

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References for this commentary are available at http://www.ebmentalhealth.com/supplemental.

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