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Primer for Prescription Medications: The First Long-Acting Atypical Antipsychotic

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At some time in our lives most of us have forgotten to complete an entire course of antibiotics. Patients with schizophrenia are no different with their medications. Long acting formulations of conventional antipsychotics, namely, haloperidol and fluphenazine decanoates, have greatly improved compliance and subsequently decreased relapse rates and re-hospitalizations over extended periods of time.[1] These medications are usually dispensed every 2 to 4 weeks as an intramuscular injection (IMJ). If a dose is missed, the case manager can alert the patient and the treatment team. Although this option ensures medication adherence, the side-effect profile of traditional agents carries an increased risk of tardive dyskinesia and extrapyramidal symptoms compared to the atypical antipsychotics.[2,3]

In 2003 a long-acting injection, Risperdal Consta, was approved for treatment of schizophrenia. It contains the same active ingredient, risperidone, as the atypical Risperdal and has a similar risk-versus-benefit ratio.

Risperidone's exact mechanism of action in the treatment of schizophrenia is unknown, as with all antipsychotics. It's proposed that its activity is mediated through a combination of dopamine2 and serotonin2 receptor antagonism. The efficacy of Risperdal Consta was established via a 12-week placebo-controlled trial in schizophrenic patients and extrapolated from the established efficacy of oral Risperdal in this population. Its effectiveness for longer than 12 weeks has not been evaluated in controlled trials, so patients should be reassessed periodically.

Risperdal Consta contains risperidone micro-encapsulated in polylactide-co-glycolide to make micro-spheres. These are suspended in a diluent prior to injection. After the first IMJ in the gluteal region, the main release of the drug starts from 3 weeks onward, is maintained from 4 to 6 weeks, and subsides by 7 weeks. Oral antipsychotic supplementation should be maintained for the first 3 weeks. It is administered every 2 weeks; steady-state plasma concentrations are reached after 4 injections.

As with most atypical antipsychotics, precautions should be maintained regarding development of neuroleptic malignant syndrome, tardive dyskinesia, hyperglycemia and diabetes mellitus, and, in elderly and demented patients, cerebrovascular and cardiovascular adverse events. It is classified as category "C" (there is no current evidence of fetal damage) in pregnancy. Some notable drug interactions with risperidone are hepatic enzyme inducers, like carbamazepine, which decrease plasma concentrations of risperidone and its active metabolite 9-hydroxyrisoeridone, and cytochrome 2 D6 enzyme inhibitors, like fluoxetine and paroxetine, which increase its levels.

In patients who have never taken the oral dose or those with hepatic or renal impairment, safety with a small oral test dose should be evaluated before starting Risperdal Consta. The starting dose is 25 mg IM every 2 weeks; dose increments should not be considered before 4 weeks. It is supplied as 25 mg, 37.5 mg, and 50 mg of risperidone in a dose pack. The diluent and needle, specially coated to prevent disintegration of the suspended microspheres, are supplied in the kit.[4]

Currently, Risperdal Consta is the only long acting atypical antipsychotic available in the United States. In the treatment of schizophrenic outpatients, it has shown better clinical outcomes and lowered health care costs over 1 year than its comparators, long acting haloperidol decanoate, oral risperidone, and oral olanzapine.[5] However, the choice of a particular antipsychotic for a patient depends on several factors, such as side-effect profile, past history of drug efficacy, and tolerability. Therefore, the future development of other long acting formulations of such atypical agents will further assist in the treatment planning and rehabilitation of this patient population in the community.

Endnotes

1. N. R. Schooler, "Relapse and rehospitalization: Comparing oral and depot antipsychotics," *Journal of Clinical Psychiatry* 64, no. 16 (2003): 14-7.

2. A. D. Schmetzer, "Primer for prescription medications: The antipsychotic medicines-conventional," *Annals of the American Psychotherapy Association* 5, no. 4 (2002): 26-27.

3. A. D. Schmetzer, "Primer for prescription medications: The antipsychotic medicines-atypical," *Annals of the American Psychotherapy Association* 5, no. 5 (2002): 26-27.

4. D. Duplay, *Physicians' Desk Reference, 59th Edition* (Montvale, NJ: Thompson PDR, 2005).

5. N. C. Edwards, M. F. Rupnow, C. L. Pashos, M. F. Botteman, R. J. Diamond, "Cost-effectiveness model of long acting risperidone in schizophrenia in the US, *Pharmacoeconomics* 23, no. 3 (2005): 299-314.

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