Introduction

Side Effects of Antipsychotic Medications: Physician's Choice of Medication and Patient Compliance

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More than 50% of all new prescriptions written in the United States today for the ongoing treatment of schizophrenia are for atypical antipsychotics. This is an impressive accomplishment, especially when only 10%—perhaps far less in some countries—of worldwide prescriptions are written for atypical antipsychotics. There is emerging interest in whether the newer atypical antipsychotics should generally be substituted for typical antipsychotics and in how to distinguish among the atypical agents when selecting treatment for an individual patient.

All 3 of the atypical antipsychotics that are currently available—risperidone, olanzapine, and quetiapine—have shown efficacy over placebo in clinical trials, and risperidone has shown efficacy over haloperidol in short-term clinical trials[1–3] and over olanzapine for the control of positive symptoms at 6 months.[4]

The atypical antipsychotics were developed to maximize efficacy while minimizing the extrapyramidal symptoms (EPS), which have limited the use of traditional neuroleptics. When used within the therapeutic dose range, all 3 atypical antipsychotics are associated with significantly fewer EPS than haloperidol.

Since EPS are less problematic with the newer agents, clinicians have focused on other side effects that may lead to noncompliance and long-term consequences. Weight gain, in particular, a frequent side effect of antipsychotic treatment, is associated with increased morbidity and mortality. Individual risk factors such as family history of diabetes and cardiovascular disease and current body mass index should be considered when selecting an antipsychotic for an individual patient. Recent reports have linked clozapine and olanzapine with new-onset diabetes, primarily in patients who were overweight at the start of treatment.[5,6]

In a general overview of side effects caused by typical antipsychotics, George W. Arana, M.D., described the wide range of side effects that can affect every physiologic system in the body. Sexual, reproductive, and central nervous system side effects were also discussed, and the impact of medication side effects on compliance and the patient's quality of life were considered.

Despite superior efficacy, minimal EPS, and lack of hyperprolactinemia, the prototypic atypical antipsychotic clozapine has generally been underutilized for the treatment of schizophrenia because of associated serious side effects, according to Del D. Miller, Pharm.D., M.D. Since clozapine carries the risk of agranulocytosis, it is indicated only for treatment-resistant schizophrenia. However, because of mandatory blood monitoring, the incidence of agranulocytosis and its associated mortality has been greatly reduced in recent years, and most other side effects of clozapine can generally be managed medically.

The side effects associated with typical antipsychotics are usually minimal in patients taking risperidone, said Robert R. Conley, M.D. Weight gain is less likely to be problematic with risperidone treatment than with either clozapine or olanzapine treatment. Moreover, although increased prolactin levels have been reported in patients taking risperidone, little correlation has been found between prolactin levels and adverse events.

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Dr. Conley and I described the adverse events of olanzapine compared with typical antipsychotics. A recent study[7] comparing olanzapine and chlorpromazine in treatment-resistant schizophrenic patients found that the chlorpromazine group exhibited significantly more dry mouth, orthostatic changes, unsteady gait, and EPS than the olanzapine group. Compared with risperidone, olanzapine appears to cause greater weight gain but less hyperprolactinemia.

Quetiapine is the newest atypical antipsychotic to be approved by the U.S. Food and Drug Administration, reported David L. Garver, M.D. Although the efficacy of quetiapine may not compare with that of typical antipsychotics, the benign side effect profile—especially with regard to EPS and serum prolactin levels—may make quetiapine a useful alternative.

Weight gain is a common side effect of most antipsychotic agents, said George L. Blackburn, M.D., Ph.D. Psychiatric patients should receive periodic monitoring for weight change and an obesity assessment for weight-related illness. A weight gain of 5 lb (2.3 kg) or more within a 3-year period calls for preventative strategies including changes in diet and physical activity, use of support groups, and possible changes in medication.

Elderly schizophrenic patients present special challenges to clinicians because they frequently have comorbid illnesses requiring multiple medications, noted Prakash S. Masand, M.D. Thus, the effects of polypharmacy must be carefully considered. Antipsychotic side effects that are particularly problematic in this population include anticholinergic reactions, parkinsonian events, tardive dyskinesia, orthostatic hypotension, cardiac conduction disturbances, reduced bone mineral density, sedation, and cognitive slowing.

Antipsychotic agents are commonly used in the long-term treatment of bipolar patients, said Carlos A. Zarate, Jr., M.D., and antipsychotic side effects may lead to noncompliance and have a negative impact on the overall course of the illness. Because of their favorable side effect profile, thymoleptic properties, and positive effect on overall functioning, atypical antipsychotics may prove useful for bipolar patients who fail to respond to combinations of mood stabilizers.

It is important that physicians communicate with each other about antipsychotic side effects and examine the clinical significance and relevance of those side effects for clinical practice. Hopefully, by focusing on the whole risk:benefit equation—that is, efficacy, tolerability, and side effects—physicians can better understand where these issues fit into an algorithm and conceptual framework for the treatment of schizophrenia.

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