MEDICATION ADHERENCE AND ATYPICAL ANTIPSYCHOTICS

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A major deterrent to effective treatment of patients with schizophrenia is adherence to prescribed medication. Patients may not be able to follow the treatment regimen due to misunderstanding, forgetting, and a failure to establish routines that promote good adherence. Newer atypical medications have improved tolerability over conventional antipsychotics and have been expected to improve medication adherence for patients with schizophrenia, thereby preventing relapse and repeated hospitalization.

The extent to which patients are adhering to atypical drug regimens has not been widely studied. In this investigation, patients with schizophrenia receiving risperidone or olanzapine in the hospital were followed up immediately after discharge. All medication was monitored for 2 weeks during a baseline period; patients were then followed up for 3 months. Several methods were used to determine medication adherence. These included measures of baseline drug plasma concentration during the period in which medication was closely monitored, with additional blood samples obtained at 3 months. Specifically, 3 blood samples were obtained from the patients immediately after discharge (while medication intake was closely monitored) to determine the coefficient of variation (%CV) in plasma level under ideal conditions.

Two random predose blood samples were obtained 3 months after discharge, and %CV and plasma concentration differences from baseline were used as adherence measurements. In addition, study investigators conducted pill counts and used collateral reports and patient self-reports regarding medication intake to assess medication adherence at baseline and at 3 months.

The results showed that antipsychotic adherence rates were as high as 91% at baseline, when patients were closely monitored; however, at 3 months, adherence dropped to 26% based on plasma level analysis, 44% based on pill counts, and 68% based on self-reports. The significant discrepancy between plasma level, pill count, and self-report adherence rates points to the limitations inherent in all methodologies for assessing compliance with prescribed antipsychotic medications. Patients may be taking medications, but doing so incorrectly or inconsistently. Pill counts can be influenced by numerous factors, including taking more medication than prescribed on certain days and less than prescribed on others, and having old bottles of the same medication in the home. The authors suggest that environmental supports, such as pill containers, signs, and alarms, may improve medication adherence. These findings show that although some atypical antipsychotic medications that are well tolerated may increase patient willingness to comply with treatment plans, other barriers to medication adherence remain and warrant additional study and interventions.

REFERENCE

EARLY RESULTS FROM THE LARGEST STUDY TO DATE OF ANTIPSYCHOTIC THERAPIES

Based on a poster presented by Haro JM,* Edgell E,† Jones P‡ et al, on behalf of the Schizophrenia Outpatient Health Outcomes Study Group

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Six-month findings form the world’s largest observational studies of antipsychotic therapy show that patients treated with atypical antipsychotics experienced marked improvement in quality of life, although efficacy among agents sometimes varied. The Schizophrenia Outpatient Health Outcomes (SOHO) studies are 2 prospective intercontinental observational studies of the health outcomes associated with antipsychotic therapy. One study includes 10 000 patients in western Europe and another includes 8600 patients in Asia, central and eastern Europe, Latin America, and the Middle East. The combined size and scope of the studies are unprecedented in that they are collecting observational, long-term data (3 years) on patients in “real-world” settings, in contrast to the traditional clinical trial framework. The study populations comprise patients who either initiated or changed antipsychotic medication. Specifically, each study has 2 cohorts: subjects who initiated or changed to olanzapine treatment, and subjects who initiated or changed to another antipsychotic agent. Mean change in positive, negative, depressive, cognitive, and overall symptoms from baseline to 6 months is being measured using the Clinical Global Impressions-Schizophrenia scale.

At 6 months into the European study, improvements were seen across drug treatment groups. However, the odds of patient response in terms of positive symptoms were significantly higher for patients that started with olanzapine compared with patients that initiated treatment with risperidone, quetiapine, or depot typical antipsychotics. No significant differences were observed between olanzapine and the clozapine and amisulpride cohorts. At 6 months, more than 35% of patients in the European study who were taking risperidone and typical antipsychotics were also taking anticholinergic agents or experiencing movement disorders compared with 20% or less of patients treated with olanzapine or clozapine.

The SOHO study will look at more than 30 areas over the course of 3 years to assess how treatment patterns affect patients’ living conditions, clinical status, health-related quality of life, and ability to work and socialize. Rates of hospitalization will also be assessed. The study will assess treatment tolerability, compliance, victimization, violence, and resource use.

SYMPTOM IMPROVEMENT WITH LONG-ACTING INJECTABLE RISPERIDONE

Based on 2 posters:

“Can Stable Patients with Schizophrenia Improve? The Impact of Partial Compliance vs Constant Therapy,” presented by Lonchena C,* Lasser RA,* Bossie CA,* Zhu Y,* Gharabawi G,* Balessarini RJ†

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“Clinical Improvement with Long-Acting Risperidone in Patients Previously Receiving Oral Olanzapine,” presented by Jones R,* Lasser RA,* Bossie CA,* Conley RR†

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Optimal outcome in the long-term treatment of schizophrenia is limited by partial compliance—patients ‘getting by’ with variable adherence to recommended medications. Further, a leading cause of relapse in patients with psychosis is a more serious lack of adherence with daily medication regimens of
atypical antipsychotics. Because these drugs are available only in short-acting formulations, daily dosing is the only option. Several studies have explored the use of the first long-acting, injectable antipsychotic, long-acting risperidone, as an alternative drug delivery system. The hypothesis is that assured pharmacologic delivery will result in improved control of symptoms and promote optimal clinical outcome.

In an open-label study, investigators analyzed data for 336 stable patients (either outpatient or inpatient) with mild schizophrenia or schizoaffective disorder who were receiving stable doses of risperidone for 1 month and who were considered clinically stable. Patients were assigned to switch to 25, 50, or 75 mg of long-acting risperidone every 2 weeks for up to 50 weeks. The study showed substantial and significant psychiatric and movement disorder improvements in these stable patients who switched from oral atypical antipsychotic agents to injections of long-acting risperidone for 1 year. The optimal dose range appeared to be 25 to 50 mg long-acting risperidone every 2 weeks.

In a shorter, 12-week study, 67 patients with moderate or severe illness receiving oral olanzapine were switched to 4 mg daily of oral risperidone, then randomized to receive intramuscular injections of long-acting risperidone or placebo every 2 weeks. Overall, subjects in this study who received injectable risperidone showed significant improvement in total Positive and Negative Syndrome Scale scores from baseline; only 23% of these patients were rated as having marked to extremely severe illness based on Clinical Global Impression scores at study end. Patients' perception of injection-site pain was low at the beginning of the trial and decreased during the study. Adverse events in both studies for the long-acting formulation were similar to those experienced with oral therapy, with reductions in rate of movement disorders compared with oral atypical therapy.

One obvious advantage of injectable agents is that they fully resolve questions pertaining to medication compliance—questions surrounding not only missed doses, but wrong doses—allowing healthcare providers to move therapeutic conversations away from "medication checks" and toward patient goals. However, some clinicians have expressed doubts that psychotic patients, who frequently suffer from problems with motivation, depression, and even more practical issues such as transportation, will visit providers to receive injections. One possible alternative is the delivery of medication to the patient in the home by a home-health professional. Potential benefit is supported by these findings that even stable patients can achieve substantial improvement with continuous medication delivery; long-acting antipsychotics are not simply for chronic, noncompliant patients. The findings from these studies support the importance of strategies and technologies of care that promote continuous, long-term treatment of psychotic disorders.

RISPERIDONE IN BIPOLAR PATIENTS SHOWS RAPID ANTIMANIC EFFECT

Based on a poster presented by Hirschfeld R,* Keck P,+ Karcher K,‡ Kramer M,‡ Grossman F,+ Vieta E§
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Risperidone is indicated for use in patients with schizophrenia and has been proved effective in this population. Given that some symptoms are common to both schizophrenia and bipolar disorder, this study was designed to explore the efficacy of risperidone in acute mania in bipolar disorder. Whereas a previous randomized study reported that risperidone was at least as effective as haloperidol when used in combination with a mood stabilizer in the rapid control of manic symptoms in bipolar disorder,1 the current study investigated whether risperidone could be effectively used as monotherapy in manic patients. The randomized, double-blind study followed previous open-label investigations of risperidone as monotherapy in mania.2,4

Two hundred sixty-two hospitalized patients with a primary diagnosis of mania were randomized to receive either risperidone or placebo. Risperidone
was administered once daily in a flexible range to optimize efficacy, initiated at a dose of 3 mg daily, then titrated upward or downward (range 1–6 mg daily) over a 3-week period. In the 56% of risperidone patients who completed the trial, significant improvements were seen in Young Mania Rating Scale (YMRS) total scores at day 3 and at each subsequent time point of the 3-week study. These reductions were observed in patients with and without psychotic features at baseline. At study end, 43% of risperidone patients achieved a 50% or greater reduction in YMRS scores (“response”), compared with 24% of placebo patients. Risperidone also improved depression in patients with bipolar disorder. The most frequently reported adverse events in the drug treatment group were somnolence (28%) and hyperkinesia (16%). This study indicates that risperidone can significantly and rapidly reduce symptoms of acute mania when administered as monotherapy.

REFERENCES