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Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder

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Abstract

Background: Enhancing medication adherence early in the course of schizophrenia and schizoaffective disorder may substantially improve long-term course. Although extensively studied in multi-episode patients, little data exist on medication adherence by first-episode patients. *Method*: Medication adherence was assessed during the first year of treatment and following recovery from the first relapse in patients treated by a standardized medication algorithm. *Results*: During the first year of treatment, patients with poorer premorbid cognitive functioning were more likely to stop antipsychotics ($t = -2.54$, $df = 75$, $p = 0.01$). Parkinsonian side effects increased the likelihood (hazard ratio = 41.22; 95% CI = 2.30, 737.89; $p = 0.01$), and better executive function decreased the likelihood (hazard ratio = 0.40; 95% CI = 0.18, 0.88; $p = 0.02$) that patients discontinued maintenance medication after a first relapse. *Conclusion*: Interventions to ameliorate cognitive deficits and Parkinsonian side effects may enhance treatment adherence.

Keywords: Antipsychotic agents; Cognition; Neuropsychological tests; Patient compliance; Schizophrenia

1. Introduction

Although poor medication adherence complicates the treatment of schizophrenia at all illness stages, interventions to maximize adherence at illness outset may be particularly fruitful. Patients' initial perceptions about antipsychotics may influence long-term adherence. Further, data suggest that the clinical deterioration associated with schizophrenia predominantly occurs in the first 5 years after illness onset (McGlashan, 1988). Improving treatment response during this period through enhanced medication adherence may limit this deterioration.

Recent reviews of the literature on medication adherence in schizophrenia (Fenton et al., 1997;

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Kampman and Lehtinen, 1999) have identified several consistent correlates of medication refusal. These include: more severe psychopathology, lack of insight, comorbid substance abuse, presence of medication side effects, an absence of social supports from family or friends, and practical barriers such as inability to afford medications.

Despite the numerous studies of medication adherence in schizophrenia, information specifically about first-episode patients is very limited (Novack-Grubic and Tavcar, 1999). A number of factors suggest the need for separate study of recent onset patients. Due to their younger age, treatment decisions more often involve both patients and their families than is the case with multi-episode patients. Further, recent onset patients and their families lack experience with antipsychotics and with the chronic and relapsing course of schizophrenia. Their assessment of the benefits vs. liabilities of antipsychotics may differ from those of multi-episode patients who have experienced the adverse consequences associated with repeated relapses.

Our opportunity to study treatment adherence occurred in the context of a long-term study of first-episode schizophrenia and schizoaffective disorder. This allowed us to study medication adherence during different phases of treatment and to examine potential predictors of treatment refusal. Because patients received treatment within the study, we were able to determine precisely the magnitude of the benefits patients obtained from treatment and the extent of side effects.

2. Material and methods

2.1. Overview of study

The parent study has been described in detail (Robinson et al., 1999a). Conduct of the study conformed to the guidelines for human subject protection of the Long Island Jewish Medical Center Institutional Review Board. After a complete explanation of the study, subjects and, if available, a family member provided written informed consent. One hundred eighteen subjects who met Research Diagnostic Criteria (RDC, Spitzer et al., 1977) for schizophrenia or schizoaffective disorder and who had less than 12 weeks of lifelong antipsychotic treatment were assessed at baseline on measures of psychopathology and social functioning, treated according to a standardized medication algorithm and assessed prospectively. Subjects progressed from one medication in the algorithm to the next until they responded. The sequence of medications was: fluphenazine; haloperidol; haloperidol plus lithium; either molindone or loxapine; clozapine. Adjuvant medications for mood stabilization were used as clinically warranted. Benztropine, lorazepam and propranolol were given as needed for side effects. The treatment settings were an inpatient unit, day and partial hospital programs and an outpatient department. In each setting, treatment was administered by the study treatment team (psychiatrist, research social worker, and nurse). In addition to clinical management, there was a psychoeducation program for subjects and family members. Group and individual psychotherapy were provided on an ongoing basis for each subject as needed. Education about the need for adherence to treatment was a major focus of treatment. Initially, there was no limitation on study duration; later, the length of treatment in the study was set at 5 years.

2.2. Assessment of medication adherence

The standard of care for multi-episode patients is to recommend continuous antipsychotic treatment. In contrast, debate persists about the proper duration of antipsychotic treatment for patients with a first episode of schizophrenia. There is consensus about the need for antipsychotic treatment for first-episode patients during two periods: the first year after initiating antipsychotic treatment for the initial episode and the period following a first relapse of illness. Because we wished to examine medication discontinuation which was clearly against medical advice, we restricted our analyses to these two periods. After completion of the study, analysis of predictors of relapse in the sample demonstrated that antipsychotic maintenance treatment during these periods (and at other times) had clearly been beneficial (Robinson et al., 1999a).

In our study, patients who were stable after meeting response criteria were given the option of discontinuing antipsychotics while continuing in