Compliance with Refilling Prescriptions for Atypical Antipsychotic Agents and Its Association with the Risks for Hospitalization, Suicide, and Death in Patients with Schizophrenia in Quebec and Saskatchewan: A Retrospective Database Study

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ABSTRACT

Objective: The objective of this analysis was to describe the patterns of compliance with atypical antipsychotics among patients with schizophrenia in actual practice in 2 Canadian provinces and to examine the relation between degrees of compliance and the risks of hospitalization, suicide, and death.

Methods: Adults with a diagnosis of schizophrenia who filled at least 1 prescription for risperidone, olanzapine, or quetiapine were identified in the Quebec public prescription drug insurance plan database (from July 1, 2001, to December 31, 2004) and the Saskatchewan Health database (from January 1, 1999, to December 31, 2003). Compliance was assessed based on the medication possession ratio, which was estimated as the proportion of days for which medication was available over each month of follow-up (≥80% = good compliance; 50%–79% = moderate compliance; <50% = poor compliance). The association between the early and long-term effects of compliance and the risks of hospitalization, suicide, and death were examined using Cox regression, with adjustment for baseline age, sex, and use of antidepressants, sedatives, and lithium (Quebec only).

Results: A respective 41,754 and 3291 patients were identified from the Quebec and Saskatchewan databases. Approximately half of the patients in each cohort were male and were aged <45 years. Many patients had good compliance over the full follow-up period (Quebec, 61%; Saskatchewan, 45%); however, poor compliance was seen in 23% of patients from Quebec and 34% of those from Saskatchewan. Compared with poor compliance, the long-term effect of good compliance was associated with a significantly decreased risk of all-cause hospitalization (Quebec: adjusted hazard ratio [HR] = 0.60; 95% CI, 0.57–0.64; Saskatchewan: adjusted HR = 0.81; 95% CI, 0.69–0.95) and psychosis-related hospitalization (Quebec: adjusted HR = 0.37; 95% CI, 0.34–0.40; Saskatchewan: adjusted HR = 0.45; 95% CI, 0.32–0.64). The Quebec data also indicated a significant association between good versus poor compliance and a decreased risk of death (adjusted HR = 0.58; 95% CI, 0.51–0.66) and suicide (adjusted HR = 0.68; 95% CI, 0.55–0.84) that was not observed in Saskatchewan.

Conclusion: In this retrospective analysis of patients with schizophrenia in Quebec and Saskatchewan, good compliance with atypical antipsychotic medications was associated with substantial reductions in the risk for all-cause and psychosis-related hospitalizations. (*Clin Ther.* 2006;28:1912–1921) Copyright © 2006 Excerpta Medica, Inc.

Key words: risperidone, olanzapine, quetiapine, schizophrenia, compliance.

INTRODUCTION

Antipsychotic medication is an essential component of management of the symptoms of schizophrenia, and

Accepted for publication October 17, 2006.

Express Track online publication November 16, 2006.
doi:10.1016/j.clinthera.2006.11.002
0149-2918/06/$19.00

maintenance treatment is usually recommended.[1] Without appropriate medication, patients with schizophrenia often have chronic or relapsing symptoms of acute psychosis.[1,2] Since 2005, the Canadian Psychiatric Association has recommended use of atypical antipsychotics as first-line treatment, as previously unmedicated patients are particularly sensitive to the extrapyramidal and sedative adverse effects of conventional antipsychotics.[1] There is emerging evidence, however, that the effectiveness of atypical antipsychotics may be limited in actual practice because patients do not persist with treatment or fail to comply fully with the prescribed treatment (eg, by missing doses).[3–8]

The objective of this analysis was to describe the patterns of compliance with atypical antipsychotics among patients with schizophrenia in actual practice in 2 Canadian provinces and to examine the relation between degrees of compliance and the risks of hospitalization, suicide, and death.

MATERIALS AND METHODS

The Databases

The health care databases managed by Régie de l'Assurance Maladie du Québec (RAMQ) and Saskatchewan Health were used to obtain data for a large sample of Canadian patients with a diagnosis of schizophrenia who were treated with risperidone, olanzapine, or quetiapine in routine community practice. RAMQ is a department of the Quebec government that oversees health care claims, including those for ~3.5 million patients eligible for the provincial drug insurance program. This program covers all residents of Quebec aged ≥65 years, welfare recipients, and patients without private insurance. Saskatchewan provides publicly funded health insurance to nearly all of its ~1.1 million residents, and most (~91%) residents are also eligible for outpatient prescription drug benefits. The 2 databases contain information on sex, age, outpatient prescription claims (including drug code and service date), physician visits (diagnosis and dates of service), hospital admissions (date and diagnosis codes), death date, and program eligibility.

Patients in both databases are assigned a unique identification number. These numbers were anonymized when the files were released for research by RAMQ and Saskatchewan Health. The study protocols were reviewed and approved by Saskatchewan Health's Study Committee and the Commission d'accès à l'information du Québec before release of the databases.

Study Design

Patients were identified who were dispensed at least 1 prescription for risperidone, olanzapine, or quetiapine between July 1, 2001, and December 31, 2004, in Quebec, and between January 1, 1999, and December 31, 2003, in Saskatchewan. The date of the first prescription for any of these drugs was considered the index date for each patient. Those with an index prescription for clozapine were excluded from the study, as use of this atypical agent is reserved for treatment-resistant cases because of the risk of agranulocytosis. Adults (Quebec: age >15 years; Saskatchewan: age >18 years) with a recorded diagnosis of schizophrenia (*International Classification of Diseases, Ninth Revision* codes 295.0–295.9) were selected for the study.

The end of follow-up was either the time of death, the last date of service for patients who lost eligibility or had a gap in services at the end of the study period (no recorded physician visits or hospital or medication claims for the previous 6 months), or December 31, 2004, for Quebec and December 31, 2003, for Saskatchewan. For each patient, the follow-up time was the number of days between the start and end dates.

The study design is shown in **Figure 1.**

Adverse Outcomes

Hospital admission diagnosis codes were used to identify all-cause and psychosis-related admissions and attempted suicides leading to admission. Information on the date and code for cause of death was used to determine whether a patient died during the follow-up period and to identify deaths by suicide. For the purposes of this study, suicide (attempted or successful) was coded as an attempt that led either to hospital admission or to death.

Compliance

Each patient's pattern of atypical antipsychotic medication use was reconstructed from the records of prescriptions dispensed. Compliance was determined by estimating the medication possession ratio (MPR), defined as the proportion of days for which medication was available in each month of follow-up. Compliance was coded using a computer algorithm that employs the date of a prescription refill and the days'