

Study Finds Frequent Switching of Antipsychotics

BY CAROLINE HELWICK

FROM THE ANNUAL CONGRESS OF THE EUROPEAN COLLEGE OF NEUROPSYCHOPHARMACOLOGY

AMSTERDAM – A large multinational study found that one in five adult patients with schizophrenia switched medications within the previous 12 weeks, mostly because of inadequate symptom control as one-third reported a relapse on the initial drug.

Tolerability issues also were important and differed between first- and second-generation antipsychotics, reported Dr. Beata Galinska-Skok of the Medical University of Bialystok in Choroszcz, Poland.

“In the long-term management of schizophrenia, around one-third of patients treated with antipsychotic drugs change their medication every year. There is a need to better understand the dynamics of switching in real-world conditions. We performed a naturalistic multinational observational survey to evaluate the parameters of treatment discontinuation and substitutions in the management of schizophrenia in every day clinical practice,” Dr. Galinska-Skok said.

The primary objective of the cross-sectional observational study conducted in 11 countries was to identify the frequency of and reasons for switching antipsychotic treatments in patients with schizophrenia. Participating physicians were community- or hospital-based psychiatrists who reflected local psychiatric prac-

tices and patient management.

The countries represented were Algeria, Greece, India, Jordan, Lithuania, Mexico, Philippines, Poland, Slovakia, Ukraine, and Vietnam.

The registry population included 23,441 adult patients (mean age 41), of whom 22,126 were analyzable. Of those, 5,128 patients (23.2%) reported a treatment switch in the previous 12 weeks and thus constituted the switch population; 3,130 consented to the study and constitute the analysis population.

The medication that was discontinued in the previous 12 weeks was a second-generation antipsychotic for 55.6% of patients and a first-generation agent for 41.8%, while 2.6% discontinued both types. After the switch, most patients received a second-generation agent (90%) either alone (72.4%) or in combination with a first-generation agent (18.3%). The remainder received a first-generation agent as monotherapy, she reported.

Main Reason for Switching: Lack of Efficacy

Physicians could report more than one reason for switching. The survey found the main reason to be inadequate symptom control (79.4%), while the occurrence of adverse events was also common (55.3%). Other reasons frequently cited included poor quality of life (31.7%), relapse on medication (30.1%), poor compliance (25.3%), and patient request (18.3%). Two to six percent reported problems with drug availability, fi-

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Major Finding: One in five adult patients with schizophrenia switched antipsychotic medications in the previous 12 weeks, mostly because of lack of efficacy and secondarily because of side effects.

Data Source: Observational study of more than 23,000 patients from 11 countries.

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nancial or life events, and comorbid medical conditions.

“Over half the changes were motivated by an adverse event,” Dr. Galinska-Skok noted. “The nature of the adverse events differed depending on the class of antipsychotic the patient was taking before the switch. Extrapyramidal symptoms and sedation were the two adverse events that most frequently motivated switching from a first-generation agent. Sedation and weight gain were the two most frequent adverse events motivating switching from a second-generation agent.”

Extrapyramidal symptoms were observed in 36% on a first-generation agent, 12% on a second-generation agent, and 28% on the combination. Sedation was observed in 20%, 25%, and 23%, respectively. Weight gain was problematic for 10%, 26%, and 23%, respectively. ■

Antipsychotic Use Tied to Venous Thromboembolism Risk

BY KERRI WACHTER

FROM THE BRITISH MEDICAL JOURNAL

Antipsychotics are associated with an almost one-third (32%) greater risk of venous thromboembolism, according to results of a nested case-control study of more than 100,000 primary care patients in the United Kingdom.

Previous research has suggested that these drugs – also commonly used for nausea, vomiting, and vertigo – might be linked with an increased risk of venous thromboembolism (VTE). However, the results have been inconsistent.

In the current study, the association was even greater for new users of antipsychotics. Those with any antipsychotic use in last 3 months had a 56% increased risk of VTE. Patients who started taking an antipsychotic in the past 3 months had a 97% increased risk. However, the absolute risks were low, with an excess of four extra cases of VTE per 10,000 patients treated over 1 year in patients of all ages and 10 for patients aged 65 years and older.

“Our study adds to the accumulating evidence of adverse health events associated with antipsychotic drugs,” the researchers wrote in the study, published online Sept. 21 in the British Medical Journal (BMJ) 2010 Sept. 21 [doi:10.1136/bmj.c4245]. “If other studies replicate these findings, antipsychotic drugs should be used more cautiously for nausea and agitation, etc., especially among patients at high risk of thromboembolism.”

The researchers used data from the QResearch database, which includes primary care clinical records for more than 11 million people registered in the past

16 years at more than 500 U.K. general practices. The study population was an open cohort of patients aged 16-100 years, who were registered with participating practices between January 1996 and July 2007. Case patients had a first-ever record of VTE – either deep vein thrombosis or pulmonary embolism – during the study period (including post-mortem diagnoses).

Incidence density sampling was used to identify up to four control patients for each case patient. Control patients were matched by age, calendar time, sex, and practice. Control patients had no diagnoses of VTE prior to the date of the first recorded diagnosis of VTE in their matched case patient (index date).

In all, 25,532 eligible case patients – 15,975 with DVT and 9,557 with pulmonary embolism – and 89,491 control patients were included in the study. In terms of mental health disorders, the overall prevalence was 0.4% for schizophrenia, 0.3% for bipolar disorder, and 1.0% for dementia. Eight case patients and 31 control patients had more than one disorder. In all, 8.3% of case patients and 5.3% of control patients had received an antipsychotic in the previous 24 months.

Overall, antipsychotic users had a 32% greater risk of VTE than did nonusers. Among those on antipsychotics, 38% were current users and their increase in risk was 56% compared with 36% for recent users. The risk was not significantly increased for past users. Among current antipsychotic users, 15% had started a new drug within the 3 months prior to the index date. This group of new users showed a greater increase in risk (97%) than did continuing users (29%).

Patients who were prescribed atypical

antipsychotic drugs had a greater risk of VTE than did those who were prescribed conventional antipsychotics – 73% compared with 28%.

Patients who had received only one prescription in the previous 12 months had a significantly greater risk (32%) than did those receiving none.

In addition, those who were prescribed two or more different antipsychotics had a greater risk (99%) than did those who received only one (29%). ■

Disclosures: The authors reported that they have no relevant financial relationships.

Implications Could Be Far Reaching

The validity of the findings is strengthened by the large sample size and the low potential for exposure and outcome misclassification because of the detailed source of data and adjustment for a large number of confounders, according to Dr. Rosa Liperoti and Dr. Giovanni Gambassi.

It's been demonstrated that “patients with schizophrenia have an increased risk of venous thromboembolism (VTE), and this might be associated with the use of antipsychotics, especially low-potency drugs such as chlorpromazine and thioridazine.

So far, however, the possibility that the underlying psychiatric disorders themselves – and not the antipsychotics – are associated with VTE has never been excluded. This could occur by the increased concentrations of adrenaline seen during psychotic excitation increasing blood coagulation,” they noted.

In this study, in almost all cases the reason for prescription of antipsychotics could not be ascertained. Most of the antipsychotics used

were conventional agents, with prochlorperazine – probably given for nausea and vomiting – accounting for almost 80% of all prescriptions, they wrote.

“These findings indicate that VTE is directly linked to the use of an antipsychotic, and that the risk of VTE increases early after starting the drug.”

The implications are potentially far reaching. “Despite their association with serious risks and few data to support their efficacy, antipsychotics are widely used, and in 2008 they became the top selling drug class in the United States,” they wrote.

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