Antipsychotic Use Tied to Venous Thromboembolism Risk

By Kerri Wachter
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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 postmortem 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 disorder itself – 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.

Rosa Liperoti, M.D., is a specialist in geriatrics and Giovanni Gambassi, M.D., is a professor of geriatrics at Università Cattolica del Sacro Cuore in Rome. Both Dr. Liperoti and Dr. Gambassi reported that they have no relevant financial relationships. Their comments were taken from a commentary that accompanied the study (BMJ 2010 Sept. 21 [doi: 10.1136/bmj.c4216]).