

WHAT IS THE EFFECT OF RISK MINIMIZATION MEASURES ON THE RISK OF ANTIPSYCHOTIC-ASSOCIATED STROKE IN ELDERLY PERSONS?

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Introduction: Two risk minimization measures (RMMs) in the form of safety warnings, were issued by the UK drug agency in March 2004 and March 2009, on the safety of antipsychotic (AP) use in elderly persons with dementia. However, the effect of these RMMs has not been evaluated to date.

Objectives: To investigate the effect of the risk minimization measures issued by the UK drug agency on the absolute risk of stroke among elderly AP users.

Methods: A cohort of incident AP users (at least one year of AP-free period) was identified from The Health Improvement Network (THIN) in 2000-2012. THIN provides data on the patients' diagnoses as well as drugs prescribed by the general practitioners, including dose and duration of treatment. Patients aged between 65 and 89 years with no cancer diagnosis registered at any time were selected. Incident cases of antipsychotic-associated stroke were identified in the three study periods as patients having a stroke while exposed to APs or within 30 days after AP discontinuation. Follow-up was divided in three periods according to the RMMs issues as "before the first RMM", "after the first RMM" and "after the second RMM". Patient characteristics were evaluated at the start of AP treatment and compared among the three study periods, as were AP dose and therapy duration. The crude incidence of stroke per 1,000 person years (PYs) in AP users was calculated as the number of antipsychotic-associated stroke events divided by the cumulative AP exposure, calculated based on the defined daily dose (DDD). In order to increase the robustness of findings, the risk of stroke was compared to the crude incidence of acute liver injury (ALI) across the three periods, as ALI is not known to be associated to AP.

Results: Preliminary data suggest that patient cardiovascular characteristics changed after the RMMs, with the frequency of congestive heart failure and ischemic heart disease decreasing after both RMMs. In general, no clear pattern in treatment duration was seen but there was an increase in duration after each RMM for any AP use. No change in mean dose was seen in the three periods. The crude absolute risk of stroke per 1,000 PYs during AP exposure before the first RMM was 24.31 (95% IC: 21.32- 27.6), decreasing to 13.37 (11.33- 15.66) after the first RMM, and further decreasing to 9.9 (7.14- 13.40) after the second RMM. In contrast, no statistically significant difference was observed in the absolute risk of ALI in the periods: 1.56 (0.91-2.51), 3.06 (2.15-4.23) and 1.26 (0.46-2.79) per 1,000 PYs before the first RMM, after the first RMM and after the second RMM, respectively.

Conclusions: The RMMs led to a decrease in the absolute risk of stroke in a cohort of elderly AP users.