Hyponatraemia as an Adverse Drug Reaction of Antipsychotic Drugs A Case-Control Study in VigiBase

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Abstract

Background: Hyponatraemia due to antipsychotic use is a potentially serious problem; however, it is not known whether it is an adverse drug reaction (ADR) to antipsychotic use or is due to the underlying psychiatric disease.

Objective: To estimate the strength of the association between antipsychotics and hyponatraemia or syndrome of inappropriate antidiuretic hormone secretion (SIADH), using information reported to the WHO Collaborating Centre for International Drug Monitoring, the Uppsala Monitoring Centre (UMC).

Setting: The WHO global individual case safety report database system (VigiBase) maintained by the UMC.

Study Design: Case-control study, with cases being reports of hyponatraemia/SIADH, and controls being reports of other ADRs. Each case was sampled with ten controls sequencing in time from the date the corresponding case was entered into the database. The potential contribution of the chemical structures and receptor affinity (dopaminergic and/or serotonergic) of the antipsychotics was studied, as was the influence of concomitant use of other medications known to cause hyponatraemia.

Main Outcome Measures: The strength of the association between antipsychotic use and hyponatraemia in comparison with other drugs was expressed as reporting odds ratio (ROR), a measure of disproportionality, with corresponding 95% CIs, adjusted for age, sex and concomitant medication associated with hyponatraemia. In addition, stratification by the presence or absence of concomitant medication was performed.

Results: Up to August 2008, 3 881 518 suspected ADRs were reported and filed in VigiBase, with 912 reports on hyponatraemia related to antipsychotics. The adjusted ROR for the association between antipsychotic use and hyponatraemia was 1.58 (95% CI 1.46, 1.70). The adjusted RORs did not vary for the different chemical structures or dopamine D2 and serotonin 5-HT2A receptor affinity profiles. The ROR was 3.00 (95% CI 2.65, 3.39) for the association between hyponatraemia and antipsychotic use in the absence of concomitant medication associated with hyponatraemia, and 1.16 (95% CI 1.06, 1.28) in the presence of concomitant medication associated with hyponatraemia.

Conclusions: Antipsychotic use may be associated with reporting of hyponatraemia. Moreover, the concomitant use of medication associated with hyponatraemia potentially leads to under-reporting of antipsychotic-associated hyponatraemia. We advise testing patients whose psychiatric and/or physical condition deteriorates while on antipsychotics for hyponatraemia.

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