HYPERSALIVATION ASSOCIATED WITH OLANZAPINE AND VALPROATE COMBINATION: A CASE REPORT

To the Editor:

Severe cases of bipolar disorder often require polypharmacy regimens in order to achieve symptom remission. Nevertheless, polypharmacy has the drawback of augmenting potential undesirable consequences. Hypersalivation related to antipsychotic use has been described most frequently as a clozapine adverse effect. We here report a case of hypersalivation associated to concomitant use of olanzapine and valproate in a patient with bipolar disorder.

A 75-year-old female was referred in December 2008 to our University Hospital inpatient unit because of agitation and grandiosity. At admission, the patient fulfilled Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for a manic episode without psychotic features, with a Young Mania Rating Scale (YMRS) score of 33. She was on a daily dose of haloperidol 10 mg, chlorpromazine 300 mg, paroxetine 20 mg, and olanzapine 2.5 mg. Immediately after admission, all drugs except olanzapine were discontinued, which was progressively increased up to 10 mg/day. The patient was also taking alendronate 70 mg weekly and acetylsalicylic acid 100 mg/day. Due to the persistence of mood symptoms, olanzapine was increased up to 15 mg/day and valproate 1,000 mg/day was introduced. After four days using both medications, the patient began to complain about hypersalivation. This side-effect became prominent, with a YMRS score of 1, and was receiving olanzapine 5 mg/day and of valproate 1,000 mg/day (re-introduced after ECT sessions), and presenting no signs of hypersalivation.

Reports of hypersalivation associated to olanzapine and/or valproate use are rare. In a MEDLINE search using the expression “(hypersalivation OR sialorrhea) AND (olanzapine OR valproate)” 19 papers were found. An initial case report described a patient who presented hypersalivation after an increase in olanzapine dose (10–15 mg/day). The authors suggested that olanzapine, due to its structural analogy and similar receptor-binding profile to clozapine, could increase saliva production by sympatetic cholinergic agonism as well as by parasympathetic cholinergic agonism. Since hypersalivation occurred only when olanzapine was increased to 15 mg/day and after the introduction of valproate 1,000 mg/day, this side effect could be secondary to olanzapine dose itself, to valproate introduction, or to the interaction of both psychopharmacs. Thus, hypersalivation may have been occurred due to any of these mechanisms. Another possibility is the existence of a pharmacokinetic interaction between olanzapine and valproate, which is a potent hepatic enzymes inhibitor. We found no reports regarding alterations in the pharmacokinetic of olanzapine and valproate when administrated together.

A Cochrane meta-analysis, despite confirming the reduced incidence of hypersalivation among patients treated with olanzapine in comparison with those using clozapine (risk ratio 0.08; 95% CI 0.02-0.31), registered two cases of hypersalivation during olanzapine use.

A more recent study confirmed a low occurrence of hypersalivation among patients treated with olanzapine (10% vs. 80%, in comparison with clozapine). Together with the previous reports, the case here described should encourage physicians to monitor patients taking olanzapine for the occurrence of hypersalivation.

Sincerely,
Christian Kieling, MSc
Clarissa Severino Gama, PhD
Brisa Simões Fernandes, MSc

REFERENCES

Dr. Kieling is a psychiatrist in the Bipolar Disorders Program, Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil. Dr. Gama is a professor in the Bipolar Disorders Program at the Hospital de Clinicas de Porto Alegre; is professor in the Molecular Psychiatry Unit at the Hospital de Clinicas de Porto Alegre (HCPA), Universidade Federal do Rio Grande do Sul in Porto Alegre, Brazil; and professor in INCT for Translational Medicine in Brazil. Dr. Fernandes is psychiatrist in the Bipolar Disorders Program at the Hospital de Clinicas de Porto Alegre; is psychiatrist in the Molecular Psychiatry Unit at the HCPA, Universidade Federal do Rio Grande do Sul in Porto Alegre, Brazil; and psychiatrist in INCT for Translational Medicine in Brazil.

Faculty Disclosures: Dr. Fernandes is supported by a scholarship from Conselho Nacional de Pesquisa (CNPq), Brazil. Dr. Gama has received grant/research support from CAPES, CNPq, FINEP-HCPA, and Endeavour Award, is a consultant/advisor to and has received consulting fees from Actelion; is on the speaker’s bureau of and has received honoraria from AstraZeneca and Lundbeck. Dr. Kieling reports no affiliation with or financial interest in any organization that might pose a conflict of interest. These agencies had no role in study design, acquisition and interpretation of data or writing the report.

Submitted for publication: February 28, 2010; Accepted for publication: March 9, 2010. First published online: March 1, 2011.

Please direct all correspondence to: Brisa Simões Fernandes, Hospital de Clinicas de Porto Alegre, Av Ramiro Barcelos 2350. ZIP 90035-903. Porto Alegre RS, Brazil. Tel: 5531-33598845; Email: brisaf@gmail.com