HYPER SALIVATION ASSOCIATED WITH OLANTZAPINE 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. Hyposalivation related to antipsychotic use has been described most frequently as a clozapine adverse effect. We here report a case of hyposalivation 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 acetylseriacid 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 hyposalivation.

A Cochrane meta-analysis, despite confirming the reduced incidence of hyposalivation 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 hyposalivation during olanzapine use. After 10 days of combined use of olanzapine and valproate, the patient persisted with manic symptoms and hyposalivation.

Electroconvulsive therapy (ECT) was initiated, conforming to the protocol instituted by our service and valproate was discontinued, with a complete remission of hyposalivation during the following week. Manic symptoms remitted after 8 sessions of ECT, presenting only a transient short-term memory deficit as a side effect. The patient was discharged euthymic, 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 hyposalivation.

Reports of hyposalivation associated to olanzapine and/or valproate use are rare. In a MEDLINE search using the expression “(hyposalivation OR sialorrhea) AND (olanzapine OR valproate)” 19 papers were found. An initial case report described a patient who presented hyposalivation 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 sympathetic αadrenergic antagonist as well as by parasympathetic cholinergic agonism.

Since hyposalivation 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 the olanzapine dose itself, to valproate introduction, or to the interaction of both psychopharmacics. Thus, hyposalivation 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 administered together.

REFERENCES


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Letters

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