

PLASMA CONCENTRATIONS OF QUETIAPINE DURING COADMINISTRATION WITH ANTIEPILEPTIC DRUGS IN PSYCHIATRIC PATIENTS

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Quetiapine is a second-generation antipsychotic widely used in the treatment of schizophrenia and bipolar disorder. It is extensively metabolised in the liver mainly via CYP3A4 and, to a lesser extent, via CYP2D6. Quetiapine is often prescribed in combination with antiepileptic agents, particularly those with mood stabilizing properties. As many antiepileptics are known to influence the activity of drug-metabolizing enzymes, aim of the present study was to evaluate the effect of comedication with antiepileptic drugs on plasma concentration/dose (C/D) ratios of quetiapine in psychiatric patients. Plasma samples from 59 psychiatric patients (31 females and 28 males, aged 23 to 60 years), most suffering from bipolar disorder, treated with quetiapine alone (n=22) or in combination with valproic acid (n=11), carbamazepine (n=5), lamotrigine (n=10), oxcarbazepine (n=4) topiramate (n=7) were collected. Plasma concentrations of quetiapine were measured by HPLC. Quetiapine dose ranged from 50 to 900 mg/day. The median C/D ratio in patients on quetiapine alone was 0.16 (range 0.01-0.83). Comedication with carbamazepine caused a significant decrease in the C/D ratio of quetiapine (median 0.04, range 0.01-0.06; $p < 0.01$), while combined treatment with lamotrigine, oxcarbazepine and topiramate did not significantly affect the C/D ratio. Dose normalized concentrations of quetiapine tended to be higher among patients comedicated with valproic acid than in the control group, but difference did not reach statistical significance. These findings demonstrate that carbamazepine decreases markedly the plasma concentrations of quetiapine, probably by inducing CYP3A4-mediated metabolism. This interaction is likely to be clinically significant and it may result in decreased efficacy. In case of combined administration of carbamazepine with quetiapine, higher doses of the antipsychotic may be needed. Conversely, valproic acid, lamotrigine, oxcarbazepine and topiramate did not cause any major change in quetiapine pharmacokinetics.