

THERAPEUTIC DRUG-MONITORING OF BUPROPION FOR DEPRESSION

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Introduction: Therapeutic Drug-Monitoring (TDM) for bupropion is limited by bupropion's instability at room temperature and by the absence of a well-defined therapeutic reference range. Further it is unclear to what extent bupropion and its metabolites contribute to therapeutic effects, though hydroxybupropion seems to account for the major antidepressant effects.

Aim: The aim of this examination was to check if measurement of only hydroxybupropion is useful to guide the antidepressant therapy with bupropion.

Methods: Hydroxybupropion plasma levels were measured by high performance liquid chromatography with ultra violet detection and related to therapeutic effects measured by the Clinical Global Impression Scale for improvement.

Results: The study included 52 patients (50% female). Patients who were very much improved according to CGI had significantly ($p=0.042$) higher hydroxybupropion serum levels than patients with moderate or minimal improvement (mean \pm SD, 1113 \pm 576 ng/ml, 825 \pm 398 ng/ml and 475 \pm 331 ng/ml, respectively). Receiver operating characteristics analysis revealed significant predictive properties of hydroxybupropion serum levels ($p=0.002$) for improvement with a lower threshold level of 858 ng/ml. Women attained significantly higher serum levels than men and also exhibited a better therapeutic effect ($p=0.018$), though they did not receive significantly higher doses.

Conclusions: Measurement of hydroxybupropion plasma levels can be used to optimize the therapeutic outcome of patients treated with bupropion. Plasma levels between 850 and 1500 ng/ml can be regarded as optimal. Potential sex differences in bupropion pharmacokinetics, probably due to differential activities of CYP2B6, should be taken into account.