Publication

Electroencephalographic and behavioral convulsant effects of hydrobromide and hydrochloride salts of bupropion in conscious rodents.

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Abstract

A novel bromide salt of the antidepressant bupropion (bupropion HBr) has recently been developed and approved for use in the United States. Given previous use of bromides to treat seizures, and that the existing chloride salt of bupropion (HCl) can cause seizures, it is important to determine if the HBr salt may be less likely to cause seizures than the HCl salt. In the present animal studies this was evaluated by means of quantified electroencephalogram (EEG), observation, and the rotarod test in mice and rats. Both bupropion salts were tested at increasing equimolar doses administered intraperitoneally. The results in mice showed that bupropion HCl 125 mg/kg induced a significantly higher ten-fold increase in the mean number of cortical EEG seizures compared to bupropion HBr (7.50 +/- 2.56 vs 0.75 +/- 0.96; $p = 0.045$), but neither drug caused any brain injuries. In rats bupropion HBr 100 mg/kg induced single EEG seizure activity in the cortical and hippocampal (depth) electrodes and in significantly ($p < 0.05$) fewer rats (44%) compared to bupropion HCl, which induced 1 to 4 convulsions per rat in all rats (100%) dosed. The total duration of cortical seizures in bupropion HCl-treated rats was significantly longer than the corresponding values obtained in bupropion HBr-treated rats (424.6 seconds vs 124.5 seconds respectively, $p < 0.05$). Bupropion HCl consistently induced more severe convulsions at each dose level compared to bupropion HBr. Both treatments demonstrated a similar dose-dependent impairment of rotarod performance in mice. In conclusion, these findings suggest that bupropion HBr may have a significantly lower potential to induce seizures in mice and rats, particularly at higher doses, compared to bupropion HCl. Determination of this potential clinical advantage will require human studies. If confirmed by such studies, it is likely that this potential beneficial clinical benefit would be due to the presence of the bromide salt given the long history of the use of bromide to treat seizure disorders.