The results of this study give tentative support to the notion that central CCK pathways are intimately involved in the pathology of PD and suggest that CCK-B antagonist may have therapeutic potentials.

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P-2-24

Anxiolytic activity of single doses of the 5-HT3 antagonist zacopride

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Key words: Zacopride; Generalised anxiety disorder; Anxiolytic; 5-HT3 antagonist

5-HT3 antagonists such as ondansetron, zacopride, and tropisetron exhibit anxiolytic potential in several animal models (Costall et al., 1988). The purpose of the present study was to test if single doses of zacopride possessed acute anxiolytic activity, using a design previously elaborated (Ansseau and von Frenckell, 1991). After a completely drug-free period of at least 1 week, 14 inpatients with DSM-IIIR generalized anxiety disorder (13 F, 1 M; mean age = 40.7 years) and a Hamilton anxiety score of at least 15 (mean = 31.7 ± 5.7) received every other day a single oral dose of zacopride 10 μg, zacopride 200 μg, diazepam 5 mg, and placebo in a double-blind and crossover design. Assessments included Hamilton anxiety scale performed at baseline and 2 and 6 h later and Norris visual analogue scales completed hourly during 6 h. Two patients did not complete the trial due to spontaneous improvement and were replaced. Statistical analysis used 3-way ANOVA (subjects, drug, sequence) with repeated measures. Results showed better anxiolytic activity of zacopride 10 μg ($P = 0.05$) and diazepam 5 mg ($P = 0.02$) compared to placebo on the Hamilton anxiety scale as well as a superiority of zacopride 10 μg over placebo on three items of the Norris scales: troubled/tranquil, proficient/incompetent, happy/sad; a superiority of zacopride 10 μg over diazepam on the item proficient/incompetent; and a superiority of diazepam over zacopride 200 μg on the items attentive/dreamy and proficient/incompetent. Two patients reported side effects after zacopride 10 μg, four after zacopride 200 μg, three after diazepam 5 mg, and four after placebo; the numbers of reported side effects were two after zacopride 10 μg, nine after zacopride 200 μg, six after diazepam 5 mg, and four after placebo. These findings support an acute anxiolytic activity and an excellent tolerability for zacopride at low dose.

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