Pilot study of flesinoxan, a 5-HT1A agonist, in major depression


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Flesinoxan is a highly potent and selective 5-HT1A full agonist (Ki = 1.7) with at least 80-times weaker affinity for any other receptor. Flesinoxan is active in several animal models of depression such as the behavioural despair test in rats and down-regulates beta-adrenoreceptor response.

In this pilot open study, flesinoxan (4 mg/d) was administered orally for 4 weeks in 16 major depressive, mostly treatment resistant inpatients exhibiting a score of at least 19 on the Hamilton depression scale. Weekly ratings including Hamilton depression scale, MADRS, and Clinical Global Impressions (CGI).

Preliminary results from the first 12 patients showed considerable improvement in depressive symptomatology, with mean MADRS scores (SD) dropping from 33 (9.0) to 10.0 (7.2) after 4 weeks of treatment and 11 patients classified as much or very much improved on the CGI. The tolerance of flesinoxan was excellent, with only 4 patients exhibiting side-effects.

In addition, the effect of flesinoxan on temperature regulation as well as on EEG sleep during a placebo-controlled challenge night (after 2 baseline placebo nights) and at the end of the treatment will be presented and discussed.

Ipsapirone in the treatment of bulimia nervosa – an open study

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Changes in serotonergic neurotransmitter system are known to be pathobiocchemical correlates of eating disorders. Ipsapirone is a member of the azapirone group and binds selectively to 5-HT1A receptor binding sites. It has a bimodal effect, at presynaptic sites it has agonistic, at postsynaptic sites partial agonistic properties.

17 female out-patients with bulimia nervosa (DSM-III-R 307.51) entered the study. There were two drop-outs before the end of the first week (suicide attempt and non-compliance) and another one after three weeks (lack of therapeutic success). The duration of the study was four weeks. No psychotherapy was carried out during the study and no concomitant medication, except oxazepam for sleep disturbances, was allowed. In the first week the daily dose of ipsapirone was 7.5 mg, in the future the dose was adjusted according to the clinical symptoms, in the second week this was on average 9.33 mg, in the third and fourth 9.83 mg.

Results: the average weight of the patients was 61.90 kg prior to treatment and 61.93 kg at the end. The scores in the Hamilton Depression Rating Scale decreased from 15.73 before treatment to 5.13 after four weeks (ANOVA: p=0.000; F=13.08; df=4/56), the scores in the Clinical Global Impressions from 5.40 to 3.26 for item 1 (p=0.000), from 3.53 to 2.73 for item 2 from day 7 to day 28 (p=0.014) and increased from 1.95 to 2.83 for item 3 (p=0.003).

The total score for the Eating Attitudes Test-26 improved from 33.46 to 25.33 (t-test:p=0.006, t=2.89, df=14).

Statistically significant improvements in the Eating Disorder Inventory appeared in factor 1 (desire for thinness, p=0.001), factor 2 (bulimia, p=0.001), factor 4 (ineffectiveness, p=0.032), factor 7 (interceptive awareness, p=0.005) and factor 8 (maturity fears, p=0.046).