Letter to the Editor

Sirs,

_Trazodone in the treatment of behaviour in frontotemporal dementia_

Frontotemporal dementia (FTD) is the second most common primary degenerative dementia after Alzheimer’s disease (AD). FTD is characterized by early changes in personality and social conduct compared with AD, which could lead to institutionalizing patients even at a mild stage of dementia. No treatment of FTD is known so far. FTD patients have no cholinergic deficit contrary to AD and the anticholinestasic agents are not indicated in FTD. FTD post-mortem studies have found a marked loss of postsynaptic serotonin receptors, especially in the frontal, temporal, and hypothalamic regions (Sparks and Markesberry, 1991). Serotonergic dysfunction could explain different symptoms linked with impulsiveness (Van Praag et al., 1990), frequently present in FTD patients. 5-HT2 antagonists have positive effects on negative symptoms related to prefrontal functions in animals and in humans. One FTD patient improved with an alpha-2 antagonist agent (Sahakian et al., 1994). Trazodone, a low serotonin reuptake inhibitor, has other specificity: a high affinity for 5-HT2 receptors and a potency to block alpha-1 and alpha-2 adrenergic receptors. In AD patients, 150 mg of trazodone decreases irritability, anxiety, restlessness and affective disturbances with a good tolerance (Lebert et al., 1994). Trazodone is referenced as a treatment of behavioural disorders in the recent practice guidelines of AD and other dementias (American Psychiatric Association, 1997).

**METHODS**

We therefore conducted an open-label study with trazodone in 14 consecutive FTD outpatients diagnosed according to the Lund and Manchester Groups’ (1994) criteria including SPECT pattern of an isolated frontotemporal uptake decrease. Neuropsychological testing was performed using the battery previously described (Pasquier et al., 1995). Affective symptoms were not consistent with the diagnosis of major depression. The diagnosis was confirmed histologically in one patient. Informed consent was given by the caregiver after the procedure had been fully explained. Mean age of the patients was 70.5 years (3.5) and mean MMSE score was 9.8 (8.6). Trazodone was administrated daily in three 50 mg oral doses during 4 weeks, and in three 100 mg doses during the following 2 weeks. Neuroleptics were withdrawn at least 6 weeks before baseline assessment, and other psychotropics for one week. We used the Neuropsychiatric Inventory (NPI) (Cummings et al., 1994) to assess the intensity of the behavioural symptoms at baseline and at the end of each dosing interval. The administration of NPI scale was performed by the same psychogeriatrician who was blinded to the pre-drug scores when administering the post-drug assessment. NPI sub-scores were compared between baseline and treatment using the Wilcoxon matched-paired test.

**RESULTS**

Trazodone improved the behaviour in all FTD patients (Table 1). Delusions, aggression, anxiety and irritability decreased significantly with 150 mg of trazodone. Three hundred milligrams of trazodone were necessary to decrease depression, disinhibition, and aberrant motor behaviour. There were no side effects except for one patient who presented with transient lipothymia with 300 mg of trazodone. MMSE score was unaffected by the treatment.

FTD patients had high scores of disinhibition, apathy and aberrant motor behaviour on the NPI, in agreement with the other studies (Levy et al., 1996). Serotonin selective reuptake inhibitors decreased disinhibition, depressive symptoms and compulsions in an open-study in FTD patients.
The mechanism of action of trazodone is dose-dependent. At low doses, trazodone exerted a 5-HT antagonist action, whereas at higher dosages trazodone exerted 5-HT agonist effects (Maj et al., 1979). The necessity of higher doses in FTD than in AD to improve some behavioural changes is an argument for a specific damage of the serotonergic system in FTD. In FTD, the effect of trazodone differs from that of an adrenoceptor antagonist (Sahakian et al., 1994). These preliminary results suggest that trazodone could be helpful in FTD patients and require a double-blind trial with higher doses than in AD.

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REFERENCES


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