Letters to the Editor


Tolerance to tacrine, arterial hypotension and leuko-araiosis in Alzheimer's disease

SIR—The baroreflex regulation of blood pressure is modulated by cholinergic systems [1]. Alzheimer's disease (AD) is more often associated with sympathetic dysfunction than fronto-temporal lobe dementia, in which the cholinergic system is relatively spared [2]. In patients with AD, orthostatic hypotension is associated with the severity of the cognitive decline—possibly because of chronic hypoperfusion of the white matter [3]. Orthostatic hypotension could also influence the response to cholinesterase inhibitors; Velnacrine non-responders had a more severe decrease in systolic postural blood pressure before treatment than responders [4].

Amar et al. [5] reported a high rate of withdrawal from tacrine in patients with AD with leuko-araiosis, especially because of agitation. We examined a possible relationship between tolerance to tacrine, orthostatic blood pressure and leuko-araiosis in patients with AD. Forty-one consecutive patients with AD with mild or moderate dementia were included. They were free from heart disease, diabetes mellitus or delirium. They were not taking any drugs with hypotensive side effects. Drug dosage had been stable for at least 1 month before the start of the study. Median age was 73.9 years (range 57-88), the median Mini-Mental State Examination score [6] was 19.6 (range 29-9) at baseline. Leuko-araiosis was assessed on computed tomography scan using Rezek's score [7].

Patients received 40 mg/day of tacrine for 6 weeks, 80 mg/day for 6 weeks, then 120 mg/day. Orthostatic hypotension (defined according to Bannister's criteria [8]) was noted at baseline and after 2 weeks of tacrine at 120 mg/day. The Mann–Whitney U-test was used for statistical analysis. Thirty-six patients were treated with tacrine without obvious side effects. Five patients (14%) were withdrawn prematurely: three because of gastritis and nausea, one because of agitation and one because of abnormal liver function tests. The age of withdrawn patients was higher than that of the others [80.2 years (73-88) versus 73.1 years (57-87); U = -1.97, P = 0.04]. The Rezek score did not differ between the groups: in withdrawn patients it was between 0 and 15 points. Seventeen patients had orthostatic hypotension: none was withdrawn. However, systolic blood pressure in supine position was significantly lower in withdrawn patients [123.6 mmHg (110-150) versus 142.6 mmHg (118-182); U = -2.43, P = 0.01]. Furthermore, orthostatic hypotension disappeared whilst on tacrine in 13 patients (42% versus 10%).

In conclusion, it appears that patients with low blood pressure have a lower tolerance of tacrine and that tacrine has an effect on orthostatic hypotension. A relationship between blood pressure dysregulation, cognitive decline, tolerance to anticholinesterase drugs in AD and white matter changes should be further investigated. Anticholinesterase drugs might also benefit patients with AD by decreasing orthostatic hypotension.

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