Parkinsonism Onset in a Patient Concurrently Using Tiapride and Donepezil

Donepezil was approved by the U. S. Food and Drug Administration in November 1996 for treating patients with mild-to-moderate Alzheimer’s disease. The use of donepezil has been associated with the worsening of (1, 2) and occurrence of parkinsonism (3). In 1999, donepezil was approved for use in Japan. The instructions for physicians, however, do not describe this potential adverse effect. The occurrence of severe parkinsonism in a patient concurrently using tiapride and donepezil is reported.

A 79-year-old woman with a history of visual hallucinations and mild dementia visited a psychiatrist. She and her family members denied that she had had difficulty in walking. No medications had been previously prescribed. She was prescribed 25 mg of tiapride once daily. The dose was increased to 25 mg twice daily 2 weeks later; her visual hallucinations disappeared. Four weeks after starting tiapride, she was prescribed 3 mg of donepezil once daily to alleviate the cognitive symptoms. Two weeks later, the dose was increased to 5 mg once daily, and one week after that, she started to walk with a stoop and required assistance. Therefore, she was referred to our clinic.

She was afebrile, her face was expressionless, and she spoke in a low voice. Her cranial nerve functions were intact. She was unable to stand or walk unaided. She had a marked stooped posture while standing or sitting on a stool. Barré arm and leg signs were negative. All four limbs showed severe bradykinesia and mild plastic rigidity; there was no obvious laterality. She had no tremor at rest or during action. Ankle jerks were hypoactive on both sides, but other tendon reflexes were normal. Sensation was intact. A neck X-ray showed no narrow canal. Cranial MR images demonstrated multiple small infarcts in the thalamus, basal ganglia, and cerebral white matter on both sides, suggesting a diagnosis of multi-infarct dementia. However, there was no fresh infarct. Both tiapride and donepezil were discontinued. On the following day, her gait disturbance began to improve. In ten days, she could walk without assistance and the rigidity had disappeared.

Because the temporal relationship between the ingestion of donepezil and the occurrence of parkinsonism was so noticeable, it is highly likely that donepezil in combination with tiapride caused the severe parkinsonism. Donepezil enhances central cholinergic activity by inhibiting acetylcholinesterase in the brain. Thus, the use of donepezil and dopamine D2 blockers must have caused the acetylcholine/dopamine imbalance in the striatum, producing parkinsonism (4). Clinicians should be aware of this possible interaction when dopamine-blocking drugs are used with donepezil.

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References