Letter to the Editor

Galantamine in the Treatment of Minor Depression With Mild to Moderate Alzheimer's Dementia in an Elderly Woman

To the Editor: Depression is present in about 20%–40% of dementia patients; 15%–50% of Alzheimer's dementia patients have depression.^{1,2} Depression is common in the early stages of the disease and remains fairly constant through most stages of Alzheimer's dementia.³ Depression exacerbates the cognitive deficits of the preexisting dementia. In Alzheimer's dementia, mild to moderate depression may also manifest as new onset of agitation, wandering, apathy, insomnia, or change in functional status. Depressive symptoms in dementia should be viewed as a cause of significant and treatable "excess disability."⁴

Case report. Ms A, an 80-year-old woman, presented with a 2-year history of cognitive decline and an 8-month history of minor depression. Depression features included low mood with decreased interest in social activities, being less energetic, psychomotor slowing, and being more withdrawn and lonely. Sleep and appetite were good. She met only 3 of the 9 features of the *DSM-IV* criteria for major depressive disorder. Her Geriatric Depression Scale (GDS)⁵ score was 11/30. Her Cornell Scale for Depression in Dementia⁶ score for depression in dementia was 13. Her Mini-Mental State Examination (MMSE)⁷ score was 22/30, and she met the *DSM-IV* criteria for Alzheimer's dementia. Computed tomography scan of the brain revealed generalized atrophy.

Ms A was started on galantamine 8 mg orally twice a day, which was subsequently increased to 16 mg orally twice a day after 4 weeks. Her minor depression features responded very well with galantamine monotherapy after 2 months. At that time, her MMSE score was 23/30, her GDS score was 4/30, and her Cornell Scale for Depression in Dementia score was 6.

Depression is associated with defects of multiple neurotransmitters, including serotonin, dopamine, catecholamine, and acetylcholine. Depression in Alzheimer's dementia is linked to catecholaminergic deficit or degeneration of serotonergic neurons, and this process is also known to occur early in Alzheimer's dementia.⁸

Galantamine is an acetylcholinesterase inhibitor and an allosteric modulator of nicotinic acetylcholine receptor (nAChR) and is used in the treatment of dementia. Nicotinic acetylcholine receptors exist not only on neuronal cell bodies and dendrites but also on those located on axon terminals and are involved in the modulation of multiple neurotransmitter releases. Neuronal nAChR is a family of ligand-gated ion channels that are widely distributed in the brain and are controlled by acetylcholine and nicotine receptor agonists. In the genetically depressive rats, nicotine showed antidepressant-like effects through the involvement of $\alpha 4\beta 2$ nicotinic acetylcholine receptor subtype. The $\alpha4$ subunit in combination with the $\beta2$ subunit mediates dopaminergic and nonadrenergic release.9 Modulation of nAChR facilitates the release of a number of neurotransmitters, including acetylcholine, dopamine, norepinephrine, serotonin, γ-aminobutyric acid (GABA), and glutamate.¹⁰ Striatal nicotinic acetylcholine receptors with high affinity for nicotinic agonists are involved with the release of a number of neurotransmitters, including dopamine.¹¹ Dopamine deficiency is associated with anhedonia, lack of interest, and psychomotor slowing (bradyphrenia), and it may arise as a consequence of cholinergic defects involving nAChR. Studies suggest galantamine

in addition to mediating cholinergic neurotransmission also through nicotinic acetylcholine receptors may influence several other neurotransmitter systems, possibly modulating the activity of serotonin, dopamine, glutamate, and GABA in certain nerve tracts.^{12,13} So, it is possible that galantamine, a cholinesterase inhibitor used in the treatment of dementia, may also have some antidepressant effect.

If large studies prove this effect, we may not need to use an antidepressant in addition to a cholinesterase inhibitor in patients who have depression with dementia. This means less medication usage and potentially less adverse effect to these patients.

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