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Anti-dementia drugs: what difference do they make?

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Editorial

Alzheimer's disease (AD) is a treatable disorder. Two classes of anti-dementia agents have emerged in the recent past: anti-oxidants and cholinesterase inhibitors. A recent study[1] showed that the anti-oxidants alpha tocopherol (vitamin E) and selegiline slowed the progress of AD. Patients treated with either agent alone or with both agents in combination progressed to end-point more slowly than patients on placebo. Patients on placebo reached one of the end-points – death, nursing home placement, progression to severe AD, or significant loss of activities of daily living – in approximately 400 days, whereas patients on active agent required approximately 600 days to reach the same end-points. Both these agents have anti-oxidant properties; selegiline is a monoamine oxidase-B inhibitor that reduces free radical generation and alpha tocopherol has free radical capture capabilities. These agents are applied to patients in mild or moderate phases of AD, where slowing the progression of the illness and maintenance of patients at higher levels of function are the principal goals. Slowing the progression of the disease in more advanced phases of the illness may be less desirable.

Cholinesterase inhibitors address the cholinergic deficiency in AD and have been developed for patients with mild to moderate severity of dementia. The average response is a four-point improvement on a cognitive scale equivalent to reversal of approximately seven months of decline.[2–4] Patients usually present for treatment several years after the onset of symptoms and most patients will not be treated with these agents in the later phases of the disease when cognitive impairment is severe. Thus, the treatment opportunity window is limited to approximately five years, and a seven- to 12-month reversal of symptoms represents a substantial and clinically compelling response. In addition to changes in cognition, cholinesterase inhibitors also have a beneficial effect on behaviour, reducing apathy, visual hallucinations and purposeless activity such as pacing.[5,6] Cognitive and behavioural abnormalities in AD produce distress in caregivers, and improvement in either of these domains ameliorates caregiver burden.[5]

Cholinesterase inhibitors exert less potent effects than required of an ideal anti-dementia agent. Although their beneficial effects are sustained relative to placebo, there is continuing decline in patients receiving anti-dementia therapy. Anti-amyloid agents, anti-inflammatory drugs, and agents affecting apoptosis or excitatory amino acid toxicity have promise as drugs that will defer the onset or slow the progression of AD. These agents, however, do not improve existing symptoms. Cholinesterase inhibitors[7] improve symptoms but appear to exert little influence on disease course. Thus, a combination of anti-dementia drugs, including compounds that will interfere in the basic disease process and agents that improve symptoms will comprise an optimal anti-dementia regimen. Cholinergic drugs are likely to continue to play an important role in anti-dementia therapy despite the emergence of newer, more powerful agents.

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