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Dementia

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CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 78.

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Dementia is characterized by chronic, global, nonreversible deterioration in memory, executive function, and personality. Speech and motor function may also be impaired in persons with dementia.

Median life expectancy for persons with Alzheimer disease and Lewy body dementia is about six years after diagnosis, although many persons with these conditions may live much longer.

Randomized controlled trials of dementia are often not representative of all persons with dementia; most trials are of six months' duration or less, are not in primary care, and are in persons with Alzheimer disease. Few randomized controlled trials address vascular dementia, and fewer still address Lewy body dementia.

Some cognitive symptoms of dementia may be improved with acetylcholinesterase inhibitors such as donepezil, galantamine, and rivastigmine.

- Acetylcholinesterase inhibitors may improve cognitive function and global function scores compared with placebo at 12 to 26 weeks in persons with Alzheimer disease. However, they may be associated with an increase in adverse effects, particularly gastrointestinal symptoms (anorexia, nausea, vomiting, or diarrhea).

We do not know whether cognitive stimulation, music therapy, reminiscence therapy, omega-3 fatty acids (fish oil), statins, or nonsteroidal anti-inflammatory drugs are effective at improving cognitive outcomes in persons with cognitive symptoms from dementia, because we found insufficient evidence.

In persons with cognitive symptoms, memantine may modestly improve cognitive function and global function scores in

persons with Alzheimer disease over 24 to 28 weeks, and may modestly improve activities of daily living scores in persons with moderate to severe Alzheimer disease.

- Although memantine is associated with a statistically significant increase in cognition scores in some population groups, the clinical importance of some of these results is unclear.

We found inconsistent evidence on the effects of Ginkgo biloba on cognitive outcomes, which varied by the analysis performed.

- We found no evidence that Ginkgo biloba improves activities of daily living outcomes, but the available evidence was weak.

Acetylcholinesterase inhibitors may marginally improve neuropsychiatric symptoms compared with placebo in persons with behavioral and psychological symptoms of dementia, but they are also associated with adverse effects.

- We do not know whether antidepressants (clomipramine, fluoxetine, imipramine, or sertraline) improve depressive symptoms in persons with Alzheimer disease that is associated with depression.

Many randomized controlled trials were small and short-term, and adverse effects were sparsely reported.

Memantine may be associated with a small improvement in neuropsychiatric symptoms compared with placebo in persons with behavioral and psychological symptoms of dementia, but it is also associated with adverse effects.

We do not know whether diazepam, lorazepam, aromatherapy, cognitive behavior therapy, exercise, carbamazepine, or sodium valproate/valproic acid is effective at improving neuropsychiatric symptoms in

persons with behavioral and psychological symptoms of dementia, because we found insufficient evidence.

Some antipsychotics may improve neuropsychiatric symptoms or aggression in persons with behavioral and psychological symptoms of dementia, but antipsychotics are also associated with an increased risk of severe adverse events such as stroke, transient ischemic attack, or death.

Caution: Regulatory bodies have issued alerts that conventional and atypical antipsychotics are associated with an increased risk of death in older persons treated for dementia-related psychosis.

Definition

Dementia is characterized by memory loss (initially of recent events), loss of executive function (such as the ability to make decisions or sequence complex tasks), other cognitive deficits, and changes in personality. This decline must be serious enough to affect social or occupational functioning, and reasonable attempts must be made to exclude other common conditions, such as depression and delirium.

Alzheimer disease is a type of dementia characterized by an insidious onset and slow deterioration, and involves impairments in memory, speech, personality, and executive function. It should be diagnosed after other systemic, psychiatric, and neurologic causes of dementia have been excluded clinically and by laboratory investigation.

Vascular dementia is often caused by multiple large or small vessel disease. It often presents with a stepwise deterioration in cognitive function, with or without language and motor dysfunction. It usually occurs in the presence of vascular risk factors (diabetes mellitus, hypertension, arteriosclerosis, and smoking). Characteristically, it has a more sudden onset and stepwise progression than Alzheimer disease, and often has a patchy picture of cognitive deficits.

Lewy body dementia is a type of dementia that involves insidious impairment of cognitive function with parkinsonism, visual hallucinations, and fluctuating cognitive abilities. Nighttime disturbance is common, and there is an increased risk of falls.

Careful clinical examination of persons with mild to moderate dementia and the use of established diagnostic criteria accurately identify 70% to 90% of causes confirmed postmortem. In all types of dementia, individuals will experience problems with cognitive functioning

Clinical Questions

What are the effects of treatments on cognitive symptoms of dementia (Alzheimer disease, Lewy body dementia, or vascular dementia)?

Likely to be beneficial	Acetylcholinesterase inhibitors (donepezil, galantamine, rivastigmine) Memantine (evidence of statistical benefit, but results of unclear clinical importance)
Unknown effectiveness	Ginkgo biloba Nonsteroidal anti-inflammatory drugs Nonpharmacologic interventions (cognitive stimulation, music therapy, reminiscence) Omega-3 fatty acids (fish oil) Statins

What are the effects of treatments on behavioral and psychological symptoms of dementia (Alzheimer disease, Lewy body dementia, or vascular dementia)?

Likely to be beneficial	Acetylcholinesterase inhibitors (donepezil, galantamine, rivastigmine; evidence of marginal benefit) Memantine (evidence of marginal benefit)
Trade-off between benefits and harms	Antipsychotic medications (limited evidence of effectiveness; however, associated with severe adverse effects, including cerebrovascular events and death)
Unknown effectiveness	Antidepressants (clomipramine, fluoxetine, imipramine, sertraline) in persons with depression and dementia Benzodiazepines (diazepam, lorazepam) Mood stabilizers (carbamazepine, sodium valproate/valproic acid) Nonpharmacologic interventions (aromatherapy, cognitive behavior therapy, exercise)

and are likely to experience behavioral and psychological symptoms of dementia. Where possible, we have divided outcomes into cognitive or behavioral/psychological, although there is often considerable crossover between these outcomes, both clinically and in research. This review deals solely with persons who have Alzheimer disease, Lewy body dementia, or vascular dementia.

Incidence and Prevalence

About 6% of persons older than 65 years and 30% of persons older than 90 years have some form of dementia. Dementia is rare before 60 years of age. Alzheimer disease and vascular dementia (including mixed dementia) are each estimated to account for 35% to 50% of dementia, and Lewy body dementia is estimated to account for up to 5% of dementia in older persons, varying with geographic, cultural, and racial factors. There are numerous other causes of dementia, all relatively rare, including frontotemporal dementia, alcohol-related dementia, Huntington disease, normal-pressure hydrocephalus, human immunodeficiency virus infection, syphilis, subdural hematoma, and some cerebral tumors.

Etiology and Risk Factors

The cause of Alzheimer disease is unclear. A key pathologic process is deposition of abnormal amyloid in the central nervous system. Another early change is abnormal phosphorylation of tau, an intracellular structural protein. This results in apoptosis and neurofibrillary tangles. Disease-modifying agents in development target both processes. Most individuals with the relatively rare condition of early-onset Alzheimer disease (before 60 years of age) exhibit an autosomal dominant inheritance due to mutations in presenilin or amyloid precursor protein genes. Several gene mutations (on the amyloid precursor protein, presenilin 1, and presenilin 2 genes) have been identified. Later-onset dementia is sometimes clustered in families, but specific gene mutations have not been identified. Down syndrome, cardiovascular risks, and lower premorbid intellect may be risk factors for Alzheimer disease. Alzheimer disease and vascular pathology often coexist.

Vascular dementia is related to cardiovascular risk factors, such as smoking, arteriosclerosis, hypertension, and diabetes. Lewy body dementia is characterized by

the presence of Lewy bodies (abnormal intracellular inclusions consisting of α -synuclein) in the cortex. Brain acetylcholine activity is reduced in many forms of dementia, and the level of reduction correlates with cognitive impairment.

Prognosis

Alzheimer disease usually has an insidious onset with progressive reduction in cerebral function. Diagnosis is difficult in the early stages. Median life expectancy after diagnosis is about six years, although many persons with Alzheimer disease live much longer. We found no reliable data on prognosis for vascular dementia. Persons with Lewy body dementia have an average life expectancy of about six years after diagnosis. Behavioral problems, depression, and psychotic symptoms are common in all types of dementia. Eventually, most persons with dementia have difficulty doing simple tasks without help.

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