Drug Update

Treatments for Cognitive Impairment in the Older Adult

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Current Drug Treatments for Alzheimer’s Disease

Cholinesterase Inhibitors: Four drugs approved using cognitive battery and behavioral assessment (ADAD-cog/CGIC)

- Tacrine (Cognex) – Used rarely due to potential for liver toxicity.
- Donepezil (Aricept) – Tolerated better. At 6-months showed improved cognitive and behavioral ratings with moderate to severe AD.

- Tariot, P.N. and Federoff, Alz Dis Assoc Disord 17(4), July-Sept. 2003
Rivastigmine (Exelon) – Has had a high rate of gastrointestinal side effects. No placebo trials longer than six months.

Galantamine (Reminyl) – Pts. on this drug at 6 months or longer showed cognitive improvement at or above baseline.

Tariot, 2003
Antiexcitotoxic Strategies

- Memantine – In combination with CHE-I in clinical trials appears safe, tolerated and effective (European use only to date). Just now available in US.

- Tariot, 2003
Untreated patients declined “relentlessly” in most studies. Treated patients “benefit” cognitively and behaviorally on assessment and showed some preservation over time.

Tariot, 2003
Antioxidants

- Vitamin E and Selegilene – “Probably” effective for AD treatment, not so much for cognition, but in behavior.
- Ginko Biloba – Effectiveness is controversial.
- “Cocktails” of these supplements may show promise.

Tariot, 2003
Anti-inflammatory Medications

- Preliminary evidence suggests probable benefit, but more research trials are needed.
- Tariot, 2003
Hormones

- Studies indicate nerve growth factor (NGF) may reverse cholinergic atrophy in the nucleus basalis.
- Hormones – Estrogen may have cholinergic and protective effects.
- Recent evidence from the Woman’s Health Initiative Study showed an increased risk for dementia.

Tariot, 2003
Other Treatments

- Antiamyloid strategies
- Normalizing Tau Phosphorylation
- Lithium - Potential new drug target
- Combining Donepezil and Vitamin E in AD
  Alz Dis and Assoc Disord 17(2), 2003
Measures used to approve cognitive drugs

- The FDA requires a significant drug-placebo difference on measures of cognitive and global change.
- Most commonly used measures in drug studies have been:
  
  Alzheimer’s Disease Assessment Scale - Cognitive (ADAS-Cog)
  

  Clinical Global Impression (CGI) or (CIBIC-plus)
  
ADAS-Cog

A 70-item exam that assesses language, memory, praxis and visuospatial skills. High scores reflect more impairment.

Studies of individual items of ADAS-Cog showed pts. On 80 mg of tacrine improved sign on recall, naming, language and word-finding.

Cummings, 2003
Mohs (1997) investigated additions to the ADAS that would assess cognitive functions not found on the original ADAS, including delayed verbal fluency, non-verbal memory, attention/concentration, word finding, executive functioning and praxis. Delayed verbal memory most useful in differentiating AD. Mohs, R.C. Alz Dis Assoc Dis 1997
CIBIC-Plus

- Rates pts on a 7 point scale
  - No change to mild, moderate and marked improvement.
Critique of CHE-I Studies

- Some studies indicate that effects are minimal on cognition and functioning.
- There seems to be evidence to suggest these drugs delay time to nursing home placement and decreased healthcare costs.
- Some reviewers suggest that more studies are needed in the areas of use, gauging response, switching to other CHE-I’s, higher doses.

Critique (cont.)

- Samples were well educated, wealthy, younger old, had few physical illnesses, few behavioral disturbances, few minorities, always in structured settings. Cummings – 2003

Global ratings appropriate but insensitive

Tested for only 3 to 6 months. Is there real change in that amount of time?

Benefit of these drugs in slowing progression over long-term (> 1 yr.) seldom studied.

High dropout rates. Pryse-Phillips, 1999
CHE-I use with other dementias

- Donepezil (Aricept) good with Alzheimer’s and Supranuclear palsy.
- Rivastigmine (Exelon) good with vascular dementia and Alzheimer’s with VD.
- Galantamine (Reminyl) good with Lewy body
- Donepezil not good with Huntington’s
Other uses (cont.)

- Exelon effective with Parkinson’s disease (cognition and behavior).
  Cumming 2003
Prevention

- Early diagnosis with neuropsychological evaluation: Identifying patients with impairment in delayed verbal memory and executive functioning most helpful.

- Early detection (before DX) and treatment with anti-dementia drugs may be helpful according to some drug studies.

DeKosky, D. Alz Dis Assoc Disord, 17 (4), 2003