

Comparative effectiveness and safety of cognitive enhancers for treating Alzheimer's dementia: A systematic review and network meta-analysis

Summary

We conducted a systematic review and network meta-analysis (NMA) including randomized control trials (RCTs), non-RCTs, and observational studies to compare the safety and effectiveness of cognitive enhancers donepezil, galantamine, rivastigmine, or memantine, in any combination. Overall our results suggest that cognitive enhancers have minimal effects on cognition, as determined by a minimal clinically important difference (MCID), yet were relatively safe. Across all effectiveness outcomes donepezil was likely the most effective therapy.

Implications

While not considered to be “serious adverse events”, side effects (namely nausea, vomiting, diarrhea and headache) from drug use affect quality of life. Our findings should help all concerned make tailored decisions about risks and benefits of using cognitive enhancers in patients with Alzheimer's Disease (AD).

Reference: Tricco AC, Ashoor HM, Soobiah C, et al. Comparative Effectiveness and Safety of Cognitive Enhancers

for Treating Alzheimer's Disease: Systematic Review and Network Metaanalysis. J

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What is the current situation?

- Global economic burden of AD to the healthcare system and individuals is substantial at an estimated \$818 billion US dollars per year.
- Cognitive enhancer medications can be used to treat patients with AD.
- Although the safety and efficacy of cognitive enhancer medications were examined in previous systematic reviews, only RCTs were included, limiting applicability of the findings to ‘real world’ patients.

What is the objective?

- To examine the comparative effectiveness and safety of cognitive enhancers for AD through a systematic review and NMA.

How was the review conducted?

- MEDLINE, EMBASE, The Cochrane Library, CINAHL, and Ageline were searched from inception until March 9, 2016.
- Studies of AD patients examining donepezil, galantamine, rivastigmine, or memantine in any combination, compared with each other or control (no treatment, placebo, best supportive care) were included.
- Two reviewers independently performed study selection, data abstraction, and quality appraisal of included articles; discrepancies were resolved through discussion.
- Bayesian random-effects pairwise meta-analysis was conducted for each treatment comparison and outcome.
- Cognitive enhancers were ranked using the surface under the cumulative ranking) curve (SUCRA).

What did the review find?

- 110 RCTs, 21 non-randomized controlled trials, and 11 cohort studies that were published between 1996 and 2015 were included.
- Donepezil is likely the most effective agent for AD across all effectiveness outcomes examined.
- For cognition, only donepezil reached the MCID threshold on the Alzheimer's Disease Assessment Scale cognition subscale (ADAS-cog scale) and thus is likely a first choice for patients and clinicians considering cognitive enhancers.
- There were no increased risks of serious harms, falls or bradycardia among AD patients.
- Donepezil, galantamine, and rivastigmine caused more patients to experience nausea and vomiting, which may result in decreased quality of life and cessation of therapy.