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Title **Cholinesterase Inhibitors for Alzheimer's Disease: A Systematic Review of Randomized Controlled Trials**

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Aim

To critically examine evidence related to the efficacy, safety, and acceptability of using cholinesterase inhibitors (ChEIs) in individuals with mild to moderate Alzheimer disease (AD).

Conclusions and results

Twenty-five clinical trials that collectively measured 29 outcomes were used in this review. Cholinesterase inhibitors had a modest impact on functional performance and global outcomes. The clinical significance of this improvement is difficult to predict. Patients on galantamine and rivastigmine experienced adverse events (AE) that led to a greater likelihood of discontinuing the treatment, although ChEIs did not cause an increase in the number of patients experiencing serious AE or death. Donepezil did not improve quality of life (QoL) or prevent institutionalization, but whether or not this is a class effect remains to be determined. Comparisons suggest that ChEIs have comparable efficacy, but methodological limitations prevent definitive conclusions.

Recommendations

Not applicable.

Methods

A comprehensive search strategy was developed to identify published and unpublished literature. Studies were selected if they reported on randomized, parallel group design trials of at least 12 weeks and if trial participants had evidence of mild to moderate, possible or probable AD, based on established diagnostic criteria. Trials comparing a ChEI with placebo or with another treatment were included, and there were no language restrictions. Meta-analysis was performed when sufficient quantitative data were provided. Where applicable, sensitivity analyses were performed for quality of trials and language of publications. The benefit and harm of using ChEIs to manage mild to moderate AD was determined by examining changes in functional performance, global improvement, quality of life (QoL), adverse events, and serious adverse events. The effects that using ChEIs had on rates of institutionalization and persistence with therapy were also examined.

Further research/reviews required

The knowledge gaps that continue with ChEIs include the impact of these drugs on outcomes, eg, rate and timing of institutionalization, beneficial effects on QoL, functional performance, and long-term effectiveness.

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