

EFFICACY AND SAFETY OF DONEPEZIL IN PATIENTS WITH ALZHEIMER DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION

- Alzheimer's disease (AD) is a neurodegenerative disorder characterized by the presence of neurofibrillary tangles and amyloid plaques.^[1]
- The prominent symptoms include dementia and loss of cognitive functions.^[1]
- AD is one of the most prevalent neurological disorders with a prevalence of 46.0 (40.2 to 52.7 million) across the world.^[2]
- Global prevalence of AD was 26.6 million in 2006 and its burden is expected to increase to four fold by year 2050, wherein 1 in every 85 people will be suffering from AD.^[3]
- Donepezil, an acetylcholinesterase inhibitor was approved in 1997 by USFDA for the treatment of mild to moderate AD.^[4]

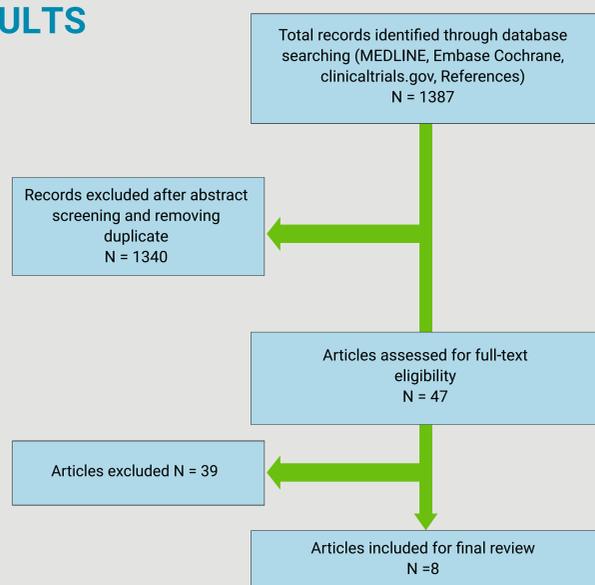
OBJECTIVE

- To evaluate the efficacy and safety of donepezil versus placebo for the treatment of AD patients.

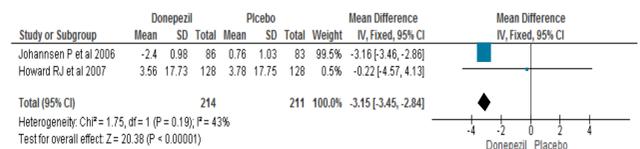
MATERIALS AND METHODS

- Literature searches were conducted in MEDLINE, Embase, the Cochrane Library, and clinicaltrials.gov. No language or date restrictions were imposed.
- In addition, references of included studies were searched for relevant studies.
- All randomized controlled trials (RCTs) comparing donepezil versus placebo among AD patients were included.
- Outcomes:
 - Primary: Cognitive function measured using Alzheimer's Disease Assessment Scale (ADAS) and Neuropsychiatric Inventory (NPI)
 - Secondary: Patients With Any One Of the Adverse Event (PWA0AE)
- Two authors independently selected papers, extracted data assessed quality and discrepancies were resolved through discussion.
- Study quality of included trials were assessed using the Cochrane Risk of Bias Tool.

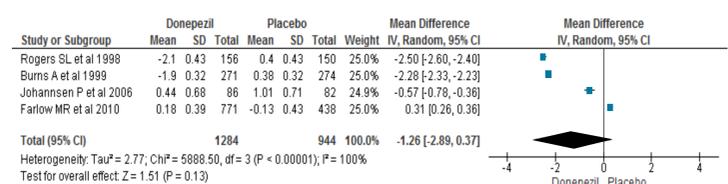
RESULTS



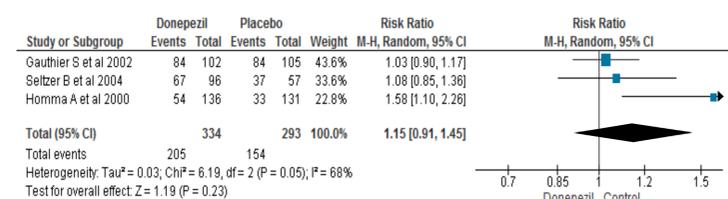
- A total of 8 RCTs involving a total of 3151 patients were included in this meta-analysis.
- A total of 1703 patients received donepezil and a total of 1448 patients received placebo.
- Overall, the risk of bias of included trials was low (3 studies) to moderate (5 studies)
- Most common adverse events reported with donepezil were dizziness, confusion and insomnia



The **Cognitive improvement using Neuropsychiatric Inventory** was better with donepezil group than the placebo (MD=-3.15; 95%CI -3.45 to -2.84, 2 studies)



The **Cognitive improvement using ADAS-cog scale** was comparable between the donepezil group and the placebo (MD=-1.26; 95%CI -2.89 to 0.37, 4 studies)



Patients with any one of the adverse event were comparable between the donepezil group and placebo (RR= 1.15; 95%CI 0.91 to 1.45, 3 studies)

DISCUSSION

- Our review suggests an improved cognitive function and behavioural aspects in donepezil monotherapy group when compared to control group, assessed by using NPI scale. Also, it was found to be comparable by ADAS-cog scale.
- Lanctot KL et al. in his study (n=1723) showed a significantly improved global response in donepezil group when compared to placebo among AD patients.^[5]
- In another study, Burns A et al. documented that donepezil was well tolerated among AD patients when compared to placebo; however more number of patients reported cholinergic adverse events.^[6]
- Study conducted by Birks JS et al. showed greater beneficial effect in terms functional aspects among patients receiving 10mg donepezil when compared to group receiving 5 mg donepezil.^[7]
- Whitehead A et al. further revealed greater improvement in cognitive and clinician-rated global function with the higher dose of donepezil.^[8]

CONCLUSIONS

- Donepezil use can lead to significant improvement in behavioural and cognitive functions in patients suffering from AD with minimum side effects as compared to placebo.

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