Effects of cholinesterase inhibitors on cognition of people with vascular cognitive impairment: a systematic review and network meta-analysis

Azmil H Abdul-Rahim[1], Ceri E Battle[2], Susan D Shenkin[3], Jonathan Hewitt[4] and Terence J Quinn[5].

1) Institute of Neuroscience and Psychology, University of Glasgow, Glasgow, UK. 2) Welsh Centre for Emergency Medicine Research, ABM University Health Board, Swansea, UK. 3) Geriatric Medicine, Department of Clinical and Surgical Sciences, University of Edinburgh, Edinburgh, UK. 4) 3rd Floor, Academic Building, Llandough Hospital, Cardiff University and Aneurin Bevan Health Board, Cardiff, UK. 5) Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK.

University of Glasgow

BACKGROUND

Cholinesterase inhibitors (ChIs) may benefit people with vascular cognitive impairment (VCI). We performed a systematic review and network meta-analysis to compare the efficacy of ChIs on cognition of people with VCI.

METHODS

We systematically searched multidisciplinary databases from inception to June 2019 for randomised, placebo-controlled trials of ChI (i.e. Donepezil, Rivastigmine and Galantamine) in people with VCI. We assessed all included studies for risk of bias using the GRADE criteria. We used random effects models to create summary estimates (mean difference [MD]) of efficacy at six months, based on Alzheimer's Disease Assessment Scale-cognitive (ADAS-Cog), first in pairwise analyses versus placebo and then in a comparative network of all drugs. ADAS-Cog is a scale from 0 to 70, with higher score indicates greater cognitive impairment.

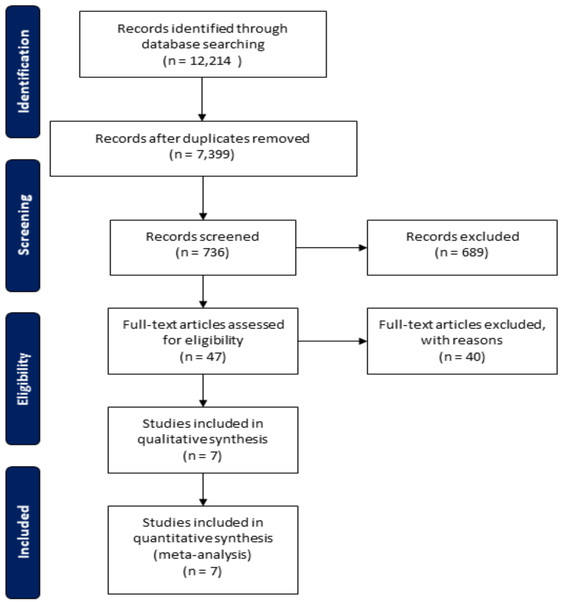


Figure 1: PRISMA diagram.

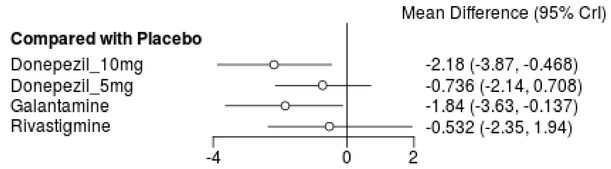


Figure 2: Pairwise summary estimates (mean difference [MD]) of cognition at 6 months using ADAS-Cog scale.

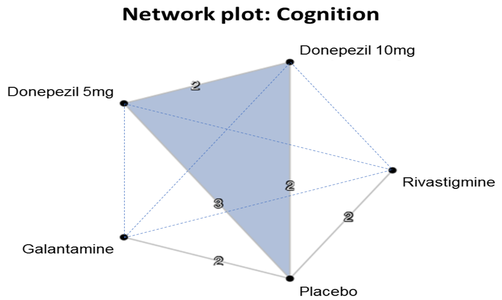
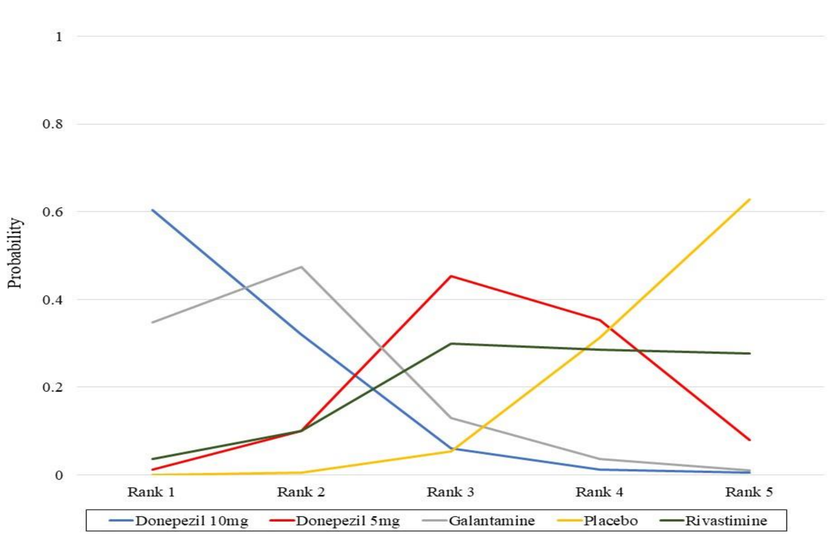


Figure 3: Comparative network plot of all ChI agents.

RESULTS

After reviewing 12,214 citations, we selected 47 studies for full-text screening. We extracted data from 7 studies. Data were available for Donepezil (n=3 trials, 1,601 participants); Rivastigmine (2 trials, 748 participants); Galantamine (2 trials, 1,188 participants) **[Figure 1]**. Overall, risk of bias was moderate. Pairwise summary estimates suggest beneficial effects versus placebo for Donepezil 5mg (MD: -0.74, 95%CI: -2.14 to 0.71), Donepezil 10mg (MD: -2.81, 95%CI: -3.87 to -0.47) and Galantamine (MD: -1.84, 95%CI: -3.63 to -0.14), but not Rivastigmine (MD: -0.53, 95%CI: -2.35 to 1.94) **[Figure 2]**. On network meta-analysis, the ranking probability based on the surface under the cumulative ranking curve suggested that Donepezil 10mg has the highest probability of favourable effects on cognition, followed by Galantamine, Donepezil 5mg and Rivastigmine **[Figures 3 and 4]**.



Rank	Intervention
1	Donepezil_10mg
2	Galantamine
3	Donepezil_5mg
4	Rivastimine
5	Placebo

Figure 4: Ranking probabilities (*rankogram*) of ChI agents for outcome of cognition at 6 months.

CONCLUSIONS

The various ChIs show differential effects in VCI, our data suggest donepezil 10mg is most efficacious but even for this drug effect size is modest. (Note: A 4-point ADAS-Cog change at six months is considered clinically-meaningful).

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Correspondence: Azmil.Abdul-Rahim@glasgow.ac.uk