TOOLS FOR PRACTICE #417 | July 6, 2026

Deprescribing Cholinesterase Inhibitors: Good or bad idea?

CLINICAL QUESTION

What are the effects of deprescribing cholinesterase inhibitors?

BOTTOM LINE

Benefits of cholinesterase inhibitors are unclear, especially when dementia progresses. In patients with moderate-severe Alzheimer's dementia, deprescribing cholinesterase inhibitors, on average, worsens cognition by 1-2 points on the Mini-Mental-State-Examination (MMSE). Randomized Controlled Trials (RCT) have not assessed the proportion of patients with clinically meaningful worsening of cognition or neuropsychiatric symptoms.

EVIDENCE

- Results statistically significant unless indicated.
- MMSE (1-30, high=better),[1,2] clinically meaningful difference: 1.4-2.
- Neuropsychiatric inventory (NPI) (1-144, low=better),[2] clinically meaningful difference: 8.
- Severe dementia, participants already on anticholinesterase inhibitors (mostly >2 years):
    - Participants with MMSE~9:
        - 146 participants, randomized to placebo (with taper) or continuation donepezil for 52 weeks.[2]
            - MMSE: Baseline ~9, changed to ~3.5 (placebo) versus ~5.5 (donepezil).
            - NPI: Not statistically different.

        - 40 participants, randomized to placebo (with taper) or continuation donepezil/galantamine for 8 weeks.[3]
            - MMSE: Not statistically different.
    - MMSE~1:
        - 65 participants, randomized to placebo or continuation donepezil/memantine (no taper) for 12 weeks.[4]
            - Cognitive examination (1-25, higher=better): Donepezil/memantine 0.9 better.
            - NPI: Not statistically different.
- Moderate dementia:
    - MMSE~19-21:
        - 202 participants tolerating donepezil but without benefits after 12 weeks, randomized to placebo (no taper) or continuation for another 12 weeks.[5]
            - MMSE: Baseline ~19, changed to ~19.5 (placebo) versus ~20.5 (donepezil).
            - NPI: Donepezil 3.2 better.
        - 96 participants tolerating donepezil after 12 weeks, randomized to placebo (no taper) or continuing donepezil for 12 weeks.[1]
            - MMSE: Baseline 21, changed to ~19 (placebo) versus ~21 (donepezil).
            - NPI: Donepezil 6.2 better.
- Overall adverse events: No difference.[6]
- Systematic review including two RCTs with galantamine: Similar. [6]
- Limitations: Poor adherence; industry funding; [1,5] unclear if scale changes reflect return to baseline (as if medication never started) versus clinical worsening; limited functional assessment data.[6]

CONTEXT

- Patients with adverse effects should stop cholinesterase-inhibitors.[6,7]
- Long-term use is controversial due to short duration/limitations of RCTs. [6,7]
- Guideline: Consider stopping in those without benefits through shared decision-making with individuals/caregivers.[7]
    - Possible severe withdrawal reactions in case reports (agitation, hallucinations).
    - Tapering recommended, example: Halve dose every four weeks.
    - Monitor, consider re-initiation if worsening of condition.

REFERENCES

1. Holmes C, Wilkinson D, Dean C *et al.* Neurology. 2004;63: 214-19.
2. Howard R, McShane R, Lindesay J *et al.* New Engl J Med. 2012;366: 893-903.
3. Hermann N, O'Regan J, Ruthirakuhan M *et al.* J Am Med Dir Assoc. 2016 Feb;17(2): 142-7.
4. Hong YJ, Choi SH, Jeong JH, *et al.* J Alzheimers Dis. 2018;63(3): 1035-1044.

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5. Johannsen P, Salmon E, Hampel H *et al.* CNS Drugs. 2006;20(4): 311-25.
6. Parsons C, Lim WY, Loy C, *et al.* Cochrane Database Syst Rev. 2021 Feb 3;2(2): CD009081.
7. Reeve E, Farell B, Thompson W *et al.* Med J Aust. 2019 Mar;210(4): 174-179.

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