DEMENTIA

Prescribing for Alzheimer's disease in primary care DTB2014;52;69

Although current NICE guidance is that these drugs should be initiated by a specialist, in many parts of the UK responsibility for the continued prescription of these drugs is being transferred to primary care. We find ourselves with a number of learning needs: *when should they be started, which drug, dose changes, common side effects, any benefit from switching and when should they be stopped?*

The DTB recently reviewed the evidence. They remind us that there are *currently no interventions that cure or alter the long-term progression of dementia.*

All of the available drugs have modest efficacy but are generally well tolerated. The four approved and licensed available drugs are:

- **The acetylcholinesterase inhibitors (AChEIs): donepezil, galantamine and rivastigmine**
    - Licensed and approved by NICE as recommended options for mild to moderate AD
- **Memantine** (a different mode of action, an NMDA antagonist)
    - Licensed and approved by NICE as an option for moderate to severe AD, and for those who cannot take AChEIs

How effective are they?

- **AChEIs:** there is level 1a evidence from a systematic review of trials that compared to placebo they modestly improve cognitive function compared to placebo (by an average of 3 points on a 70 point scale, considered the minimal clinically significant change) in mild, moderate and severe disease
    - The NNT is 12 to achieve a significant benefit in cognitive function after 12 weeks
    - The NNH is also 12 over the same time to have an adverse effect
    - Modest benefits are also seen for a range of other outcome measures, such as activity of daily living (ADL) and behaviour
    - One study has shown that when patients develop severe AD, continued treatment with donepezil (as compared to stopping it) is worthwhile in terms of preserving cognition and function
- **Memantine:** there is level 1a evidence that Memantine has a small beneficial effect in moderate and severe AD, but not in mild AD
    - At 6 months benefits were seen in cognition, mood, behaviour and ADL
- Combination treatment of AChEI and memantine: studies have shown conflicting results, but a meta-analysis (1a) failed to show clinically significant benefit for combination therapy

Whilst these mean effects seem modest, another paper BMJ2012;344:e2986 highlighted

- The modest overall benefit hides the fact that a small number of patients derive a substantial benefit whereas most do not, encouraging a 'trial of treatment' approach.
- There is evidence that at 6 months patients on donepezil worsen less than on placebo (NNT of 6), so apparent 'non-responders' may still be getting some benefit compared to placebo.
- Some authors then feel that a positive response to treatment would be considered 'reduced worsening than expected if left untreated'

What about adverse events?

- AChEIs: cholinergic stimulation commonly causes nausea, vomiting, diarrhoea, headaches and insomnia
    - These adverse effects tend to occur at the start of therapy or dose increases and are often transient; slow dose titration or dose reduction will often help