Use of antidepressants to treat depression in dementia

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Position Statement 81

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Background

It is estimated that the number of dementia cases worldwide currently totals 35.6 million, with these numbers expected to double approximately every 20 years until 2050 (World Health Organisation, 2012). Estimates of the prevalence of major depression in dementia range from 11-25% (International Psychogeriatric Association, 2012). These figures represent an enormous and growing burden of illness within the field of aged psychiatry, yet the literature on the efficacy of pharmacotherapy for major depression occurring during the course of a dementing illness is sparse. Randomised controlled trials are few and of variable quality.

Evidence

Early small studies (including the DIADS study, Lyketsos et al. 2000; 2003) showed moderate to strong efficacy for sertraline, and in 2005 an expert consensus guideline recommended the use of antidepressants as the treatment of choice for depression in dementia (Alexopoulos et al. 2005). A recent systematic review and meta-analysis of placebo-controlled trials in this population produced only equivocal evidence of antidepressant efficacy; however the meta-analysis included only 330 people (Nelson and Devanand, 2011).

The largest single study of antidepressants in dementia enrolled 326 patients who were randomised to either placebo, sertraline or mirtazapine and failed to demonstrate significant differences in outcome across all groups at 13 and 39 weeks (Banerjee et al 2011). This supported findings from the DIADS-2 study, based on 131 subjects, which found no efficacy for sertraline over placebo (Rosenberg et al. 2010). While the Banerjee study has been criticised for its methodological problems, most specifically the recruitment and type of patients studied, doses used and limitations of the Cornell Scale for Depression in Dementia (CSDD) (Macfarlane et al. 2012), it remains the best evidence available upon which to base clinical practice.

What might best be highlighted within the Banerjee study is the observation that all groups improved, regardless of the intervention they received. It should be noted that participants in the study were all in receipt of services from specialist old-age psychiatry services within the UK, and that the psychosocial interventions offered within these specialist models of care may well have constituted an ‘active placebo’ effect that was received by all groups, thus diluting out any additional effects from antidepressant medications. There are also concerns that the treatment group may have included a significant number of patients with dysthymia or mild depressive symptoms, which are less likely to respond to medication treatment than those with melancholic depression. Moreover, the study highlighted the importance of the role of ‘normal care’ and what this might involve, specifically in regards to psychosocial and environmental interventions for which there is strong supportive evidence (e.g. for exercise and behaviour management) (Burns et al. 2012).

A double-blind discontinuation study (Bergh et al. 2012) found that discontinuation of antidepressants in 63 persons with dementia and neuropsychiatric symptoms led to an increase in depressive symptoms compared to those 68 that remained on antidepressants. However, as the authors noted, most patients appeared to tolerate the discontinuation as they remained within the same subscore group of the CSDD. Accordingly, the authors recommended vigilance for development of depressive symptoms on discontinuation.
Cost Benefit Analysis

Because pharmacological intervention studies of antidepressants in dementia are limited in quality and number, and because these studies have shown that these medications are associated with a range of adverse events, most notably sedation, falls, bleeding, SIADH, tremor, gastrointestinal and respiratory effects, and all cause mortality (e.g. Rosenberg et al. 2010; Banerjee et al. 2011, Coupland et al. 2011) the potential benefits must be weighed against the risks.

Recommendations

The College supports the following principles:

- The current evidence for antidepressant efficacy in dementia is equivocal and requires further development. Clinicians should act on the basis of careful consideration of all the factors at hand, as well the most up-to-date research.

- Clinicians treating depression in patients with dementia should expect improvement. Therapeutic nihilism is not justified.

- People with dementia and depression should have access to mental health care from professionals with knowledge of how to adapt such care for age and the presence of dementia.

- Choice of treatment should be based on comprehensive assessment of each individual, their history, mental state and risk. Assessments should include active involvement from family, whānau and carers.

- Clinicians need to be conscious of the need to differentiate major depression from dysthymia and the behavioural and psychological symptoms of dementia (BPSD) in this patient group; and that this differentiation may require review over time due to the clinical challenges entailed.

- Patients with dementia and depression who are referred to old-age psychiatry services should receive psychosocial interventions in the first instance, followed by consideration of antidepressants if there is no response.

- Individual patient factors including suicide or other risk, a past history of antidepressant response, presence of symptoms of melancholic depression and levels of distress should be considered indicators for an early trial of antidepressants.

- Antidepressant initiation must be accompanied by a clear plan to monitor efficacy and side effects.

- Antidepressant cessation should also be accompanied by a clear plan to monitor symptom recurrence and re-evaluation of treatment as required.
References


Lyketsos CG, DelCampo L, Steinberg M, et al. Treating depression in Alzheimer disease: Efficacy and safety of sertraline therapy, and the benefits of depression reduction: The DIADS. *Arch Gen Psychiatry* 2003; 60:737-746


World Health Association/Alzheimer’s Disease *International Dementia: A Public Health Priority*

Disclaimer

This information is intended to provide general guide to practitioners, and should not be relied on as a substitute for proper assessment with respect to the merits of each case and the needs of the patient. The College endeavours to ensure that information is accurate and current at the time of preparation, but takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available.
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Contact: Senior Manager, Practice Policy and Partnerships

<table>
<thead>
<tr>
<th>Date</th>
<th>Version</th>
<th>Approver</th>
<th>Description</th>
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<tbody>
<tr>
<td>14/02/2015</td>
<td>1.0</td>
<td>B2015/1 R22</td>
<td>New Document</td>
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<tr>
<td>02/2018</td>
<td></td>
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<td>NEXT REVIEW</td>
</tr>
</tbody>
</table>

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