NICE or not so nice: dementia clinical guideline

The National Institute for Health and Clinical Excellence (NICE) is no stranger to controversy, but rarely have their decisions ignited such heated debate as their recommendation of drugs to treat dementia. Professor Clive Ballard and Samantha Sharp of the Alzheimer’s Society study the data, marshall their thoughts and articulate concerns about the new recommendations.

The National Institute for Health and Clinical Excellence (NICE) Dementia Clinical Guideline provides over 100 evidence-based recommendations for health and social care professionals, service managers and commissioners. It covers the range of care that should be routinely available, focusing on diverse but key issues such as services for people with mild dementia, training for staff in residential and nursing homes, and brain imaging. It is, however, disappointing the release of these guidelines has been overshadowed by NICE’s guidance for antideementia drugs, published on the same day.

The NICE guidance states cholinesterase inhibitors (donepezil, rivastigmine, galantamine) should be restricted to people with Alzheimer’s disease (AD) of moderate severity, defined by NICE as a score on the Mini-Mental State Examination (MMSE) cognitive screening test of between 10 and 20. The prescription of memantine, licensed for moderate to severe AD, is not recommended outside clinical trials. The NICE appraisal confirmed the evidence from more than 30 randomised placebo-controlled clinical trials, expert clinical opinion (British Association of Psychopharmacology (BAP) guidelines) and people receiving treatment (Table 1) that cholinesterase inhibitors are clinically effective, across the full licensed range of mild-moderate AD. The average clinical response to treatment is a

Table 1. Benefits reported by carers of people with dementia taking one of the four licensed drug treatments

<table>
<thead>
<tr>
<th>Benefit</th>
<th>No of responses</th>
<th>Percentage of all responses</th>
<th>Percentage of people reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slowed/ stabilised stress</td>
<td>1045</td>
<td>25%</td>
<td>39%</td>
</tr>
<tr>
<td>Happier/ brighter/more aware/more active</td>
<td>550</td>
<td>13%</td>
<td>21%</td>
</tr>
<tr>
<td>Improved/ helped memory loss</td>
<td>491</td>
<td>12%</td>
<td>18%</td>
</tr>
<tr>
<td>Calmer/ less aggressive</td>
<td>324</td>
<td>8%</td>
<td>12%</td>
</tr>
<tr>
<td>Improved/ helped memory loss</td>
<td>238</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>More independent/ taking care of personal needs</td>
<td>219</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Showed an interest in things</td>
<td>167</td>
<td>4%</td>
<td>7%</td>
</tr>
<tr>
<td>Improved conversation/ speech</td>
<td>183</td>
<td>4%</td>
<td>7%</td>
</tr>
<tr>
<td>Better quality of life</td>
<td>137</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Restored/ more confident</td>
<td>105</td>
<td>2%</td>
<td>4%</td>
</tr>
</tbody>
</table>
modest but meaningful improvement, enabling people to function above their baseline level of impairment for six to 12 months with additional benefits for confidence and mood (Table 1). After this time period there is provisional evidence of ongoing benefit from open label trials. The debate is entirely about cost.

NICE use a complex formula to estimate the cost of gaining Quality Adjusted Life Years (QALYs). This model is based on a single cross-sectional US study using an instrument not validated for assessing people with AD and previously considered to be unreliable by NICE. From the appraisal report, 39 per cent of people overall and 34 per cent of people with mild AD respond to cholinesterase inhibitors. The method of evaluating cost-effectiveness recommended by all stakeholders, including the Department of Health, was a responder analysis. This assumes that only individuals experiencing improvement continue to receive therapy, mirroring usual prescribing practice. The magnitude of clinical benefit was more than doubled in responders compared to the overall group, with a cost per QALY of £21k–£30k, within NICE’s usual cost-effectiveness threshold of £30k. NICE’s other assessment models may also demonstrate cost-effectiveness if full-time care is correctly costed and carer benefit taken into consideration. Cholinesterase inhibitors give tangible clinical benefits at a cost of only £2.50 a day. To withhold treatment on the basis of unsound models and cherry picking unfavourable cost-effectiveness data seems blatantly unreasonable but, above all, makes no clinical sense. People with AD will be denied treatment at the stage of illness where they value it most. In addition, doctors will find it difficult to maintain a good therapeutic relationship in these circumstances and will have to cope with increased monitoring demands because of the requirement to evaluate people regularly until they decline.

NICE guidance regarding memantine is equally
disappointing. NICE did not thoroughly consider the cost-effectiveness of memantine because they did not believe it to be clinically effective. This is in direct contradiction to systematic evaluations of the evidence by Cochrane as well as the Food and Drug Administration (FDA) and European Agency for the Evaluation of Medicinal Products (EMEA). NICE’s analysis of patient level data indicated that 55 per cent of patients are defined as responders, and the clinical response was more substantial in people with behavioural symptoms. This is particularly important as memantine is currently the only current treatment licensed for people with severe Alzheimer’s disease and the current guidance is likely to encourage more widespread prescription of atypical neuroleptics, which are of similar cost to memantine, have similar efficacy with respect to behavioural symptoms and are associated with considerable risk of serious adverse outcomes including stroke and death.

**The Dementia Guideline**

The NICE Dementia Clinical Guideline, published in parallel, does at least provide a framework for assessing and treating people with Alzheimer’s disease. The inflexible reliance on MMSE described in the guidance is by NICE’s own admission discriminatory, meaning people with a learning disability, a first language other than English, high or low levels of education will not have equitable access to treatment. It is notable that the NICE Dementia Clinical Guideline Development Group previously urged NICE to accept their model was flawed and to recommend that both the cholinesterase inhibitors and memantine be available on the NHS, consistent with other guidelines produced by professional bodies such as BAP.

Among the important recommendations for health and social care professionals, service managers and commissioners, the guideline
Key points

- NICE’s figures show only a five per cent difference in proportion of responders in the mild group compared to the overall group.
- A basic responder analysis show that the cholinesterase inhibitors are cost effective across the full licensed range of mild-moderate Alzheimer’s disease.
- The NICE Clinical Guideline recommend that all staff working with older people should receive training in dementia and the Memory Assessment Service should be the single point of referral for people with suspected dementia.

References


Discussion

The NICE Clinical Guideline recommends that the memory assessment service should be the single point of referral for people with suspected dementia. There was concern the drugs guidance would put these services at risk, due to decreased referrals, so the emphasis on their importance is welcomed. The guideline also contains helpful recommendations around the treatment of non-cognitive symptoms, present in up to 75 per cent of people with dementia. It is particularly strong in identifying the approaches health and social care staff should take to manage and ameliorate these symptoms. These recommendations must be supported by provision of appropriate training to ensure multidisciplinary teams have the skills to enable their implementation. Leading on from this, the guideline recommends further research into the effect of staff training in person-centred dementia care on behaviour that challenges, as well as the investigation of cholinesterase inhibitor drugs and memantine as a treatment for non-cognitive symptoms.

Conclusion

While there are a number of positive recommendations within the NICE Clinical Guidelines that will enable improvements in the care of people with dementia, it should not be a choice between good care and appropriate pharmacological treatment. Drug therapy is an important element of the overall treatment and care of people with dementia. It is clear from the clinical evidence people with mild Alzheimer’s disease benefit from cholinesterase inhibitors and that memantine is a preferable treatment for people with behavioural problems in the context of severe dementia than atypical neuroleptics. As highlighted by the Royal College of Psychiatrists, the duty of care for doctors is to provide the best clinical treatments[2]. Guidance, based on an inaccurate, pseudo-evidence-based evaluation, contradicting what is clearly best practice can only hinder the quality of clinical care.

Conflict of interest: The Alzheimer’s Society is the leading care and research charity for people with Alzheimer’s disease, other forms of dementia and their carers. Professor Clive Ballard and Samantha Sharp are employed by the charity. As co-director of King’s College CARD, Professor Ballard has received consultancy fees, honoraria for presentations and research funding from some companies.

*NICE was invited to respond to a preview of this article but were unable to compose a response in time for this issue. Their response will be sent to peer review for publication when submitted.