NICE 2011 recommendations on the management of Alzheimer's disease by acetylcholinesterase inhibitors & memantine

CHARLES SCERRI

The National Institute of Clinical Excellence (NICE) has lately overturned its decision to restrict the use of acetycholinesterase inhibitors and memantine in patients diagnosed with Alzheimer's disease (AD). It is estimated that such a policy U-turn will offer access to a significant number of individuals who were previously denied these medications. This short article will focus on the latest developments and recommendations by NICE on the use of these pharmacological agents in the managment of AD.

AD is the most common form of dementia accounting for about 50-70% of the cases. It is the most common neurodegenerative disorder in the elderly with a prevalence rate that increases exponentially from 2-3% in the general population at the age of 65 years to that exceeding 40% after the age of 85 years. Given the trend towards an increase in the elderly population worldwide, the prevalence of AD is expected to double in the next forty years. In Malta, it is estimated that currently the number of individuals with dementia almost reaches 4,500. This figure is expected to almost double, reaching 2% of the Maltese population by the year 2050[1]. In addition to the huge costs involved in the medical management of AD, its psychosocial burden on caregivers and society in general is enormous.

Pathologically, AD is characterised by the presence of amyloid plaques and neurofibrillary tangles in the brain coupled with significant loss of cholinergic tracts in areas associated with learning and memory. The disease is a multistage process initially characterised by a decline in short-term memory, faulty judgment and personality changes. At later stages, memory decline worsens and activities of daily living and communication skills become gradually impaired. In the final stages, the patient becomes mute, withdrawn, incontinent and unable to walk with the consequence of becoming bedridden and prone to illness and infection.

Acetylcholinesterase inhibitors (AChEIs) were the first pharmacological agents for the management of AD approved by the relevant health authorities. Locally, three AChEIs are clinically available: donepezil, rivastigmine and galantamine. Their major therapeutic effect is reported to be their ability to maintain cognitive function compared to placebo over a three year period or less[2,3]. These drugs are particularly useful in mild to moderate stages of AD. A later addition to the list of drugs recommended for use in AD patients was memantine, a compound that appears to block pathologic neural toxicity associated with prolonged glutamate release[4]. In randomised clinical trials, this drug demonstrated the ability to delay cognitive decline and is recommended for the use in moderate to severe AD.

In 2006, NICE advised that donepezil, rivastigmine and galantamine should only be used to treat moderate stage AD and that memantine should be reserved for clinical studies involving individuals with moderately severe to severe AD. This meant that in the UK, these drugs could not be used to treat the disease in its mild form via the NHS. As expected, these restrictions were met with strong resistance and various organisations across the UK voiced their concerns about this approach, highlighting the need for NICE to reassess its views. These included Alzheimer's Society, Age Concern, Counsel and Care, Dementia Care Trust, the Royal College of Nursing, the Royal College of Psychiatrists and the British Geriatrics Society.

Even Alzheimer's Europe called for NICE to revise its recommendations and allow patients at all stages of the disease to have access to the various drug treatments.

The discussion on the use of such drugs continued and after considering evidence from a number of recent scientific publications on the cost-effectiveness of these agents as well as feedback from drug manufacturers, professional and patients groups and other consultees, NICE reversed its

continued on page15

continued from page13

NICE 2011 recommendations on the management of Alzheimer's disease by acetylcholinesterase inhibitors & memantine

decision through the publication of a technology appraisal report in March 2011[5]. Recommendations set out in this guidance report include:

- The three acetylcholinesterase inhibitors (AChEIs) donepezil, galantamine and rivastigmine are recommended as options for managing mild to moderate AD;
- Memantine is recommended as an option for managing AD for people with moderate or severe AD;
- Treatment should be recommended only by specialists and when considered to have a worthwhile effect on the cognitive, functional and behavioural symptoms;
- Patients should be reviewed regularly and treatment adjusted depending on the symptoms as reviewed by a specilised team. The carer's view should also be consulted at follow-up;
- Although treatment with AChEIs should be started with the drug with the lower acquisition cost, an alternative AChEI could be prescribed if found to be appropriate based on adverse event profile, patient compliance, medical comorbidity and dosing regimens;
- Communication difficulties and sensory or learning disabilities should be taken into consideration when assessment scales are used to determine the severity of AD;
- Healthcare professionals should not rely solely on cognition scores in circumstances in which it would be inappropriate to do so, such as in sensory impairments, communication difficulties or level of education.

In conclusion, these latest recommendations by NICE are in line with accumulating evidence showing that these drugs enhance activities of daily living, reduce behavioural disturbances, slow cognitive impairment and decrease caregiver stress thus delaying institutionilisation. Unfortunately in Malta, AD is not among the list of chronic disorders on the Fifth Schedule of the Social Security Act and therefore these drugs are only available in the community as an out-of-pocket expense. It is hoped that the local health authorties follow the example of the majority of countries in the European Union and reimburse AD drugs to all those individuals suffering from this debiliating disease.

References

1 Abela S, Mamo J, Aquilina C, Scerri C. Estimated prevalence of dementia in the Maltese Islands. *Malta Medical Journal* 2007; 19(2):23-6.

2 Mohs RC, Doody RS, Morris JC et al. "312" Study Group. A 1-year, placebo-controlled preservation of function survival study of donepezil in AD patients [published correction appears in Neurology 2001: 57: 1942]. *Neurology* 2001; 57:481-8.

3 Raskind MA, Peskind ER, Truyen L, Kershaw P, Damaraju CV. The cognitive benefits of galantamine are sustained for at least 36 months: a long-term extension trial. *Archives of Neurology* 2004; 61:252-6.

4 Danysz W, Parsons CG, Mobius HJ. Neuroprotective and symtomalogical action of memantine relevant for Alzheimer's disease – a unified glutamatergic hypothesis on the mechanism of action. *Neurotoxicity Research* 2000; 2:85-98.

5 National Institute of Clinical Excellence. Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disese: NICE technology appraisal guidance 217. Available from: www.nice.org.uk/nicemedia/live/13419/53619/53619.pdf