Management of behavioural and psychological symptoms in dementia: NICE guidelines and evidence-based decision-making

Janet Sultana BPharm(Hons)

Department of Neuroscience, Institute of Psychiatry, United Kingdom
Emial: janet.j.sultana@kcl.ac.uk

Educational aims

- To briefly review the different dementia syndromes and some associated psychiatric symptoms
- To summarise NICE guidelines on the management of challenging psychiatric behaviour in dementia and the evidence base behind the guidance

Key words
Dementia, antipsychotics, behavioural and psychological symptoms in dementia, NICE guidance, evidence

Dementia is an age-related progressive syndrome that often presents with psychiatric symptoms such as hallucinations, aggression and agitation. The management of such symptoms in dementia is particularly important when it puts the patients themselves and their carers at risk. The NICE guidance for pharmacologically managing psychiatric symptoms in dementia and the evidence base is summarised with particular focus on antipsychotic drug use. Alternative approaches to psychiatric symptoms in dementia are briefly discussed as a substitute for antipsychotic use.

Introduction

The dementia syndromes associated with neurodegeneration present with progressive cognitive decline that may involve amnesia, aphasia, apraxia, agnosia and often psychological and psychiatric symptoms[1]. 7 million people suffer from dementia in Europe[2]. In Malta, the prevalence rate for 2015 is projected to be 1.25%, affecting a total of 4892 people from different age groups[3].

Identifying the aetiology of dementia and hence making a specific dementia diagnosis (Alzheimer's disease, vascular dementia etc.) is critical, because this influences the management of dementia and the associated psychiatric symptoms. It is challenging to make a definitive diagnosis because there is no single and authoritative diagnostic test to identify most dementia syndromes.[4] In addition, it has been disputed whether the underlying pathology can be reliably elicited in living patients after a multi-centre post-mortem study in the UK found a mismatch between the diagnosis of the dementia type and the actual neuropathology present in the brain.[5]

Secondary causes of dementia include traumatic brain lesions, frontotemporal dementia, subcortical dementia and focal dementia. Frontotemporal dementia tends to present with marked behavioural rather than memory problems.Examples of subcortical dementia and focal dementia are Parkinson's disease dementia and progressive aphasia respectively.

A study by the Medical Research Council UK investigated the prevalence of a spectrum of psychological and psychiatric symptoms in patients with dementia.[9] An example of the overlap between dementia and psychiatric or psychological symptoms such as irritability, hallucinations, agitation and anxiety are found in Table 1.

The presence of these symptoms was much more marked in patients with dementia rather than patients without dementia.

Irritability, hallucinations, agitation and anxiety can give rise to difficult behaviour in patients with dementia and this must be managed accordingly because the welfare of the patients themselves and also their carers and co-residents in nursing homes could be affected.

The National Institute for Clinical Excellence (NICE) has issued guidance for the management of non-cognitive symptoms and challenging behaviour in dementia. The guidance has defined these symptoms as illustrated in Table 3.

Table 1: Dementia type in order of decreasing prevalence, starting with the most common[1,2,6,7,8]

Dementia type	Prevalence	Aetiology
Alzheimer's disease	60-70%	Amyloid deposition and hyper-phosphorylated tau which lead to neuronal death; clinical progression tends to be gradual
Vascular dementia	32%	Neuronal death caused by ischaemic insults in the CNS; clinical progression tends to be incremental
Mixed dementia	10-40%	A combination of Alzheimer's disease with cognitive decline related to vascular pathology
Lewy body dementia	15%	Neuronal death caused by α-synuclein accumulations in neurons. The clinical presentation often involves Parkinsonian symptoms
Other causes	5%	Secondary causes of dementia, frontotemporal dementia, subcortical dementia and focal dementia

Table 2: The prevalence of selected psychiatric and psychological symptoms in patients with and without dementia, expressed as the percentage prevalence per population[9]

	% Population prevalence		
Symptoms Assessment criteria	**Participants without dementia** (N=2050)	**Participants with dementia** (N=587)	**P value**
Irritability Participant has been more angry or irritable lately, interviewer observes severe hostility or angry response	12.8	28.8	<0.001
Depression Assessed using Cambridge Mental Disorders of the Elderly Examination depression algorithm	8.6	20.5	<0.001
Hallucinations Hearing voices; visions; smells or gustatory hallucination	3.7	15.1	<0.001
Agitation Inappropriate verbal, vocal or motor activity; observed restlessness during interview	3.6	9.0	<0.001
Anxiety Suffering from fear or panic attacks, often trembles or interviewer observed severe bodily features of anxiety	6.3	8.9	0.068

Table 3: Definitions of non-cognitive symptoms of dementia and challenging behaviour as used in the NICE 2011 guidelines[10]

Non-cognitive symptoms of dementia	Challenging behaviour
Hallucinations	Aggressive behaviour
Delusions	Agitation
Anxiety	Wondering, hoarding
Marked agitation	Shouting
Aggressive behaviour	Sexual disinhibition

Antipsychotic drugs

Antipsychotic drugs should not be used for non-cognitive symptoms that are *mild to moderate* in Lewy body dementia due to the risk of severe adverse effects. They should also not be used in *mild to moderate* behavioural symptoms in Alzheimer's disease and dementia of vascular or mixed origin due to the risk of cerebrovascular-associated morbidity and mortality. Antipsychotic drugs can however be considered in dementia patient who develop non-cognitive symptoms such as psychosis and agitation that are severe and distressing, provided that health care workers discuss the risks and benefits of antipsychotic treatment.

Practice points 2

Considerations for prescribing antipsychotics in dementia[10]

- The increased risk of stroke has to be justified by benefits of antipsychotics.
- Cognition has to be monitored and patients switched to other drugs if necessary.
- Co-morbidities such as depression should be considered in the decision to start antipsychotics.
- Antipsychotic dose should be started at low levels and titrated up.
- The duration of treatment is limited to the minimum necessary and should be reviewed every three months.
- In dementia with Lewy bodies, vigilantly monitor for neuroleptic sensitivity reactions which can lead to cognitive and functional impairment and can even be fatal.
- As an alternative to antipsychotics, the use of AChEIs may be appropriate in dementia with Lewy bodies and all stages of Alzheimer's disease but not vascular dementia.

Acetylcholinesterase inhibitors

An acetylcholinesterase inhibitor (AChEI) can be considered in patients with dementia having Lewy bodies that have challenging non-cognitive behaviour as defined in Table 2. It may also be appropriate for Alzheimer's disease of all severities if non-pharmacological management is inappropriate or ineffective, or if antipsychotic treatment has been unsuccessful or cannot be used. AChEIs should not be used in vascular dementia for psychiatric symptoms unless as part of clinical studies.

Key points

- Psychiatric symptoms such as aggression and agitation are common in dementia.
- Commonly used antipsychotic agents present more risk than benefit in neuropsychiatric symptoms of dementia and are not very effective.
- Acetylcholinesterase inhibitors can be helpful in managing difficult behaviour in dementia but are not a substitute for ensuring that elderly patients, especially in institutionalised care homes, are treated in a holistic manner. This includes adequate pain management.
- The UK Alzheimer's society put it simply: "Professionals are often not aware that symptoms such as restlessness and shouting out can be the expression of unmet needs".[29]

Evidence behind the guidance: Pharmaceutical care issues with antipsychotics

The main pharmaceutical care issues with antipsychotic agents in dementia lie with their safety and efficacy. The main risks are the development of neuroleptic sensitivity syndrome, risk of stroke and risk of death. Neuroleptic sensitivity syndrome is characterised by the development of adverse effects such as the precipitation or aggravation of extrapyramidal symptoms and significant physical deterioration, and possibly death, after antipsychotic drug administration.[11] Patients with Lewy body dementia are particularly sensitive to the negative effects of antipsychotics.[12] It had been suggested that this is linked to the Parkinsonian component of Lewy body dementia almost a decade ago.[13] This is not surprising, as it is known that antipsychotics that antagonise the dopaminergic system can worsen Parkinsonian symptoms that are a result of central dopaminergic deficit.[14] The gravity of neuroleptic sensitivity in Lewy body dementia becomes apparent when considering that it can result in or contribute significantly to death. One study that followed hospitalised patients with dementia found that the time from antipsychotic administration to death varied from 9 days to 12 months at most.[6] This study provided clinicians with two important warnings: the severity of neuroleptic sensitivity symptoms may not be related to the *dose* of the antipsychotic or *whether it is a typical or atypical agent*. The consequences of antipsychotic prescribing in Lewy body dementia could therefore be particularly serious, especially considering evidence from a randomised double-blind placebo controlled trial showing that not only is quetiapine not effective in treating agitation in dementia but also that quetiapine can accelerate cognitive decline.[15] The Cochrane Dementia and Cognitive Improvement Group have shown that risperidone and olanzepine *modestly* reduce aggression and risperidone can have a *modest* beneficial effect on psychosis but both are linked to significantly increased risk of extrapyramidal symptoms and cerebrovascular adverse effects.[15] Another safety concern with the use of typical and atypical antipsychotics is the increased risk of stroke which can be increased between three- and five-fold.[16] The sum of this evidence suggests that commonly used antipsychotics are only marginally effective in selected psychiatric symptoms such as aggression and agitation but significantly increase the risk of patient harm and death.[17]

Alternative management of psychiatric symptoms in dementia

Acetylcholinesterase inhibitors were found to have a beneficial effect in irritability, anxiety and disinhibition.[17] Donepezil and galantamine, for example, were found to be of potential benefit in severe Alzheimer's disease.[18] This suggests that cholinergic deficits play a role in neuropsychiatric symptoms. Although memantine (an NMDA receptor antagonist) is not clearly mentioned in the NICE guidelines for management of non-cognitive symptoms in Alzheimer's disease[19], it was also found to be beneficial in agitation and aggression in Alzheimer's disease.[20] Despite this evidence for pharmacotherapy, it is important not to underestimate the role of non-pharmacological interventions. Agitation and aggression may be the result of pain, loneliness, boredom and depression which can be addressed through socialising, reminiscence therapy, aromatherapy, music therapy, art therapy and multi-sensory approaches to name a few.[21] Interventions involving support and training of nursing home staff to change their clinical approach and deliver a more 'person-centered' approach resulted in the reduced prescription of antipsychotics without a worsening of neuropsychiatric symptoms.[22,23] Another important perspective on management of difficult behaviour in dementia comes from pain studies. Elderly persons in institutionalised care homes may experience a significantly distressing amount of pain that goes unnoticed and untreated. One study found that only 15% of elderly persons who were in pain were given analgesics while another smaller study showed that 'difficult' elderly patients on antipsychotics were successfully managed with regular paracetamol dosing, and their behaviour did not regress on stopping the antipsychotics.[24]

Conclusion

More than 9 out of every 10 dementia patients will experience at least one symptom of behavioural and psychological symptoms such as aggression and irritability, as well as relatively more subtle but common depressive symptoms.[25] It seems clear that such symptoms are more common in patients with dementia than patients without dementia[4], however it has been suggested that for a long time this aspect of dementia had not been given the attention it merits.[26] Both pharmacological and non-pharmacological management of dementia have been the subject of many trials[27] which have in turn been incorporated into clinical guidance. There is much to be done in the way of optimising the benefits of treatments and reducing the risks of pharmacological and non-pharmacological management. Nevertheless, the evidence base for the management of behavioural and psychological symptoms in dementia is growing, allowing clinicians and researchers to continue improving global outcomes in dementia.

References

1. Burns B. Dementia (Clinical Review). BMJ 2009; 338:b75.
2. World Health Organisation. Dementia: A public health priority. [Internet]. Geneva: World Health Organisation; 2012 [cited 11 May 2012]. World Health Organisation Switzerland: Geneva. Available from: http://whqlibdoc.who.int/publications/2012/9789241564458_eng.pdf
3. Abela S, Mamo J, Aquilina C, Scerri C. Estimated prevalence of dementia in the Maltese Islands. Malta Med J. 2007;(2):23-26.
4. van der Flier WM, Scheltens P. Epidemiology and risk factors of dementia. J Neurol Neurosurg Psychiatry. 2005;76:v2-v7.

5. Neuropathology Group (Medical Research Council Cognitive Function and Aging Study). Pathological correlates of late-onset dementia in a multicentre, community-based population in England and Wales. Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS). Lancet. 2001;357(9251):169-75.
6. Ballard C, Grace J, McKeith I, Holme C. Neuroleptic sensitivity in dementia with Lewy bodies and Alzheimer's disease. Lancet. 1998; 351(9108):1032–3.
7. Mulugeta E, Molina-Holgado F, Elliott MS, Hortobagyi T, Perry R, Kalaria RN, Ballard CG, Francis PT. Inflammatory mediators in the frontal lobe of patients with mixed and vascular dementia. Dement Geriatr Cogn Disord. 2008;25(3):278-86.
8. Aarsland D, Sardahaee FS, Anderssen S, Ballard C; Alzheimer's Society Systematic Review group. Is physical activity a potential preventive factor for vascular dementia? A systematic review**.** Aging Ment Health. 2010 May;14(4):386-95.
9. Savva GM, Zaccai J, Matthews FE, Davidson JE, McKeith I, Brayne C. Prevalence, correlates and course of behavioural and psychological symptoms of dementia in the population. BJP 2009, 194:212-219.
10. National Institute for Clinical Excellence [Internet]. NICE pathways: Dementia intervention. London: National Institute for Health and Clinical Excellence [updated 2011; cited 17 March 2012]. Available from http://pathways.nice.org.uk/pathways/dementia/dementia-diagnosis-and-assessment#content=view-node%3Anodes-pharmacological-interventions-for-non-cognitive-symptoms&path=view%3A/pathways/dementia/dementia-interventions.xml
11. McKeith I, Fairbairn A, Perry R, Thompson P, Perry E. Neuroleptic sensitivity in patients with senile dementia of Lewy body type. BMJ 1992; 305:673-8.
12. Karim S, Byrne EJ. Treatment of psychosis in elderly people. APT. 2005;11: 286-296.
13. Byrne EJ, Burns A, and Waite J. Neuroleptic sensitivity in dementia with cortical Lewy bodies. BMJ. 1992; 305(6862): 1158 9.
14. Marras C, Kopp A, Qiu F, Lang AE, Sykora K, Shulman KI, Rochon PA. Antipsychotic use in older adults with Parkinson's disease. Mov Disord. 2007 Feb 15;22(3):319-23.
15. Ballard C, Margallo-Lana M, Juszczak E, Douglas S, Swann A, Thomas A, O'Brien J, Everratt A, Sadler S, Maddison C, Lee L, Bannister C, Elvish R, Jacoby R. Quetiapine and rivastigmine and cognitive decline in Alzheimer's disease: randomised double blind placebo controlled trial. BMJ 2005;330:874.
16. Douglas J, Smeeth L. Exposure to antipsychotics and risk of stroke: self controlled case series study. BMJ 2008;337:a1227.
17. Ballard CG, Waite J, Birks J. Atypical antipsychotics for aggression and psychosis in Alzheimer's disease. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. No.: CD003476. DOI: 10.1002/14651858.CD003476.pub2.
18. Schwab W, Messinger-Rapport B, Franco K. Psychiatric symptoms of dementia: Treatable, but no silver bullet. CCJM. 2009; 76(3):167-174.
19. Masterman DL. Role of cholinesterase inhibitors in managing behavioural problems in Alzheimer's disease. J Clin Psychiatry 2004;6(3):126 131.
20. Wilcock GK, Ballard CG, Cooper JA, Loft H. Memantine for agitation/aggression and psychosis in moderately severe to severe Alzheimer's disease: a pooled analysis of 3 studies. J Clin Psychiatry. 2008;69(3):341-8.
21. Salzman C, Jeste D, Meyer RE, Cohen-Mansfield J, Cummings J, Grossberg G, Jarvik L, Kraemer H, Lebowitz B, Maslow K, Pollock B, Raskind M, Schultz S, Wang P, Zito JM, Zubenko GS. Elderly Patients with Dementia-Related Symptoms of Severe Agitation and Aggression: Consensus Statement on Treatment Options, Clinical Trials Methodology, and Policy. J Clin Psychiatry.. 2008; 69(6): 889-898.
22. Fossey J, Ballard C, Juszczak E, James I, Alder N, Jacoby A, Howard R. Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial. BMJ 2006;332:756.
23. Douglas S, James, Ballard C. Non-pharmacological interventions in dementia. APT. 2004;10: 171-177.
24. Huffman JC, Kunik ME. Assessment and understanding of pain in patients with dementia. Gerontologist 2000; 40(5):574-581.
25. Steinberg M, Shao H, Zandi P, Lyketsos CG, Welsh-Bohmer KA, Norton MC, Breitner JCS, Steffens DC, Tschanz JT, Cache County Investigators.. Int J Geriatr Psychiatry. 2008; 23: 170–177.
26. Lawlor B. Managing behavioural and psychological symptoms in dementia. The Brit J Psychiat. 2002;181: 463-465.
27. Henry G, Williamson D, Tampi RR. Efficacy and tolerability of antidepressants in the treatment of behavioral and psychological symptoms of dementia, a literature review of evidence. Am J Alzheimers Dis Other Demen. 2011;26(3):169-83.
28. National Institute for Clinical Excellence. NICE technology appraisal guidance 217 Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of NICE technology appraisal guidance 111). [Internet]. London: National Institute for Health and Clinical Excellence; 2011 [cited 11 May 2012]. Available from http://www.nice.org.uk/nicemedia/live/13419/53619/53619.pdf
29. Alzheimer's Society UK [Internet].London: Alzheimer's Society [updated 2012; cited 17 March 2012]. Available from http://alzheimers.org.uk