

Introduction

Clinical Effectiveness of Atypical Antipsychotics in Dementia

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In the developed world, life expectancies are higher than ever before. As a result, an increasing number of people are at risk of neurodegenerative disease in old age. While the predominantly motor disturbance of Parkinson's disease may be complicated by subcortical dementia in some patients, Alzheimer's disease and dementia with Lewy bodies (DLB) are the two most common forms of cortical dementia.

The hallmark cognitive decline of dementia is accompanied by behavioral and psychological signs and symptoms of dementia, such as agitation, aggression, paranoia, other psychotic symptoms, sleep disturbance, and disturbed mood. This heterogeneous group of signs and symptoms has a devastating impact on the day-to-day lives of patients and their caregivers, and is often the trigger for placement of patients in nursing home care. Addressing these distressing signs and symptoms is a key goal of treatment in patients with dementia, and a range of psychosocial and pharmacologic interventions exist. Recently, the clinical effectiveness of atypical antipsychotics in dementia was considered by 4 experts at a symposium held at the 11th International Psychogeriatric Association congress (Chicago, Ill., Aug. 17–22, 2003). The following series of articles reports on this highly successful, CME-accredited meeting.

Professor Brian A. Lawlor from the University of Dublin, Ireland, underlines the nature and clinical significance of the expected behavioral and psychological signs and symptoms. These can lead to significant impairment of quality of life for patients and their caregivers. Indeed, the development of these signs and symptoms has a greater impact on caregiver burden and need for institutionalized care than cognitive deficits. Consequently, such behavioral features are now recognized as an important therapeutic target in dementia, and the identification of particular problematic symptoms and their context is valuable. Approaches to management, including behavioral therapies and caregiver support, are reviewed. The need for evidence-based, well-tolerated pharmacotherapies in this particularly vulnerable patient population is also highlighted. Atypical antipsychotics play a key role in the treatment of such behavioral features, especially agitation and psychosis, although the side effect profile of individual agents is likely to have an impact on treatment decisions.

In the second article, Professor Pierre N. Tariot and coauthors from the University of Rochester, N.Y., reinforce the view that the main goal of pharmacotherapy in patients with dementia is to relieve distressing agitation and/or psychosis. Clinical experience with the established atypical antipsychotics risperidone, olanzapine, and quetiapine, as well as preliminary findings with aripiprazole, is described. Although these agents show similar efficacy, differing tolerability profiles have been reported in Alzheimer's disease populations. Head-to-head com-

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parisons of atypicals are lacking thus far, but the results of a comparative effectiveness study funded by the National Institute of Mental Health are due to be reported in 2004.

Dr. Andrius Baskys, a geriatric psychiatrist and Assistant Professor at the University of California, considers whether DLB provides a “litmus test” for developing extrapyramidal symptoms (EPS). Characteristics of this rapidly progressive, dementing disorder include fluctuating cognition, hallucinations and delusions, and mild parkinsonism, while other symptoms include frequent falls, agitation at night, and depression. Extensive loss of dopaminergic and acetylcholinergic neurons contributes to the pattern of symptoms in DLB. However, these neurotransmitter deficits make patients especially vulnerable to the antidopaminergic and anticholinergic action of various antipsychotic drugs. Patients with DLB (and Parkinson’s disease) are particularly susceptible to developing EPS and complications of neuroleptic sensitivity, which makes the treatment of psychotic symptoms a complex issue. This review examines the efficacy, dopamine- and acetylcholine-receptor affinities, and EPS risk of atypical antipsychotics in DLB and Parkinson’s disease–related psychosis. Quetiapine in particular appears to be an attractive candidate for the treatment of these patient types, not least because of its low propensity for EPS.

Achieving improvements in quality of life is a key consideration in the treatment of behavioral and psychological signs and symptoms associated with dementia. In the final article, Professor Clive Ballard and Dr. Marisa Margallo-Lana of the University of Newcastle upon Tyne, United Kingdom, explore the relationship between treatment of these symptoms and signs and “real-world” improvements in daily life, particularly among patients living in residential and nursing home care since they are most likely to be affected. Although improvements in symptoms are apparent in patients with dementia, the long-term effects of atypical antipsychotics (and any associated side effects) on quality of life remain to be demonstrated. Professor Ballard and Dr. Margallo-Lana present some preliminary evidence to suggest that quality-of-life benefits may be gained in patients who require ongoing pharmacotherapy for such behavioral features by changing the antipsychotic used to one with a more favorable tolerability profile. However, the urgent need for systematic assessment of quality-of-life variables in clinical studies is emphasized. Measurement of these outcomes would enable psychiatrists to make informed decisions regarding treatment and rational choices between available antipsychotic agents.

The faculty would like to thank the clinicians and patients who have participated in the research presented here, and all those who attended the meeting for the stimulating debate that followed.

Since this symposium, an update to safety information for olanzapine has been issued to doctors in the United States, Canada, and Europe describing results from clinical studies in elderly patients with dementia.^{1–3} These results showed that a higher proportion of patients experienced strokes or related events following treatment with olanzapine, compared with placebo (1.3% vs. 0.4%, respectively). In addition, further to similar safety updates on risperidone in Canada (2002) and the United States (2003) [please see Tariot et al.⁴ in this supplement], a warning has recently been issued in the United Kingdom highlighting the increased risk of stroke associated with risperidone treatment in elderly patients with dementia.⁵

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