THE AMERICAN JOURNAL of MEDICINE®

Pharmacological Management of Psychosis in Elderly Patients with Parkinsonism

Mehrul Hasnain, MD,[a] W. Victor R. Vieweg, MD,[b,d,f,h] Mark S. Baron, MD,[c,g] Mary Beatty-Brooks, MA,[e] Antony Fernandez, MD,[b,f] Anand K. Pandurangi, MD[f]

[a]Department of Psychiatry, Western Regional Integrated Health Authority, Sir Thomas Roddick Hospital, Stephenville, Newfoundland, Canada; [b]Department of Psychiatry, [c]Department of Neurology, [d]Department of Medicine Services, and [e]Department of Medical Media, Hunter Holmes McGuire Veterans Affairs Medical Center, Richmond, Va; and [f]Department of Psychiatry, [g]Department of Neurology, and [h]Department of Internal Medicine, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond.

ABSTRACT

Parkinsonism is a characteristic feature of Parkinson's disease and dementia with Lewy bodies and is commonly seen in Alzheimer's disease. Psychosis commonly appears during the course of these illnesses. Treatment of parkinsonism with antiparkinsonian medications constitutes an additional risk factor for the appearance or worsening of psychosis. Conversely, treatment of psychosis with antipsychotic drugs in patients with parkinsonism might worsen the underlying movement disorder, especially in the elderly. In this article, we review parkinsonian conditions in the elderly and offer guidelines to assess and manage comorbid psychosis. We focus on the pharmacologic management of psychosis with atypical antipsychotic medications and briefly review the role of acetylcholinesterase inhibitors.

 • *The American Journal of Medicine (2009) 122, 614-622*

KEYWORDS: Antipsychotic drugs; Basal ganglia; Dementia; Lewy bodies; Parkinson's disease; Psychosis

Parkinsonism refers to motor features characteristic of Parkinson's disease, including bradykinesia, rigidity, resting tremor, and postural instability. These features occur commonly in the elderly. When defined as the presence of 2 or more of the parkinsonian features, the prevalence of parkinsonism in community-dwelling individuals is approximately 14.9% for those aged 65 to 74 years, 29.5% for those aged 75 to 84 years, and 52.4% for those aged more than 85 years.[1] Historically, parkinsonism has been viewed as a benign concomitant of aging, and its under-recognition has been reported in acute and long-term care settings.[2,3]

Psychosis commonly appears during the course of various parkinsonian conditions in the elderly. Up to 40% of patients with Parkinson's disease develop psychosis.[4] Visual hallucinations appear most commonly in individuals with dementia with Lewy bodies.[5] Although neurologists or psychiatrists may be periodically involved in the care of patients with parkinsonism and psychosis, the internist should have mastery of these conditions because of the primary role in the care of the growing geriatric population. In this article, we briefly review common conditions associated with parkinsonism that internists and geriatricians will encounter in practice; discuss the common pathophysiologic and interconnecting features of parkinsonism, psychosis, antiparkinsonian medications, and antipsychotic drugs; and provide guidelines for pharmacologic management of psychosis comorbid with parkinsonism.

COMMON PARKINSONIAN CONDITIONS IN THE ELDERLY: AN OVERVIEW

Parkinson's Disease

In addition to the characteristic parkinsonian motor features noted earlier, Parkinson's disease also has nonmotor features, including impaired olfaction, sleep disturbances, fatigue, apathy, autonomic dysfunction, depression, anxiety, psychosis, and cognitive abnormalities.[6] Parkinson's disease affects approximately 0.3% of the population by age 65

Funding: None.

Conflict of Interest: Dr Pandurangi is on the speaker's bureau of Astra-Zeneca, Bristol Myers Squibb, Janssen, and Pfizer Pharmaceuticals. The other authors do not have any potential conflict of interest to disclose.

Authorship: All authors had access to the data and played a role in writing this manuscript.

Requests for reprints should be addressed to Mehrul Hasnain, MD, Sir Thomas Roddick Hospital, 142 Minnesota Drive, Stephenville, Newfoundland A2N 2V6, Canada.

E-mail address: mehrul_hasnain@yahoo.com

0002-9343/$ -see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.amjmed.2009.01.025

years with the prevalence increasing to more than 4% in those older than 85 years.[7] Parkinson's disease induces substantial disability and reduced life expectancy.[8] Psychosis, particularly when accompanied by visual hallucinations, is common in patients with Parkinson's disease and is associated with reduced quality of life and early institutionalization because of its impact on both patient and caregiver.[9,10] Dementia occurs late in Parkinson's disease (Parkinson's disease with dementia) but is predictable if the patient lives long enough.[11]

Dementia with Lewy Bodies

Dementia with Lewy bodies accounts for up to 30.5% of demented patients.[12] Progressive dementia, fluctuating cognition, recurrent visual hallucinations, and parkinsonism constitute its core clinical features. Features suggestive of dementia with Lewy bodies include rapid eye movement sleep behavior disorder, severe neuroleptic sensitivity, and low dopamine reuptake in basal ganglia on functional neuroimaging. Repeated falls, transient loss of consciousness, severe autonomic dysfunction, and depression support the clinical diagnosis of dementia with Lewy bodies.[5] Patients with Lewy body dementia often have varying degrees of Alzheimer's disease neuropathology[13] that might contribute to the clinical presentation.

Alzheimer's Disease with Extrapyramidal Signs

Alzheimer's disease is the most common form of dementia. Its prevalence is approximately 1% for those 65 to 69 years of age, increasing to 40% to 50% among persons 95 years of age and older.[14] Clinical features include progressive memory loss, impaired judgment and decision-making, disorientation, and reduced vocabulary. The prevalence of extrapyramidal features in patients with Alzheimer's disease varies between 12% and 92%.[15] A recent literature review reported psychosis in 41% of patients with Alzheimer's disease.[16] Concurrent extrapyramidal features and psychosis predict faster cognitive and functional decline, increased likelihood of nursing home placement and reduced survival.[17]

PATHOPHYSIOLOGY OF PARKINSONISM AND PSYCHOSIS

Parkinsonism and the Basal Ganglia

Parkinson's disease is the prototype of parkinsonism and drives our understanding of this syndrome. Loss of dopaminergic neurons in the substantia nigra par compacta projecting into the striatum marks the pathology of Parkinson's disease[18] (Figure 1). Dopamine deficiency in the nigrostriatal pathway leads to excessive inhibition of thalamic activity. This reduces feedback from the thalamus to the motor cortex and is probably the major factor explaining motor dysregulation.[19] Similar neuronal loss in the substantia nigra also occurs in dementia with Lewy bodies[20] and Alzheimer's disease.[21]

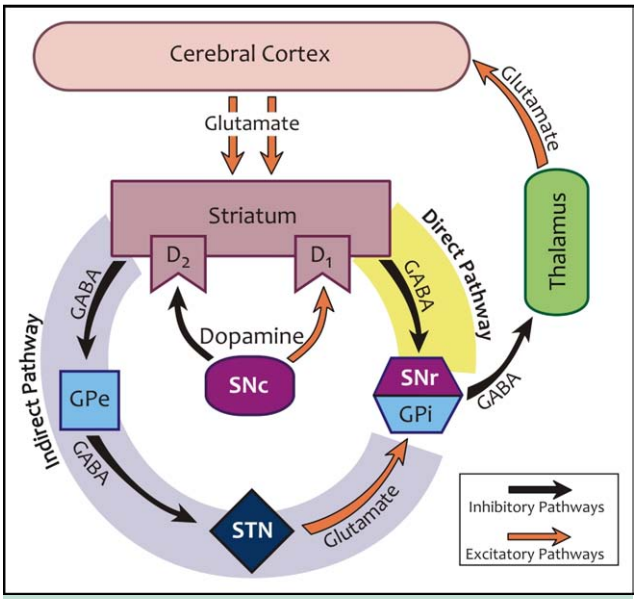

Figure 1 Cortical-basal ganglia-thalamic-cortical loop showing the major connections and neurotransmitters.

Psychosis

Psychosis is "loss of contact with reality." Hallucinations and delusions are core "positive" features. "Negative" features include apathy and psychomotor retardation. The pathophysiology of psychosis is complex and may involve various neurotransmitters and brain regions. Increased dopaminergic activity, particularly in the mesolimbic pathways, and dysfunction in the dopaminergic and serotonergic systems have been implicated in various types of psychosis.[22-24] For psychosis comorbid with parkinsonism, cholinergic deficit[25] and an imbalance between the cholinergic and monoaminergic systems[26] have been proposed as possible mechanisms.

Link between Parkinsonism and Psychosis

Dopaminergic dysfunction links parkinsonism and psychosis. An oversimplification states that this link moves in opposite directions and involves different neural pathways. Parkinsonism is a "hypo-dopaminergic" condition involving the nigrostriatal pathways. Medications used to treat parkinsonism increase dopaminergic transmission and may cause or worsen psychosis by increasing dopaminergic transmission in brain areas implicated in psychosis. In contrast, psychosis is a "hyper-dopaminergic" condition involving the mesolimbic system. Antipsychotic medications lower brain dopaminergic transmission and can cause or worsen parkinsonism by diminishing dopaminergic transmission in the nigrostriatal pathways.