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Dementia in Parkinson's Disease

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Parkinson's Disease (PD) has long been considered a condition affecting motor functions only. It is now appreciated that PD patients begin to experience subtle cognitive difficulties, which may proceed to a state of dementia. Dementia may be a major risk factor for nursing home placement of PD patients. Recent estimates suggest that 40% of all PD patients suffer from dementia. Parkinson's Disease Dementia (PDD) together with Lewy Body Dementia (DLB) account for approximately 20% of all cases of dementia.

Risk factors for dementia include advancing age, atypical features of PD, duration of disease, motor disability, depression and psychosis. The need to identify these at-risk patients early may intensify, as dementia treatments improve.

In order to diagnose PDD, a patient needs to meet criteria for the diagnosis of both PD and of dementia (DSM-IV). In PDD, the symptoms of dementia start after the onset of motor deficits and dementia needs to have started a minimum of 1 year after the diagnosis of PD. This somewhat arbitrary rule differentiates PDD from DLB. The defining feature of PDD is an impairment of executive functions (the ability to plan, organize and regulate goal-directed behavior). Attention and memory are also affected.

Clinical features of dementia associated with PD

- Impaired attention with fluctuations
- Impaired executive functions
- Impaired memory
- Impaired visuospatial functions
- Language largely preserved except for verbal fluency
- Praxis largely preserved
- Personality changes
- Multiple behavioral symptoms

Adapted from: Murat Emre: The Lancet Neurology Vol.2 April 2003 229-237

Dementia in Parkinson's Disease (continued from page 1)

Difficulties in making the diagnosis:

Cognitive decline in PD may be a slow process, starting with minor changes in the speed of mental processing (bradyphrenia), and other changes which include impairment of executive functions and visuospatial difficulties. These changes may occur in a subtle fashion, and affected patients may not initially meet the criteria for a diagnosis of dementia, if standard DSM criteria are utilized. For example, it may not be possible to tell if an impairment in activities of daily living is caused by physical or cognitive problems. Drug effects or depression may further affect the evaluation in a negative manner. As noted, there is significant overlap between Parkinson's dementia (PDD) and Lewy Body dementia (DLB) and clinicians often experience difficulties in differentiating between each of these conditions.

Since both these conditions share pathological and clinical features, the question has been asked as to whether they are the same entity. (Ref: D. Aarsland, CG Ballard G. Halliday: Are Parkinson's Disease With Dementia and Dementia With Lewy Bodies the Same Entity? J Geriatr Psychiatry Neurol 2004; 17: 137-145) Some workers in this field prefer to think of the two disorders as being part of the same spectrum.

Relationship to AD

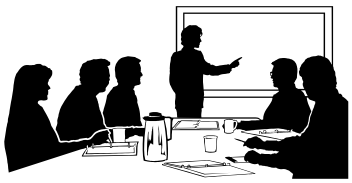
In addition to the overlap with DLB, Alzheimer Disease (AD) may occur concurrently in patients with PD, making the differential more difficult. AD may not only be difficult to separate out from PDD clinically, but the two conditions may also overlap pathologically. AD-type pathology is found in a large proportion of severely demented PD patients at autopsy, but not in non-demented PD patients. This may represent concurrent AD and PDD. However the neurochemical changes associated with the two conditions, when they occur separately, are also similar. PDD results from a brain cholinergic deficit making it similar to Alzheimer Disease (AD). Studies using PET imaging have suggested that cortical ACHE deficits were more extensive in PDD patients compared with AD of approximately equal degree of dementia severity (ref: N.I. Bohnen et al: Cortical Cholinergic Function Is More Severely Affected in Parkinsonian Dementia Than in Alzheimer Disease: Arch Neurol Vol. 60 Dec 2003, 1745-1748).

An additional finding was that cortical ACHE activity in patients with PD was intermediate between the PDD patients and AD affected patients. This study, done on live patients has been interpreted as supporting post-mortem studies showing that in early PD, there is degeneration of the forebrain cholinergic system and that this worsens with the onset of dementia. Neuropsychological assessment may be helpful in order to differentiate between the various closely related clinical situations described above, and should be considered in the work-up of these patients.

Treatments in PPD

Dopaminergic drugs are used in the treatment of PD, but any cognitive benefits of these drugs may be simply due to non-specific effects on alertness and mood. Potential benefits may be neutralized by side effects such as delirium and psychosis. Apart from a few open label studies there has been little data to support the use of anti-dementia drugs in PDD. The recent EXPRESS study is the first international, multicentre, double-blind, placebo controlled study to demonstrate the efficacy and safety of a ChEI in the treatment of PDD. Results showed that patients treated with Rivastimine experienced a significant improvement in cognition, global function, behavioral problems and activities of daily living, compared to placebo. Studies with other ChEI drugs are currently underway. Drugs of this group may be considered as a treatment option in improving quality of life. Although there has also been some interest in hormone replacement therapy, selegiline and vitamin E to lower the risk of dementia in PD patients, there is little scientific evidence to support their use at the present time.

Innovative Physician Education For You!



We will come to your office and do a one to one session with you (20-30 minutes) or a 4-6 member breakfast or lunch and learn session (40-60 minutes). We will provide the food!

Physician educators will include: Anna Byszewski, Bill Dalziel, Tony Guzmàn, Barbara Power, Tilak Mendis, Inge Loy-English, and Louise Carrier

To find out more information, please call: 523-4004

The Role of Memantine (EBIXA®) for Moderate to Severe Alzheimer's Dementia

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On December 15, 2004, Memantine was approved in Canada for monotherapy or adjunctive use (add-on to cholinesterase inhibitors: Aricept, Exelon, Reminyl) for moderate to severe Alzheimer Disease (AD) (generally MMSE 5-19).

Two neurotransmitters can now be modulated in Alzheimer Disease and related dementias: acetylcholine by cholinesterase inhibitors to increase the signal and glutamate by Memantine, a NMDA receptor antagonist to decrease the background noise.

So What Is the Evidence?

1. Reisberg B, New England Journal of Medicine 2003: 348(1333-41) showed benefits (cognition, function, global impression and behaviour) in a 28-week RCT of 252 AD patients (MMSE 3-14) with the use of Memantine 10 mg. BID. Behavioural improvement was seen in agitation / aggression and delusions. Perhaps the most meaningful clinical change was decreased caregiver assistance in activities of daily living by approximately 1.7 hours per day.
2. Tariot P, Journal of the American Medical Association 2004: 291 #3 (317-24) showed benefits (cognition, function, global impression and behaviour) in a 24-week RCT when Memantine 10 mg. BID was added on to AD patients (MMSE 5 –14) already on stable doses of Aricept.
3. Winblad B, International Journal of Geriatric Psychiatry 1999: 14 (135-46) showed benefits (cognition, function and global impression) in a 12-week RCT of 317 severe AD patients (MMSE <10) in a long-term care institutional setting. In terms of patient care needs (BGP care dependency scale), a greater than 15% reduction was seen in 65% of patients on Memantine versus 40% of patients on placebo (a 25% difference or a very robust number needed to treat (NNT) of only 4). This translates to decreased nursing workload related to improved ambulation, dressing, washing and toileting.

What About Side Effects, Precautions and Dose?

Memantine is extremely well-tolerated with very little of the GI side effects seen with the cholinesterase inhibitors and only minimal increases over placebo levels for dizziness, transient confusion and constipation. It can be taken with or without food and although it has a long half-life, the recommended dosage is to start at 5 mg. OD and add 5 mg. per week to reach an eventual dose of 10 mg. BID after 4 weeks of titration. There is no interaction with the cytochrome P450 system and therefore little in the way of drug/drug interactions. It is predominantly renally excreted and therefore in moderate renal impairment, the dose should be decreased to 10 mg. OD and it is relatively contraindicated in severe renal impairment. The concomitant use of other NMDA antagonists such as Amantidine, Ketamine and Dextromethorphan should be avoided. There have been no reported problems of bradycardia and heart block as sometimes seen with cholinesterase inhibitors.

So When Should Memantine Use Be Considered?

1. As an add-on therapy to cholinesterase therapy when a patient progresses to the moderate stage of AD.
2. As actual therapy for AD when cholinesterase inhibitors are <u>contraindicated</u> (heart conduction concerns, active ulcer or asthma), or <u>not tolerated</u>, or are <u>ineffective.</u>

The Bottom Line

Memantine is another useful drug in the treatment of dementia. It is officially approved for monotherapy or add-on use in moderate to severe AD. It currently is not covered under any provincial drug benefit plan and the cost is similar to that of cholinesterase inhibitors at approximately $5.00 per day.

Have a look at: www.dementiaeducation.ca

This site has been developed as part of the Physician Education Initiative of Ontario's Strategy for Alzheimer Disease and Related Dementias. This multi-faceted education program was developed to inform and promote practice change in regards to Alzheimer Disease and related dementias. Registered users of the site will have access to clinical tools, educational materials and teaching resources. The website hosts casebased interactive learning modules, clinical practice guidelines, various educational resources and information on community resources. Take a look…be informed!

A Helpful Resource for Your Patients

The primary purpose of the Personal Health Record is to provide persons diagnosed with dementia and their caregivers with as complete a record as possible. It is designed to:

- present the information most frequently required by service agencies in a convenient format
- provide in one location contact information that may be needed by the caregiver
- inform the various agencies of all parties involved in providing service

For more information call:
The Alzheimer Society of Ottawa at 523-4004

Top Three Reasons to Refer Your Patients to First Link

First Link Premier lien

1. Caregiver support
2. Dementia education
3. Info about community services

Local physicians have referred more than 200 patients to First Link, a support and education initiative for individuals and families with dementia. First Link is an Alzheimer Society of Ottawa program implemented in collaboration with the Dementia Network of Ottawa. When you refer a patient to First Link, they receive: a personal phone call from the Alzheimer Society, an information package about Alzheimer Disease and dementia, guidance and information about community resources and care issues.

Dr. Ian Richardson, an Ottawa family physician reports: "Patients who have made the First Link connection are generally more knowledgeable about the disease and the help available, and more secure in having someone specific to call on when they need to".

For more information:
www.alzheimerottawa.org/first_link
or phone 523-4004
for your First Link referral kit

THANK YOU

The Dementia Network of Ottawa would like to thank Janssen-Ortho, Pfizer and Lundbeck for sponsoring this edition of the Dementia Newsletter for Physicians.

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