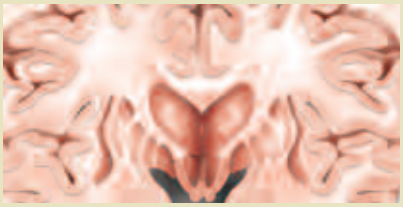
abstract



Mild cognitive impairment (MCI), the presence of cognitive difficulties without having dementia, is viewed as a preclinical state for Alzheimer's disease (AD) or another dementing illness. With the burden of AD expected to increase, research efforts have focused on interventions to delay the progression of MCI to AD. In this review, we first discuss the current conceptual understanding of MCI. Then, we outline a simplified approach to help clinicians diagnose MCI. Finally, we provide an overview of how to address the clinical needs of individuals with MCI.

Key words: *mild cognitive impairment, Alzheimer's disease, diagnosis, prognosis, treatment*

Diagnosis and Management of Mild Cognitive Impairment

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Introduction

Alzheimer's disease (AD) is a chronic, neurodegenerative disease associated with cognitive, functional, and behavioural changes. It is estimated that 280,000 Canadians over the age of 65 have AD and a projected 750,000 Canadians will have AD by 2030.[1] Given the public health burden of AD, there is increasing interest in defining preclinical disease states for AD when interventions may delay the onset of clinical dementia. Mild cognitive impairment (MCI) is a preclinical state when cognitive impairment but not dementia is present. As more data about MCI becomes available, it is important for clinicians to translate these findings into daily practice. In this review, we first provide a framework for the evolving definition of MCI. Then, we outline a simplified approach for clinicians to diagnose MCI. Finally, we provide an outline for formulating a management plan for individuals with MCI.

Definition of Mild Cognitive Impairment

There is no consensus regarding the precise definition of MCI. Conceptually, most people use the term MCI to refer to individuals with evidence of impairment on cognitive testing who do not meet criteria for dementia.[2–4] While definitions for MCI vary, Table 1 shows the criteria outlined in a 2001 practice parameter by the American Academy of Neurology on MCI.[3,5] While these criteria have been useful in predicting development of AD in clinical trials[6] and other studies, the definition does not capture the heterogeneity associated with MCI. For instance, MCI also may be a preclinical state for other dementias such as vascular dementia and Lewy Body disease.[7] Second, the focus on short-term memory deficits may limit inclusion of individuals who have very mild deficits in other areas of cognition. Third, some individuals do not complain of memory loss. Fourth, recent studies suggest that persons with MCI have subtle functional deficits.[10,11] In fact, natural history studies have shown similar associations between alternate definitions of MCI and risk of AD.[4,8,9] Finally, no consensus has been reached on how to quantify objective memory difficulties.

Diagnosis

In clinical practice, a relatively simple algorithm can be used to diagnose MCI. The algorithm is based on determining if an individual has chronic memory difficulties and whether the individual has dementia. Answers to these questions can be derived from the clinical history with corroborating evidence from bedside mental status testing. A physical examination, laboratory tests, and neuroimaging studies are also recommended in the evaluation of possible dementia, as described in previous reviews.[12,13]

Obtaining a symptom history is a valuable diagnostic tool. It provides information regarding how long memory problems have been present and what type of cognitive problems exist. As some individuals are unaware of their memory difficulties, it is worthwhile to inter-

Table 1: Definition of Mild Cognitive Impairment*

Subjective complaint of memory difficulty
Objective memory impairment
Other cognitive functions normal
No functional loss (Table 2)
No dementia (Table 3)

Source: Adapted from Petersen RC, et al. 1999.[3]

view a knowledgeable informant. Determining the symptom time course involves ascertaining when memory difficulties began, if difficulties began gradually, and if they have progressed. Memory problems can be addressed by asking if the individual repeats recent conversations, misplaces items and cannot locate them without help, has difficulties with vocabulary, or has difficulty learning new tasks. As behaviour changes coincide with cognitive changes, screening for depressive symptoms, hallucinations, and agitation is important. Also, assessing functional ability using standard scales such as the Instrumental and Katz Activities of Daily Living Scales is beneficial (Table 2). Finally, reviewing the medical history, medications, and family history offers information regarding other factors that may contribute to memory difficulties.

The examination focuses on finding objective cognitive changes and looking for other common neurologic conditions that may affect memory. The American Academy of Neurology 2001 practice parameter on dementia diagnosis concluded that general cognitive screening instruments such as a Mini-Mental Status Examination (MMSE) should be considered and that neuropsychologic batteries are useful in identifying individuals with dementia.[12] Unfortunately, complete neuropsychological batteries are impractical in a busy primary office setting and may not even be available in the community. Nonetheless, supplementing the MMSE with delayed recall of a brief story such as the Logical Memory Delayed Paragraph recall[6] can be very useful in identifying objective memory impairment. In this test, a paragraph is read to the person, immediate recollection results are recorded, and recall is tested following a 15-minute delay. It can be integrated into the office setting and can be administered by nonphysician examiners. Information on performance in nondemented older patients is available.[4,14] Objective cognitive tests can bookend a focused neurologic examination looking for signs of parkinsonism or stroke.

Laboratory and imaging studies are performed to diagnose other concomitant causes of memory difficulty. According to the American Academy of Neurology's guidelines for dementia,[12] laboratory evaluation should include a complete blood count, a metabolic profile, a thyroid stimulating hormone assay, a vitamin B12 level, and, if there is concern about the risk for sexually transmitted disease or the setting is an endemic region of the country, an RPR. Computerized tomography or magnetic resonance imaging of the brain is conducted to determine if structural findings such as stroke or mass lesions are present that could affect cognition.

Performing a focused history and physical provides the answers to whether a chronic memory problem exists and whether it represents a dementia. Using the DSM-IV criteria (Table 3), dementia is diagnosed if memory and at least one other area of cognitive impairment are present. In clinical settings, it is common to look for evidence that the impairments affect social or functional abilities and that the symptoms cannot be explained by another medical or psychiatric diagnosis. If the individual has chronic cognitive problems but does not meet criteria for dementia, the diagnosis of MCI is made.

Management and Treatment

While not everyone with MCI will progress to AD or another cause of dementia,[4] it is common and it warrants a frank discussion with the individual regarding the increased likelihood of progression. If the individual desires, his/her family should be included in the discussion. Individuals with MCI are advised to develop a network of potential personal care, medical, social service, and legal providers that may be needed as a support foundation in the future. Patients with limited insight into their cognitive impairment often exhibit similar management problems to persons with AD[15,16] and already are in need of a network despite the mildness of cognitive problems. The goal of the network is to maintain cognitive abilities, preserve functional abilities, control behavioural difficulties should they exist or emerge, and reduce caregiver burden through education, social and legal services, and treatment interventions.

As MCI is not generally understood by the lay public, it is important to describe the consequences of the condition. While the reported prevalence of MCI ranges from 5–25% depending on the cohort and definition used,[17–19] the Canadian Health and Aging Study reported prevalence in excess of 15%.[20] Several studies report that people with MCI are about twice as likely to die over the next several years as people without cognitive impairment.[10,21–23] Also, there is a two- to three-fold increased risk of long-term care placement.[21,24] Finally, it is important to state that MCI is a risk factor for developing AD. Compared to individuals without cognitive impairment who develop AD at rates of one to seven percent per year, the yearly risk for conversion from MCI to AD is 10–15%.[3,6] Other studies have shown that the risk of dementia with MCI is increased three- to eight-fold.[4,21,24]

Goals and Resources for a Treatment Plan for Mild Cognitive Impairment

The ideal treatment plan for mild cognitive impairment attempts to maintain cognitive abilities, preserve functional abilities, control behavioural difficulties, and reduce caregiver burden through education, through social services, and potentially through medications.

Table 2: Activities of Daily Living Scales to Assess Functional Ability

Do you need assistance with:
Instrumental Activities of Daily Living*
– transportation
– medications
– finances
– grocery shopping
– cooking
– housecleaning
– telephone use
Basic Activities of Daily Living**
– transferring out of bed
– walking
– grooming (brushing teeth, dressing)
– toileting (maintaining continence)
– bathing
– feeding

Source: *Adapted from Lawton MP, et al., 1969.[31]
** Adapted from Katz S, et al., 1963.[32]

Social and Legal Services

The other goal of education is to give individuals with MCI and their care providers an opportunity to self-manage the condition, and to prevent or delay adverse outcomes. While formatted for individuals with AD, some books can be useful for individuals with MCI and their families.[25,26] These resources may assist in maintaining independence and preventing care provider burnout, as shown in AD caregiver studies.[27]

Although social and legal services may not be needed immediately, making individuals with MCI and their care providers aware of long-term planning issues is important. An individual with MCI typically still has input into his or her personal decisions. Encouraging him or her to work with care providers to address safety issues such as the potential risks of driving and the eventual need to look for other means of transportation is valuable. Selecting a power of attorney for property may reduce the risk of financial abuse. Assigning a health care power of attorney to attend medical visits with the individual may facilitate compliance with medical treatment and reduce the risk of medical iatrogenesis. Providing information about resources such as the Alzheimer's Association, adult day centres, homemaker services, and assisted living facilities may be helpful. Earlier investigation of these services may make future decisions regarding them less stressful.

Pharmacological Interventions

Finding interventions to help prevent the conversion of MCI to AD has been a priority over the last few years. Currently, there are no approved medications for MCI. Efforts to use acetylcholinesterase inhibitors have produced mixed results. A study by the Alzheimer's Disease Cooperative Study group with donepezil showed no change in rate of conversion when compared to placebo over three years; however, there seemed to be an initial reduced rate of conversion compared to placebo over the first year.[6] In pooled studies of galantamine in MCI, the rate of death in the treatment group was higher than in the placebo group. Although the total number of deaths was low and the placebo group had an extremely low death rate, the United States Food and Drug Administration recommended a warning be placed in the galantamine product label that it is not recommended for use in MCI.[28] To our knowledge, data from large placebo-controlled studies of rivastigmine or memantine in MCI are not available. Therefore, the use of these AD medications should be considered off-label and patients should be provided with adequate information about the risks, benefits, and alternatives if treatment is prescribed.

The ADCS trial on donepezil also tested vitamin E 1000 IU twice a day in a parallel arm. The vitamin E group was comparable to placebo as far as three-year rate of conversion to AD.[6] In light of recent other studies showing increased harm and lack of benefit with vitamin E in other conditions, prescribing vitamin E in MCI does not appear to be beneficial.[29,30]

In the absence of robust pharmacotherapy for MCI, it is prudent to conduct follow-up evaluations at periodic intervals, such as once per year, to determine if cognitive impairment has progressed and if the patient has developed AD. If a transition occurs, approved pharmacological treatment for mild-to-moderate AD can be initiated. If individuals are interested in taking a medication for MCI, participation in clinical trials should be encouraged to maintain close monitoring of effects. Ongoing studies of MCI can be located at www.clinicaltrials.gov, a website sponsored by the National Institutes of Health, or at the Alzheimer's Disease Education & Referral Center (ADEAR) website at www.alzheimers.org/trials, which is sponsored by the National Institute on Aging.

Table 3: Definition of Dementia

The development of multiple cognitive deficits manifested by both
– memory impairment (impaired ability to learn new information or to recall previously learned information) and
– one (or more) of the following cognitive disturbances: aphasia, apraxia, agnosia, or disturbance in executive functioning.
The cognitive deficits cause significant impairment in social or occupational functioning, and represent a significant decline from a previous level of functioning.
The deficits do not occur exclusively during the course of a delirium.
The disturbance is not better accounted for by another Axis I disorder.

Source: Adapted from American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Washington, D.C.: American Psychiatric Association, 1994.

Conclusion

As no medication interventions currently exist, there is a perception that it may not be necessary to diagnose MCI. However, recognizing MCI may have an impact on maintaining the quality of life of individuals with the condition. Diagnosing MCI enables discussions about prognosis and helps individuals develop a support network. Counselling on social service resources may help maintain cognitive and functional abilities, and may prevent potential causes of morbidity. Closer monitoring for AD can occur so that approved treatments can be started early. Finally, individuals are given an opportunity to participate in clinical research looking for novel interventions for MCI. Therefore, as the population ages, it is important for all health care providers to recognize and manage MCI. ◆

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