

Mild Cognitive Impairment

A Clinical Perspective

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Introduction

Mild Cognitive Impairment (MCI), which is considered early stage Alzheimer's Disease (AD), is defined as a decline in cognitive functioning that is greater than would be expected for a patient's age and educational background and that goes beyond normal changes seen in ageing (Petersen 1999). Various cognitive domains can be affected including learning and memory, attention, executive function, language and visuospatial skills. Changes should be severe enough that they are noticed by the patient, their family and/or their clinician. While these cognitive changes should not be severe enough to interfere with basic activities of daily living some compensatory strategies may be in place for more instrumental Activities of Daily Living (ADLs) such as paying bills (Knopman 2014). Cognitive tests will reveal scores of between 1 and 1.5 standard deviations below the mean for the patients' age and education level (Albert 2011).

MCI is viewed as a transitional state between normal ageing and dementia; the annual progression rate to dementia has been shown to be 10% from clinical settings and 5% in community settings (Mitchell AJ 2009). Conversely it has also been shown from a meta-analysis that reversion rates of 23% and 10% are seen from population and clinical based studies respectively implying this is a dynamic diagnosis. Interventions to promote improved health or cognitive functioning may therefore be very useful at this stage (Canevelli 2016).

From a clinician's perspective it is important to identify those patients who are most at risk of conversion to dementia and advise accordingly. The literature has identified the following risk factors as especially relevant:

Cardiovascular risk factors

There is accumulating evidence that diabetes and insulin resistance in non-diabetic individuals is linked to a higher risk of cognitive impairment (Rawlings 2014; Crane 2013, Kim 2015). Midlife hypertension, obesity and dyslipidaemia appear to be risk factors when assessed separately, clustered into a metabolic syndrome or summed up in

cardiovascular risk scores (Solomon 2007; Cournot 2006; Yaffe 2009). In older patients however a U-shaped relationship with hypertension has been suggested to the extent that repeated episodes of cerebral hypotension may be as deleterious as chronic hypertension (Elmstahl 2014). Atrial fibrillation has also been demonstrated to be associated with worse cognitive function over time even in the absence of a cerebrovascular accident (Kalantarian 2013). The control of vascular risk is therefore imperative in a patient with mild cognitive impairment.

Behavioural factors

Moderate physical activity has been shown to be associated with a lower risk of cognitive decline in general population studies without cognitive impairment (Blondell 2014; Sofi 2010) and accumulating evidence points to its protective effects in MCI (Cammisuli 2017; Wang 2014). Smoking is also a risk factor for MCI and progression to dementia (Xue 2017; Durazzo 2014). Light to moderate alcohol appears protective against dementia in general populations compared to abstinence and heavy intake but there is conflicting evidence in the realm of MCI with one study showing a U shaped relationship (Cherbuin 2009), another finding no protective effect of alcohol intake at any level (Luck 2010) while a cohort study in a Chinese population showed light-moderate alcohol intake increased the risk of transitioning from MCI to dementia (Xue 2017). Further research on this is obviously warranted.

Psychological factors

There is moderate evidence from clinical studies that any type of neuropsychiatric symptom e.g. depression, apathy, anxiety in patients with MCI increases their risk of progression to dementia. Epidemiological studies have shown that depression on its own predicts conversion from MCI to dementia but the evidence has been inconsistent from clinical studies (Cooper 2015).

Neuropsychological factors

Patients with MCI who have deficits in multiple cognitive domains including memory are

most at risk of transition to dementia; this is converse to those who have a memory deficit only; their clinical course appears to be quite benign (McGuinness 2015; Nordlund 2010).

Anticholinergic burden

There is increasing evidence that drugs with anticholinergic effects such as antiemetics, antispasmodics, antihistamines and analgesics cause poor cognition in normal elderly populations and increase risk of future progression to MCI and dementia (Risacher 2016). Mortality rates in an Australian memory clinic study were found to be significantly higher in those on anticholinergic drugs compared to those not on (Cross 2017). Doctors should therefore reassess the requirement for any of these drugs in patients with MCI.

Dietary interventions

A recent systematic review showed there is insufficient RCT evidence on cognitive outcomes in MCI patients in terms of dietary interventions. Existing studies are heterogeneous in terms of the nature of the dietary intervention, duration, sample size and cognitive outcome measures assessed but there were some improvements in cognitive function, particularly in the domain of memory and the most consistent results for cognitive function were shown by B vitamin, folic acid and cocoa flavonol supplementation (McGrattan 2017).

From a review of observational studies there was accumulating evidence that combinations of foods and nutrients into certain patterns may act synergistically to provide stronger health effects than those conferred by their individual dietary components. In particular, higher adherence to a Mediterranean-type diet was associated with decreased cognitive decline. Moreover, also other emerging healthy dietary patterns such as the Dietary Approach to Stop Hypertension (DASH) and the Mediterranean-DASH diet Intervention for Neurodegenerative Delay (MIND) diets were associated with slower rates of cognitive decline and significant reduction of AD rate (Solfrizzi 2017).

Fortasyn Connect (Souvenaid™)

Souvenaid™ is a Food for Special Medical Purposes for use in the dietary management of early Alzheimer's Disease, and must be used under medical supervision. Souvenaid™ contains Fortasyn Connect which is designed to support the formulation and function of neuronal membranes.

Souvenaid™ has been shown to demonstrate statistically significant improvement in memory performance in patients diagnosed with mild and very mild Alzheimer's disease over 12 and 24 weeks in randomised controlled trials (Scheltens 2010,

Scheltens 2012) and continues to improve memory performance for up to 48 weeks (Olde-Rickert 2015). Souvenaid™ is well tolerated, has a positive safety profile with a high rate of compliance

LiPiDiDiet was a recently published 24-month randomised, controlled, double-blind, parallel-group, multicentre trial; it enrolled patients with prodromal Alzheimer's disease/disease/MCI. Participants were randomly assigned (1:1) to active product (125ml once-a-day Souvenaid™) or control product and were not receiving cholinesterase inhibitors at baseline. Although the intervention had no significant effect on the neuropsychological test battery (NTB) primary endpoint over 2 years cognitive decline in this population was much lower than expected, rendering the primary endpoint inadequately powered. Group differences on secondary endpoints of disease progression measuring cognition and function and hippocampal atrophy were observed which is encouraging. Further study of nutritional approaches with larger sample sizes, longer duration, or a primary endpoint more sensitive in this pre-dementia population, is needed (Soininen 2017).

Further points

There is no evidence that treatment with cholinesterase inhibitors, fish oils, individual B or E vitamins is of benefit in MCI (Cooper 2015). Patients with MCI should be followed up yearly or sooner if there is a concern regarding deterioration.

In conclusion a doctor faced with a patient with MCI can encourage and manage as appropriate to minimise the risk of transition to dementia.

Key messages appear to be:

1. Treat vascular risk
2. Encourage patients to be physically active
3. Treat underlying psychological issues
4. Reassess need for anticholinergic drugs
5. Encourage a healthy diet e.g. Mediterranean, DASH, MIND
6. Consider recommending Souvenaid™* to the patient

*Souvenaid™ is a Food for Special Medical Purposes for the dietary management of early Alzheimer's disease and must be used under medical supervision

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