

## **FOR A BETTER QUALITY OF LIFE IN ELDERLY**

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Currently, those aged 65 years or above comprise about 6% of the world's population. The reasons for this explosion in the older population in the world in general, and in the develop world in particular are many, and are not just a result of increasing life expectancy. Other factors including the declining fertility rate, declining child mortality, education and economic development play a big part. The ageing population of the world presents major challenges for society and for health services. Mental health issues are extremely important, as mental disorders, notably dementia and depression, are common in old age. Mental ill-health can profoundly affect the quality of life of elderly people and has a significant impact upon the use of health and social services.

Taking into account the fact that the mild cognitive impairment is considered as a prodromal phase of dementia, it is important to identify it early and to start the primary prevention. The primary prevention refers to the specific treatment of cognitive features and to changes of the lifestyle. The compliance and the lifestyle can stop the progression of the disease. Early detection and the treatment of mild cognitive impairment can maintain the elderly at a maximum level of functionality as much as possible. It is therefore important to improve quality of life the elderly, so that to maintain healthy and functional as long as possible, to prevent their admission to hospitals or homes-hospitals.

**KEYWORDS:** Mental health, elderly, mild cognitive impairment

### **Introduction**

The last century witnessed an unprecedented increase in the average human lifespan. The estimated total world population of older people was about 200 million in 1950 and is expected to rise to 1.9 billion by 2050 – nine-fold increase in 100 years.<sup>1</sup> Currently, about 6% of the world's population comprises those aged 65 years or above.<sup>1</sup>

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## Normal ageing

There is no satisfactory definition of the normal ageing process. It can be defined as a cumulative process of adverse changes in physiological, psychological and social functions that characterize average older people. Normal ageing as a social concept refers to an accepted range of variation in health, appearance, and performance of adults at different stages of their lives. However, it is always difficult to make a distinction between normal and pathological ageing.

According to *biological theories*<sup>1</sup>, the ageing process can be divided into primary and secondary ageing.

*Primary* ageing refers to those declines in function that are genetically controlled and *secondary* ageing consists of random changes resulting from acquired disease and trauma. These theories suggest that if the hostile events related to secondary ageing could be prevented, life would be extended, but because of primary ageing decline and death are inevitable.

*Psychological theories*<sup>1</sup> of ageing can be divided into cognitive and personality theories.

*The Cognitive theory* is based on studies of cognitive changes associated with age. In general, adults with higher intelligence and education tend to show minimum decline in their performances with increasing age, while a significant decline is observed in adults with lower intelligence and education. Older adults in general tend to perform less well in new and novel situations.

*The Personality theory*: Most studies have reported relative stability of personality traits from adulthood into late life. When personality changes occur, they appear to be related to losses, particularly those involving health and social support systems. Some studies have reported sex differences in personality in older age, men tending to become more dependent and nurturing and women tending to become more individualistic and more aggressive as they become older.<sup>1</sup>

The most frequent mental disorders in old age are: dementia, depression, anxiety disorder, drug abuse and psychosis.

## Dementia

The prevalence of dementia increases with age. Most studies have shown a prevalence of 0.8% in the 65-70 year age group which increases exponentially to 28.5% in the 90+ age group.<sup>1</sup> Dementia has an enormous impact on persons with the disorder and on those around them. The quality of life of individuals with dementia is affected by their cognitive and functional impairments, as well as the behavioral and psychological symptoms that often occur.

## Mild Cognitive Impairment (MCI)

MCI is an etiological heterogeneous condition characterized by cognitive decline greater than expected for an individual's age and education level, but that does not interfere notably with activities of daily life, subjects performing poorly on a variety of cognitive, functional and behavioral parameters, compared with normal person of the same age, but the cognitive decline is not enough severe to characterize dementia.<sup>2</sup>

For diagnosis of mild cognitive impairment are used<sup>3</sup> the Peterson criteria (2001):

- memory complaint, preferably corroborated by informant,
- impairment is 1.5 standard deviations (SD) below peer norms,
- impaired memory function for age and education,
- preserved general cognitive function,
- intact activities of daily living,

- not demented.

Use of term MCI by clinicians is increasing, as they see more and more such patients in clinical settings as the populations ages and awareness of the treatability of some forms of dementia grows. According to an evidence-based medicine review, the American Academy of Neurology recommends that MCI is a useful clinical concept worthy of attention. This is because persons with MCI progress to dementia at a rate of 10% to 15% per year, which is in contrast to the normal elderly cohort that convert at 1% to 2% per year.<sup>2</sup> The transition is usually to Alzheimer's dementia, and less commonly to vascular dementia. In referral clinic populations, most patients with a diagnosis of mild cognitive impairment either persist with mild cognitive impairment or progress to dementia, and on autopsy such patients have characteristic neuropathological findings of Alzheimer's disease, including senile plaques.<sup>4</sup>

### **Etiology of MCI**

The cognitive decline etiology includes (1) genetic factors and (2) environmental factors (viral infections, food, smoking, stress).

Fat diet increase the risk of disease. Depression is secondary to stress, and untreated depression is a major risk factor for cognitive impairment and for dementia.<sup>2</sup> Another risk factors for mild cognitive impairment are: cardiovascular disease, abnormal blood pressure, too high or too low, metabolic disorders, low levels of physical, social and mental activity, fewer years of education. People who have higher levels of social, mental and physical activity seem to have less risk of MCI and dementia.

### **Symptomatology of MCI**

The patient with MCI complains of difficulty with memory. Typically, the complaints include trouble remembering the names of people they met recently, trouble remembering the flow of a conversation, and an increased tendency to misplace things, or similar problems. In many cases, the individual will be quite aware of these difficulties and will compensate with increased reliance on notes and calendars. Most importantly, the diagnosis of MCI relies on the fact that the individual is able to perform all their usual activities successfully, without more assistance from others than they previously needed.

### **Prevention of MCI**

The *primary* prevention of MCI involves the prevention of the appearance of the disease by measures applied to the individual and the environment.<sup>5</sup> The treatment of risk factors includes the treatment of hypertension, hypercholesterolemia, diabetes, hypothyroidism, depression, sleep disorders and other psychiatric disorders that may adversely affect cognitive status.

Alcohol in moderation may slow the appearance of cognitive deterioration and dementia progression in people who already have cognitive impairment. In addition to the specific treatment related diseases mentioned above, MCI's primary prevention includes physical activities and Mediterranean diet. Other non-pharmacological interventions which may have effects on memory and their removal are: stress factors, sleep low, taken medication (anticholinergic and sedative).

*Secondary prevention* lies in identifying and treating asymptomatic or pre-symptomatic persons having a risk factor of developing the disease; if MCI, secondary prevention can be achieved by use of anti-aging treatment, such as: omega-3 acids, natural products on herbal

(vinpocetinum, Rhodiola Rosea, ginkgo-biloba), nootropics (piracetam), antioxidants (vitamin E, C, A, alpha-lipoic acid, Coenzyme Q10).

An alternative method consists in the administration of extracts of Rhodiola Rosea strain containing bioactive alkaloids, polyphenols and phenyl-propanoids. The effects on the brain function are: cognitive stimulation, memory improvement, learning improvement and improvement of abstraction capacity.<sup>6</sup> The effects of Rhodiola Rosea are augmented in combination with Piracetam or Ginseng.

Cholinesterase inhibitors are typically used to treat early and mild stages of dementia. Treatment of Alzheimer's dementia could be extrapolated and used for the treatment of slight cognitive deficit. Cholinesterase inhibitors are donepezil (Aricept R), rivastigmine (Exelon R), galantamine (Reminyl R) and tacrine (Cognex).

*Tertiary prophylaxis* prevents association factors that lead to disease, preventing complications from occurring

### **Treatment of MCI**

Presently, there is no specific treatment for mild cognitive impairment, the treatment for Alzheimer's disease could be extrapolated and used for patients diagnosed with mild cognitive impairment. The adequate treatment for mild cognitive impairment includes non-pharmacological and pharmacological treatment.

#### ***Non-pharmacological treatment***

##### *Physical activity*

Regular physical activities seems to improve the memory loss to persons over 50 years with cognitive impairment, according to a study done in Australia, publicized in Journal of the American Medical Association in 2008.<sup>7</sup>

##### *Diet*

Recent research has shown that diet plays a major role in preventing cognitive impairment and reducing the risk of MCI conversion to AD. Mediterranean diet is currently considered the most healthful diet because high intake of fruits and vegetables.<sup>8</sup> Mediterranean diet contains large amounts of beta-carotene, vitamin C, tocopherols, tocotrienols (vitamin E), polyphenols and essential minerals such as selenium, magnesium, zinc, iron, calcium and iodine.

##### *Cognitive intervention*

The goal is to slow cognitive stimulation rate of cognitive decline using functional approaches in order to strengthen cognitive function.<sup>3</sup> In art therapy it is possible to express ideas and feelings that cannot be converted in words and this is important for people with language impairment.

##### *Art therapy*

Art therapy have been used initially in Germany in the rehabilitation program of patients diagnosed with early dementia.<sup>9</sup> Art therapy is a nonverbal form of therapy that uses visual imagination. In art therapy it is possible to express ideas and feelings that cannot be converted in words. This is important for people with language impairment.

#### ***Pharmacological treatment***

Several classes of drugs have been studied for the prevention of progression to dementia, these includes: antioxidants, nootropics (piracetamum), anti-inflammatory agents (rofecoxib), hormones (estrogens), other drugs which modify brain chemical levels and cholinesterase inhibitors (donepezil, rivastigmine and galantamine).

### Antioxidants

Antioxidants (vitamin E,C,A, alpha-lipoic acid, Co-enzyme Q10) are substances which may protect brain cells from the oxidative stress.<sup>10</sup>

At least one randomized, placebo-controlled, double-blind, multi-center trial indicates that vitamin E may delay the progression of moderate-to-severe AD<sup>12</sup>, but, the research is still underway to determine its efficacy in MCI. The combination supplemental of vitamin E(400UI/day or more) and vitamin C (at least 500mg/day of ascorbic acid) but not either vitamin alone reduce significantly the incidence and prevalence of dementia. The administration of vitamin E in combination with selegiline delays the institutionalization and the progression of dementia. There are clinical trials looking at vitamin E plus selegiline ( a mono-amine-oxidase inhibitor) as a treatment for dementia and for preventing progression of cognitive impairment.<sup>2</sup>

Coenzyme Q10, or ubiquinone, is an antioxidant that occurs naturally in the body and is needed for normal cell metabolism. One of the apparent benefits that are thought to come from coenzyme Q10 is prevention of cellular damage caused by free radicals.

Selezin ACE represents a unique and balanced combination of minerals – selenium and zinc – enriched by vitamins A, C and E. All contained vitamins and minerals have antioxidant effects, which protect the human body against the negative influence of free radicals.

### Ginkgo biloba

Ginkgo biloba has been used medicinally for thousands of years. Ginkgo has been used even as treatment and as dietary supplement in Europe and in Asia. Ginkgo is used for the treatment of numerous conditions, many of which are under scientific investigation.<sup>11</sup>

Ginkgo biloba has antioxidant properties and inhibit the formation of  $\beta$ -amyloid protein with a role in forming amyloid plaques in patients with dementia. Administered in a dose of 40 mg three times a day, ginkgo improve the cerebral flow.<sup>11</sup>

### Rhodiola Rosea

Herbal alternative treatment for mild cognitive impairment, this plant grows in the mountains of eastern Europe, Siberia and the Far East at 3000 meters altitude. Its beneficial effects on the body have been mentioned 1,200 years ago in the writings of Tibetans. Reports in the alternative medicine literature indicate that its extract (bioactive alkaloids, polyphenols and phenylpropanoids including tyrosol, rosavin, rosin and rosarin) have effects on brain function . The extracts of the roots of this plant have been found to favorably affect a number of physiological functions including neurotransmitter levels, central nervous system activity, and cardiovascular function. It is being used to decrease depression, enhance work performance, enhance learning and memory, increase accuracy in mental performance for prolonged periods of time, eliminate fatigue and prevent high-altitude sickness.<sup>22</sup>

### Nootropics

Nootropics are drugs that boost brain activity and memory and enhance the brain function. *Piracetam* is the most used nootropic, increases performance in a variety of cognitive tasks, appear to be effective in dementia and mild cognitive impairment. The dose of piracetam used for cognitive decline is 1600mg/day and the side effects are few, transient and mild.

### Anti-inflammatory agents

Anti-inflammatory agents have role in reducing inflammation in the brain as having a role in reducing risk for cognitive deterioration. Researchers and clinicians have shown that individuals who consumed NSAIDs have a reduced risk of dementia, taking non-steroidal inflammatory (*ibuprofen*) taken over two years decreased risk of Alzheimer's dementia. Other

studies have demonstrated the effectiveness of *aspirin* and *acetaminophen*. *Celebrex* and *rofecoxib* (cyclo-oxygenase 2 inhibitor) had comparable effects with ibuprofen administration.<sup>10</sup>

#### Statins

Epidemiological and experimental *in vitro* and *in vivo* studies have indicated a link between cholesterol metabolism and the development of AD<sup>23</sup>. It is assumed that there is an influence of cholesterol on the formation and accumulation of amyloid-beta. In a 26-week randomized, controlled, double-blind trial, 80 mg *simvastatin* was administered to 44 patients with normal cholesterol levels and 40 patients with AD. A significant reduction in CSF A $\beta$  that correlated with a slower progression of clinical symptoms were observed.<sup>24</sup>

#### Platelet Aggregation Inhibitors (Triflusal)

The effect of the platelet aggregation inhibitor *triflusal* on cognitive parameters and conversion to dementia has been studied in patients with amnesic mild cognitive impairment. The analysis of the data showed a significant reduction in the rate of conversion to dementia. In addition to the antiplatelet effect, triflusal has an anti-inflammatory effect, which may explain a potential secondary preventive effect.<sup>25</sup>

#### Hormonal treatment in MCI

Replacing the *estrogen* lost at menopause can prevent many of the manifestations of aging including osteoporosis, cardiovascular disease and decline in cognitive functions. Hormone replacing therapy after menopause have benefits for menopausal symptoms, for cognitive function – neuro-protective inhibit neuronal apoptosis and modulate Apo-lipoprotein gene expression.<sup>2</sup>

#### Drugs that alter brain chemical levels

Medications more commonly used to reduce the symptoms of Parkinson's disease may help normalize the effects of mild cognitive impairment

#### Control of cardiovascular risk factors

Arterial hypertension is a risk factor for mild cognitive impairment. Multiple mechanisms has been proposed to explain the correlation between arterial hypertension and MCI. Arterial hypertension is a risk factor for cerebrovascular diseases, and these are risk factor for MCI.

#### Cholinesterase inhibitors

Cholinesterase inhibitors are typically used to treat the early and middle stages of dementia. Alzheimer disease treatment can be extrapolated and used for mild cognitive impairment. This is because the deterioration in the production of acetylcholine accelerates over time, as more and more brain cells become damage did. These include donepezil (AriceptR), rivastigmine (ExelonR), galantamine (ReminylR), and tacrine (CognexR).

Cholinesterase inhibitors are used for long term treatment. Cholinesterase inhibitors improve or at least retard the rate of loss of cognition, the drugs can improve a person's quality of life.

*Tacrine* considered a first generation of cholinesterase inhibitor, used for cognitive decline in 1980 is no longer use due to hepatotoxic effects.

Currently there are three FDA-approved choline-mimetics: donepezil, rivastigmine and galantamine.<sup>13-15</sup> These medication are not curative but they have been shown to minimize morbidity in AD by improving cognitive functions such as memory, language and praxis. Recent evidence also suggests that such medications are effective in managing neuropsychiatric and behavioral symptoms in AD patients.<sup>2</sup>

*Donepezil*, the second cholinesterase inhibitor, is approved for treating mild dementia. The maximum daily dose of donepezil is normally 5–10 mg. This dose is taken just once a day,

either in the morning or in the evening. It is well tolerated, the adverse events observed after administration includes nausea, vomiting, headache, insomnia and dizziness.

*Rivastigmine* is a reversible acetyl-cholinesterase and butyryl-cholinesterase inhibitor and was found to be superior to placebo in clinical trials. The maximum daily dose of Rivastigmine is 6–12 mg. The drug is taken twice a day with meals (typically breakfast and dinner).

*Galantamine* has a dual mechanism of action, an cholinesterase inhibitor and has additional properties at nicotinic receptors, increasing cholinergic activity by activating presynaptic nicotinic receptors. The maximum daily dose of galantamine is 16–24 mg, and it is also taken twice a day with meals. The side effects are usually gastrointestinal related, like nausea, vomiting, diarrhea.

#### Other substances

In addition to the above-mentioned drugs a number of other substances have been investigated in terms of their effectiveness and benefits for persons with MCI. These include intranasal *insulin*, *melatonin* and *nicotine patches*. However, only studies of small sample size and short duration exist. Based on these data, a recommendation for the use of these substances for the treatment of MCI cannot be given.<sup>21</sup>

A few substances are currently in phase II trials: *ladostigil*, a dual acetylcholine-butyryl-cholinesterase and brain selective monoamine oxidase (MAO)-A and -B inhibitor Other drugs under investigation for MCI include *levetiracetam*, *atomoxetine*, *pioglitazone*, *insulin*, *human growth hormones* and *immunoglobulins*.<sup>21</sup>

### **Conclusions**

Taking into account the fact that the mild cognitive impairment is considered as a prodromal phase of dementia<sup>20</sup>, it is important to identify it early and to start the primary prevention.

The primary prevention refers to the specific treatment of cognitive features and to changes of the lifestyle. The clinicians should advise the patients to try to maintain a healthy lifestyle. The compliance and the lifestyle can stop the progression of the disease.

Early detection and the treatment of mild cognitive impairment can maintain the elderly at a maximum level of functionality as much as possible.

It is therefore important to improve quality of life of elderly, so that they maintain health and functionality as long as possible, to prevent their admission to hospitals or homes-hospitals.

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