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Analysis of risk factors for mild cognitive impairment

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ABSTRACT

Background: The term mild cognitive impairment was introduced in the 1990s. This disorder is the stage between normal aging and dementia. Considering the developments in the age structure of the population, diseases associated with the loss of cognition come to the forefront for both scientists and the public.

Objective: The paper introduces mild cognitive impairment as well as selected results of an epidemiological case-control study which investigated whether patients with mild cognitive impairment had risk factors for possible conversion to Alzheimer's disease.

Methodology: The method involved a questionnaire survey and venous blood sampling for genetic analysis. The data were processed statistically.

Results: Information from 698 subjects (219 cases and 479 controls) has been processed to date. The cases included 1.7 times more women with cognitive impairment than men with cognitive impairment. Other statistically significant differences were found in the type of occupation, with controls more often having sedentary jobs, and lower limb ischemia, with cases recording a higher incidence. Statistically significant associations were found for the TOMM40, IDE, and CLU genes.

Conclusions: Given that amnestic MCI is considered a precursor to dementia, it is likely that the same risk factors affect the onset of the disease. Knowledge and confirmation of these risks may help prevent and early detect MCI and dementia.

KEY WORDS

Dementia, mild cognitive impairment, risk factors

BACKGROUND

Population is ageing. In 2018, almost one fifth (19%) of the population of the European Union was aged 65 and older. The increasing age is a significant risk for developing dementia, the most common type of which is Alzheimer's disease (AD).

Dementia tends to develop slowly, and is marked by an initial decline in one or several cognitive functions. The majority of older adults never show symptoms of dementia (1, 2).

The term mild cognitive impairment (MCI) was introduced in the 1990s. MIC is the stage between cognitive changes accompanying physiological aging and early dementia. The term 'cognitive decline' may in practice be confused with normal aging (3, 4, 5).

MCI is distinguished from normal cognitive aging with biochemical markers, imaging, genetic and cognitive methods. Neuropsychological assessment plays an important role in identifying the risk of dementia before any significant development of cognitive impairment (4, 6, 7).

MCI was divided into amnestic MCI and non-amnestic MCI in 2005. Both the types may be associated with diseases of varying aetiology, such as AD or vascular dementia. Amnestic MCI is referred to be the precursor of AD. The conversion of amnestic MCI to AD is estimated at 10–15% per year (8, 9).

Clinical criteria of mild cognitive impairment

- cognitive changes confirmed by family or doctor,
- absence of dementia,
- loss of episodic memory, ie ability to learn and remember new information,
- substantial impairment of one or more cognitive functions compared to age and education,
- self-sufficiency (3, 10).

Cognitive functions

Cognitive functions include memory, thinking, attention, judgment, intellect, planning, decision-making, as well as visual-spatial functions, psychomotor speed, and abstract thinking.

Memory is essential for imprinting, storing, and retrieving information. Imprinting capacity is the ability to encode, store, and retrieve new information. Working memory is crucial to cognitive processes. Cognition is a function which helps to identify a situation and respond appropriately. It is the ability to process information, respond to stimuli, and adapt to the external environment. Perception is the ability to sense external and internal stimuli, process them, and incorporate them into experience. Intellect is the ability of creative reasoning, abstraction. It is reported that the higher the intellect before the onset of dementia, the slower the course of dementia (11).

Risk factors for mild cognitive impairment

Due to the risk of conversion to more severe cognitive impairment, the probability of MCI is increased by the same risk factors as in AD. Awareness of MCI risk factors may contribute to timely prevention of dementia (12).

Risk factors can be grouped into uncontrollable and controllable factors. Uncontrollable risk factors include age, gender, and genetic factors. MCI risk increases with age. The issue of gender is disputed, with some experts reporting a higher risk in men, some in women, and some negating any difference in gender. Association studies on AD focus on genetic polymorphisms that are considered to affect the expression and modulation of gene functions associated with the pathogenesis of AD (e.g., Apolipoprotein E, amyloid precursor protein, presenilin I, presenilin II, Tau protein), and on polymorphisms in relation to the metabolism of the above proteins. Amnestic MCI is assumed to present similar genetic markers, which would allow for predicting possible AD (11, 12).

Controllable risk factors include lifestyle factors, vascular and metabolic factors, such as obesity, hypercholesterolemia, diabetes mellitus, cardiovascular and cerebrovascular diseases. Another group of factors which could be controlled are education, employment and the related socio-economic status, social activities and others (12).

AIM

The paper aimed to assess, based on an epidemiological case-control study, whether patients with mild cognitive impairment had genetic, vascular, and psychosocial risk factors predicting possible conversion to Alzheimer's disease.

METHODOLOGY

The Department of Epidemiology and Public Health, Faculty of Medicine, University of Ostrava, Czech Republic, in cooperation with the Institute of Animal Physiology and Genetics, Academy of Sciences, Czech Republic, carried out an epidemiological case-control study between 2016 and 2019 to investigate the leading risk factors for MCI.

The methods involved were a questionnaire survey and venous blood sampling for genetic analysis. The data were processed statistically.

Qualifying criteria for the selection of respondents:

1. Cases

- Subjective memory impairment.
- Memory impairment reported by a close person.
- Montreal Cognitive Test MOCA®, Czech versions 7.1, 7.2, 7.3, score of 22 to 26 points.

2. Controls

- Absence of subjective memory impairmen.
- Montreal Cognitive Test MOCA®, Czech versions 7.1, 7.2, 7.3, score above 26 points.
- The control should be of the same sex and age ± 5 years. All respondents were duly informed and signed informed consent.

RESULTS

Information from 698 subjects (219 cases and 479 controls) has been processed to date.

A statistically significant difference in gender was identified in the group of cases with cognitive disorder ($p = 0.04105$). There were 1.7 times more women with cognitive impairment than men with cognitive impairment. The mean age of both the genders in the group was approximately 62 years. Although no statistically significant difference in education was established, statistically significantly more controls had a sedentary occupation, compared to cases ($p = 0.02288$).

For most of the observed cardiovascular risk factors (for example CHD, diabetes mellitus, hypertension, and stroke), no statistically significant differ-

ence was found between the groups. The cases had a statistically significant higher incidence of peripheral arterial disease (PAD) compared to the controls ($p = 0.04312$).

In terms of substance use, a statistically significantly greater number of cases consumed alcohol daily (13.55%) compared to controls (6.98%) ($p = 0.0182$). No statistically significant relationship was found for cigarette smoking.

Genetic analysis revealed statistically significant associations in the following polymorphisms: the TOMM40 gene ($p < 0.03$), the IDE gene ($p < 0.01$), the CLU gene ($p < 0.001$).

DISCUSSION

The above data were collected from 219 cases (subjects with cognitive deficit) and 479 controls (subjects without cognitive deficit).

Although experts disagree on which gender is at greater risk for MCI (12), the sample included 1.7 times more women diagnosed with cognitive disorder.

A number of studies show that higher education has protective effects on cognitive decline (12). We have not been able to confirm this fact in our research sample. Education is, nonetheless, linked to occupation. A statistically significant difference was found between the groups in the type of employment. The cases were more likely to work manually than mentally.

Neurodegenerative research indicates and in many cases confirms a significant association of cognitive deficit (both mild cognitive impairment and dementia) with vascular risk factors. Concerning selected cardiovascular factors, the sample yielded a statistically significant difference only in PAD. Multiple studies report an association of atherosclerosis with MCI and dementia independent of cardiovascular risk factors. A 2011 systematic review compared 12 studies, of which almost all reported a significant relationship between cognitive impairment, dementia, and Alzheimer's disease and positive ankle brachial index (ABI) results (13, 14, 15).

The above confirms an association between MCI and AD. The much debated risk factors, in particular lifestyle, are preventable. A healthy diet combined with adequate exercise and stimulation of cognitive functions may clearly affect the prevention of MCI and AD (16).

The above epidemiological study yielded only partial results. The potential risks of MCI need to be further studied, as knowledge of these risks may help prevent cognitive deficit and the onset of dementia as a more severe type of cognitive impairment.

CONCLUSION

MIC is the stage between cognitive changes accompanying physiological aging and early dementia. Considering the developments in the age structure of the population, diseases associated with the loss of cognition come to the forefront for both scientists and the public. As the aetiology of MCI and AD is not fully understood yet, it is necessary to study the possible risk factors of these diseases in detail. Knowledge and confirmation of these risks may help prevent and early detect both the serious diseases.

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