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FACTORS AFFECTING THE DEVELOPMENT AND COURSE OF COGNITIVE DISORDERS IN THE EDERLY

Kubešová H.M., Meluzínová H., Weber P.

Klinika interní, geriatrie a praktického lékařství LFMU a FN Brno, Česká republika, e-mail: hkubes@med.muni.cz

The authors present an overview of the current situation in the diagnosis and treatment of cognitive disorders in the elderly. Chronic diseases that significantly affect the development of dementia are stressed- adequate treatment of these diseases having been demonstrated as an important factor delaying cognitive decline. The effect of different drug groups on cognitive performance is also discussed. The importance of nutrition in the elderly and the effects of various deficiencies that clearly play a role in the development of cognitive disorders-especially deficiencies involving vitamins B; polyunsaturated fatty acids etc. are also discussed. Another section of the article deals with the importance of physical and intellectual activities for maintaining cognitive functions. Depression is discussed as a factor that significantly enhances the development of dementia. Finally, a table of recommended preventive, prophylactic and diagnostic measures that could improve the management of cognitive deterioration in the elderly is presented.

Key words: cognitive functions – dementia - early diagnostics – secondary dementia – nutrition in the elderly – depression.

ФАКТОРЫ ВЛИЯЮЩИЕ НА РАЗВИТИЕ И ТЕЧЕНИЕ КОГНИТИВНЫХ РАСТРОЙСТВ У ПОЖИЛЫХ

Кубешова Г.М., Мелюзинова Г., Вебер П.

Клиника внутренней медицины, гериатриии и общей врачебной практики медицинского факультета Университета им. Масарыка, Брно, Чехия, e-mail: hkubes@med.muni.cz

Авторы представляют обзор текущей ситуации в диагностике и лечении когнитивных расстройств у пожилых людей. Хронические заболевания, которые значительно влияют на развитие деменции, упорное и адекватное лечение которых, представляет собой важный фактор задержки когнитивного снижения функций. Также обсуждается влияние различных групп препаратов на когнитивные функции. Важности питания в пожилом возрасте так же уделяется внимание,

обсуждается влияние различных недостатков пищевых элементов, которые, несомненно, играют роль в развитии когнитивных расстройств, особенно с участием недостатков витаминов, полиненасыщенных жирных кислот и т.д. Другая часть статьи отражает важность физической и интеллектуальной деятельности для поддержания когнитивных функций. Депрессия рассматривается как фактор, который значительно способствует развитию слабоумия. Наконец, представлена таблица рекомендуемых профилактических, диагностических мер, которые могут улучшить управление когнитивными нарушениями у пожилых.

Ключевые слова: когнитивные функции, деменция, ранняя диагностика, торичные деменции, питание в пожилом возрасте, депрессия.

Introduction. To date, it has been possible to unify in internal medicine both diagnostic and therapeutic approaches to a wide range of diseases in the form of guidelines and recommendations set up by specialist societies. Elderly patients represent a majority of the clientele of specialized outpatient departments and these patients gradually develop geriatric multi-disciplinary syndromes such as instability and falls, intellectual disorders, incontinence, immobilization, chronic wounds etc. The common denominators of these states include, among others progressive, involutional, degenerative and atherosclerotic changes. The progression of these changes leads to complications of internal diseases as well as to deterioration of the organism as a whole in the sense of frailty. Experience to date from our own population indicates that little attention is paid to the deterioration of cognitive functions.

Unfortunately, resolution of cognitive disorders in our elderly population remains highly unsatisfactory. Most cognitive disorders are diagnosed only once they are of intermediate or great severity, whereby dementia is diagnosed together or just before social problems emerge. In any case, at the time of diagnosis we are faced with a practically incurable, basically untreatable disease whose course may be at best modifiable. In such a situation, it logically appears that the most effective approach is to make use of all the preventive measures available. Today, we already have at our disposal data regarding a number of factors that have been shown to be significantly associated with the development of cognitive disorders. We may thus define individuals with an increased probability of developing a cognitive disorder [1].

Factors envisaged to potentiate the development of dementia include vascular impairment induced by hypertension, dyslipidemia, cigarette smoking and diabetes. On the other hand, a positive effect is presumed in the case of higher levels of education, regular physical activity, healthy diet and social activities [2].

Experience has shown that in some cases cognitive disorders have an easily detectable and conspicuous familial incidence– this conclusion is also supported by recent genetic

studies. The genes Abeta PP, PSEN1 and PSEN2 demonstrate typical Mendelian inheritance. Nonetheless, this type of inheritance explains only a small percentage of dementias. Non-Mendelian type of inheritance has also been uncovered in the case of APO-E; nonetheless it cannot as yet be used for prediction. Great potential for the coming years lies in the application of genomics in the prediction, early diagnosis and treatment of dementias [3].

Changes in blood pressure and the risk of developing dementia.

Consistent treatment of previously diagnosed hypertension represents an important area, where we can effectively intervene against the processes that lead to the development of dementia. We have at our disposal the results of seven large studies. Though they primarily focused on the treatment of hypertension, at least three demonstrated the positive influence of antihypertensive treatment on the development of cognitive functions in older patients. Calcium channel blockers and AT1 receptor blockers appear to be the most effective to this end. [4, 5]. Treatment using the latter group of drugs especially demonstrated significant postponement of institutionalization in patients treated for Alzheimer´s disease [6]. On the other hand, we must also pay attention to the significance of lower blood pressure values in older patients, either induced by vigorous antihypertensive therapy or occurring spontaneously. This aspect is currently the subject of discussion regarding the target blood pressure values in patients being treated for hypertension [7].

The influence of medication and other substances.

The possible role of non-steroidal anti-inflammatory drugs in the prevention of Alzheimer dementia has been discussed for many years- both the anti-inflammatory effect of this drug group and the slowing of amyloid deposition are presumed. Unfortunately, large interventional studies, which were supposed to demonstrate the efficacy of cyclooxygenase-2 blockers in the treatment of Alzheimer dementia, did not meet expectations. The only substance to have shown a positive effect via apolipoprotein E4 was naproxen in whose case a primary preventive effect is actually presumed [8].

Another much discussed substance is caffeine- three out of five longitudinal studies demonstrated the positive effect of regular coffee consumption in middle age at a dose of 3-5 cups per day on postponing the development and slowing the progression of cognitive disorders in old age- the risk decreased by up to 65%. Another two studies combined the drinking of tea and coffee and the effect was comparable. An antioxidant mechanism of action together with increased insulin sensitivity is presumed [9].

Naturally, the question arises regarding the amount of caffeine actually contained in the volume termed “cup”. Fifty milligrams of caffeine is cited as the borderline value between the sedative and excitatory dose. Thus, while coffee consumers wishing to increase their intellectual and psychological productivity would consume up to 500 mg of caffeine in 3-5 cups of Turkish coffee per day, those consuming coffee as a form of pleasant relaxation would certainly not need to consume more than 150-200 mg per day in 3-5 cups.

The influence of nutrition and metabolism.

Today, the quality of nutrition, from both a quantitative aspect and from the aspect of the proportion of individual nutrients, undoubtedly plays a role in the development of cognitive disorders. The presence of various nutrient deficiencies accelerates the decline of cognitive performance, while their increased intake may postpone and slow down the development of dementia. The negative effect of decreased vitamin B levels- vitamin B12, folic acid, thiamine, nicotinic acid- on the development of acute delirious states as well as on chronic cerebral dysfunction has been known for a considerable time. However, if low levels of vitamin B12 or folic acid were associated with hyperhomocysteinemia, the positive effect of supplementation on the decline in cognitive functions was not demonstrated [10]. More recently, a negative effect on cognitive functions has been attributed to hyperglycemia, recurrent hypoglycemia or hypertriglyceridemia [11].

A positive effect has been demonstrated in the case of Docosahexaenoic acid (DHA), which is currently designated as a promising candidate preventive drug that postpones the development of cognitive disorders, both of vascular origin and those associated with Alzheimer type of dementia. DHA is involved at multiple levels in the synthesis of beta-amyloid; it modifies the activity of kinases that hyperphosphorylate the tau-protein; it helps suppress the inflammatory activity and oxidative stress of neurons. However, according to some studies, the positive effect of DHA on the slowing of cognitive function decline is linked to a specific genotype of apolipoprotein E. Targeted administration of DHA to individuals with the appropriate genotype would be optimal [12].

A group of French authors reported the positive effect of both DHA and all polyunsaturated fatty acids (PUFA) on maintaining functional synapses, on facilitating learning and improving memory, exerting a general neuroprotective effect [13].

Much attention is being paid to vitamin D levels, whereby a significant positive correlation has been demonstrated between serum vitamin D levels and the results of cognitive function tests MMSE [14]. Moreover, a genetic association between decreased

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vitamin D levels and a predisposition to developing neurodegenerative diseases has been demonstrated [15].

An often overlooked factor that significantly aggravates both the physical state and cognitive performance of the elderly is the quantitative aspect of nutrition. Protein-energy malnutrition significantly worsens the potential of the elderly to maintain homeostasis; it increases the probability of developing acute cerebral dysfunction-delirious states and it accelerates the decline of cognitive functions from the long-term outlook [11]. According to ongoing studies, the attention being paid to the nutritional status of nursing home residents is insufficient– a survey conducted in Germany according to the Maastricht study from the Netherlands demonstrated that only one quarter of establishments for the elderly uses standardized screening tools for uncovering the risk of malnutrition. On the other hand, most establishments use a protocol or unified approach for the prevention and resolution of malnutrition. Nonetheless, malnutrition was observed in 26% of the clients of such institutions and the risk of malnutrition was detected in a further 28% [16].

Thyreopathy must be kept in mind as another of the metabolic-endocrine factors that affect the speed of cognitive function decline and nephropathies have also been recently cited as playing a role in this process. Estrogen supplementation has been shown as being effective in younger post-menopausal women, while older women were harmed rather than helped by supplementation [10].

The effect of intellectual and physical activity.

Today, it has been unequivocally demonstrated that physical, intellectual and social activity all have a positive effect on delaying the development of cognitive disorders. Two-year monitoring of a group of elderly persons with intermediate to high levels of physical activity demonstrated the unequivocally significant decrease in the risk of developing dementia compared to a group of elderly persons with low or no physical activity [17]. A group of French authors actually demonstrated the improvement of cognitive functions in elderly persons enrolled in a program of physical activities [18]. Similar results were reported by a study during which, for a period of 6 months, elderly persons underwent aerobic training, reaching 75-85% aerobic capacity, or stretching training not exceeding 50% aerobic capacity, both lasting 45-60 minutes, 4 days per week. The group that underwent aerobic training achieved improved results on their cognitive tests, improved glucose metabolism, a reduction in their percentage of body fat and improved overall fitness [19]. This approach appears to be beneficial also from the aspect of current views that compare Alzheimer dementia to type 3

diabetes, based on the finding of significant reciprocal dependence between insulin expression and the stage of dementia [20]. In a relatively high percentage of the elderly, though, disorders of the locomotor apparatus usually accompanied by pain dependent on the degree of loading may represent an obstacle to regular physical activity. For this reason, it is appropriate to pay greater attention to the diagnosis and treatment of pain in this population [21].

The mutual positive relationship between physical and intellectual activity and cognitive performance was demonstrated by a seven-week Japanese study, which involved a group of elderly persons who were exposed to greater physical (walking) and intellectual (taking photos using a cell phone and sending them) activity. Functional tests were performed at the beginning and at the end of the monitoring period. It was demonstrated that the most significant improvement occurred in those who increased both their physical and intellectual activity compared to those who were more active in only one of the two components [22].

Early detection of cognitive disorders?

The initial stages of cognitive deficits (MCI – mild cognitive impairment) continue to be the subject of much discussion involving on the one hand the possibility of predicting further progression into higher degrees of dementia and on the other the efficacy of early intervention with the aim of slowing progression. One of the interventions being studied is cognitive training whose presumed mechanism of action involves the preservation of neuroplasticity. Studies that have been conducted to date indicate the positive potential of this approach for improving cognitive performance or at least for postponing the more severe stages of dementia. Current knowledge, though, is limited by the different methods used and the relatively small groups of patients studied [23].

An even less explored area is SCI – subjective cognitive impairment, whereby tests practically cannot demonstrate cognitive impairment, yet the elderly person feels and ventilates a cognitive disorder. Six-year monitoring of patients with SCI demonstrated a several-fold higher incidence of MCI and dementia compared to patients without SCI, whereby deterioration occurred on average 3.5 years later in patients without SCI. Thus, the subjective sense of impaired memory may be considered to be a warning sign of early progression into a more pronounced cognitive disorder [24].

The authors´ as yet unpublished data show an up to fifteen-fold higher incidence of cognitive disorders in the population of community-dwelling elderly persons compared with the number of diagnosed and treated cases.

The development of a delirious state-in most cases induced by a sudden change of surroundings, acute health complications such as acute urinary tract or respiratory tract infection, trauma, dyspepsia with dehydration- is an event that may often help uncover an evolving and thus far undiagnosed cognitive disorder.

Views regarding the prognosis of delirium in older patients are undergoing developments. In 1998, we were told that the prognosis is relatively good, that most cases are reversible and that only less than 5-10% of patients progress into chronicity and dementia. This is why it was generally recommended to always consider an older patient with acute onset of a qualitative disorder of consciousness or cognitive functions to be a patient with delirium, a reversible state and to treat it as such [25]. Currently, the prevailing opinion supported by clinical studies is that delirium states aggravate one-year mortality in older patients. The longer the delirium, the worse the one-year prognosis is. It is thus necessary to use all means to prevent delirium or if it develops to shorten its duration as much as possible [26].

The effect of depression.

The overall state of mind undoubtedly influences cognitive functions- the concurrence of depression and cognitive disorders has been demonstrated repeatedly [27, 28]. The mutual influence reaching the proportions of a vicious circle is quite clear, especially in the initial stages of a cognitive disorder, when the senior is still completely aware of his/her declining cognitive abilities. The results of a study based on demonstrating the role of the suprachiasmatic nucleus in sleep disorders and the presumed positive effect of light on neuronal activity as well as overall mood in patients with cognitive disorders will be undoubtedly noteworthy. A group of elderly persons with subjective cognitive impairment, mild cognitive impairment and early stage Alzheimer dementia will be regularly exposed, twice a day, morning and evening, to white light at an intensity of 10 000 lux. The study is planned to span 2 years. If the results of this study are positive, this technique would represent an inexpensive and accessible means of positively modifying the course of cognitive disorders [29].

Conclusions for practice.

According to current knowledge, the development of cognitive disorders may be slowed down by measures listed in Table 1. Application of these measures in a concrete elderly patient will naturally unfold from a given, specific situation. Nonetheless, the more it will be possible to positively influence the lifestyle of the middle aged and elderly population,

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the more favorable the course of cognitive disorders and their consequences could be. The unequivocal requirement is for us to pay greater attention in all medical fields to the early detection of cognitive disorders and the timely initiation of appropriate therapy with the aim of slowing cognitive decline.

Table 1

Measures that mitigate the incidence and course of cognitive disorders in the ageing population

Preventive measures with a long-term effect-to be preferably applied from middle age onwards
1. Consistent compensation of attendant chronic diseases-especially hypertension, hyperlipidemia and diabetes; preferential use of medication with a demonstrated positive effect on the course of cognitive disorders. 2. Food respecting the recommendation of a healthy diet with a sufficient content of polyunsaturated fatty acids, vitamins B, especially B12, vitamin D and antioxidants. 3. Targeted cognitive training- counting from memory, planning and evaluating daily activities, active recall of information-geography, arts, history. 4. Regular physical activity with a predominance of aerobic loading, 3-4 x week for 30-60 minutes.
Preventive measures-prophylaxis
A. For the elderly
1. No downplaying of symptoms that hinder the implementation of the aforementioned measures-anorexia, biliary disorders, pain originating in the locomotor system, sensory deficits, subjectively perceived memory disorders. 2. Spending time outdoors, in the sun, with aerobic physical activity- walking, cycling, swimming, cross-country skiing, dancing. 3. Seeking social activities.
B. For carers and close family
1. Focusing on the early detection of an evolving cognitive impairment; attaching importance to the subjective cognitive impairment of the elderly person; eventually evaluating the risk according to the known medical history and concurrent diseases. 2. Ensuring an appropriate diet for the elderly person from both a quantitative and qualitative aspect. 3. Promoting physical activity, cognitive training and social activities.
C. For the healthcare system
Including the testing of cognitive functions and depression in the complex of tests that are part of regular preventive medical examinations in the persons over the age of 65.

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