

CLINICAL RESEARCH

Clinical and Neurological Status in Patients with Mild Cognitive Impairment due to Chronic Cerebral Ischemia

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Abstract

The aim of our work was to study the neurological status and cognitive function in patients with stage I and II CCI, depending on its nature.

Material and Methods: The study included 302 patients (mean age - 61.3 ± 0.3 years; 165/54.6% men and 137/45.4% women) with stage I and II CCI. Clinical and neurological examination, study of cognitive function, and MRI were performed in all patients. The degree of cognitive defect was determined by the MMSE (Mini-Mental State Exam) test and the Bourdon test (visual perception and vigilance). All the subjects were categorized into two groups. Group 1 consisted of 133 patients with the amnesic type of MCI (AT-MCI); Group 2 consisted of 169 patients with the multifunction type of MCI (MT-MCI).

Results: The highest frequency of complaints of a cerebral nature was observed in Group 2 patients with MT-MCI compared to Group 1 patients with AT-MCI. It should be noted that memory impairment occurred in all patients in Group 1. The clinical-neurological examination revealed that the subjective complaints of a cerebral nature occurred significantly more frequently in Group 2 patients compared with Group 1 patients, except for the memory disorders, which prevailed in Group 1 patients with AT-MCI. With regard to the objective symptoms, the focal neurological symptoms occurred with equal frequency in both groups. It should be noted that the symptoms of the carotid region were more frequent in Group 2 patients and the symptoms of the vertebrobasilar region in Group 1 patients. The parameters of the cognitive function related to the concentration and stability of attention were less disturbed in patients with AT-MCI compared with the patients having the MT-MCI, and those parameters correlated with the parameters of the neurological focal symptoms.

Keywords: chronic cerebral ischemia (CCI); mild cognitive impairment (MCI); neurological status.

Introduction

Chronic cerebral ischemia (CCI) is one of the main causes of dementia in elderly people. Several European studies have demonstrated the prevalence of vascular dementia (VD) in 1.6% of people over 65 years of age [1,2]. It is noted that the prevalence and severity of VD tends toward sustained growth with age. In studies with autopsy, VD was detected in 20% of patients [3,4].

In most cases, CCI is developed on the background of hypertension and atherosclerotic vascular lesions of the brain. Risk factors for VD and CCI are diabetes, hypertension,

genotype of ApoE gene (E4), and smoking [5,6]. These risk factors have a direct effect on blood vessels and vascular function. In one of the studies of risk factors for VD (smoking, hypertension and diabetes), they were closely associated with the subsequent risk of hospitalization for cognitive decline; this is seen most clearly in middle-aged patients. This association was stronger when risk factors were assessed at a young age and again at a later age [7].

Impaired cognition that is associated with CCI can vary from "central" deficit (aphasia, visual agnosia or ignoring the neurological defect) to disorders of cognitive functions in the framework for dementia (from subclinical to coarse disorders) [5,8,9]. Unlike neurodegenerative diseases such as Alzheimer's disease, there is not a single profile for cognitive disorders that would characterize VD. The most common manifestation of VD is cognitive deficit, which is more apparent than mental disorders [10-13].

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Thus, recognition of causes, identifying risk factors, and the exact knowledge of the structural, physiological and clinical features of the disease define the real possibility for effective treatment and prevention of chronic vascular pathology of the brain.

Based on the above, *the aim* of this work was to study the neurological status and cognitive function in patients with stage I and II CCI, depending on its nature.

Material and Methods

We present results of a comprehensive survey of 302 patients (165/54.6% men and 137/45.4% women) with stage I and II CCI, who were hospitalized in the department of neurology of RCH #1, CCH "Uzbekistan Temir Iulary", private hospital "Spectra neurology" named after Academician NM Madjidov", GMS and "NeuroMed-service" hospitals during 2010–2013. Written informed consent was obtained from each patient.

Among those surveyed, male patients significantly predominated over women. The mean age was 61.3 ± 0.3 years. Patients aged from 60 to 69 years composed the largest group ($n=225/74.5\%$), and patients aged from 43 to 49 years composed the smallest group ($n=5/1.7\%$). Table 1 shows the distribution of patients by age and sex. It may be noted that the development of mild cognitive impairment (MCI) was associated with age and gender; so, the risk of this disease increases in men with increasing age.

Table 1.

Distribution of patients by age and sex

Group	Sex				Age (yrs)						
	Men		Women		Mean age	43-49		50-59		60-69	
	n	%	n	%		n	%	n	%	n	%
Group 1	74	55.6	59	44.4	61.6±0.45	3	2.3	28	21.0	102	76.7
Group 2	91	53.8	78	46.2	61.1±0.39	2	1.2	44	25.4	123	73.4
Total	165	54.6	137	45.4	61.3±0.3	5	1.7	72	23.8	225	74.5

The diagnosis of MCI was verified according to ICD-10. Clinical and neurological examination, study of cognitive function, and MRI were performed in all patients. The degree of cognitive defect was determined by the MMSE (Mini-Mental State Exam) test and the Bourdon test (visual perception and vigilance). The distribution of patients into groups was done according to the classification of O.S. Levin (2010). Group 1 consisted of 133 patients with the amnesic type of MCI (AT-MCI); Group 2 consisted of 169 patients with the multifunction type of MCI (MT-MCI). Analysis of the age and sex gradation revealed that the AT-MCI and MT-MCI were more common among men over the age of 60 years.

The exclusion criteria were age less than 35 and older than 75 years, CCI stage III, other etiologies of encephalopathy, stroke, diabetes, epilepsy, organic diseases of the brain and spinal cord (the hereditary, demyelinating, and degenerative diseases, tumors), blood diseases and autoimmune diseases. Control group included 30 healthy subjects without any objective manifestations of CCI.

Statistical analysis was performed using the statistical

software «Statistica». For data with normal distribution, inter-group comparisons were performed using student's t-test. The mean (M) and standard error of the mean (SEM) were calculated. The difference was considered reliable when $P < 0.05$.

Results and Discussion

The main subjective symptoms (Table 2) were headache, dizziness, tinnitus, a decrease of memory and attention, disorders in the emotional sphere, and decreased performance. Therefore, a headache was more frequent in the Group 2 patients compared to the Group 1 patients. An unsystematic dizziness was also more frequent in patients in Group 2 compared to patients in Group 1. Decreased memory was found in 133 (100%) patients in Group 1 and 145 (86.8%) patients in Group 2. Fatigue and decreased performance took place in 100 (76.9%) and 123 (92.4%) patients in Group 1 and 134 (80.2%) and 141 (84.4%) patients in Group 2, respectively. These symptoms were associated with decreased attention in 123 (92.4%) patients in Group 1 and 142 (85%) patients in Group 2. Sleep disturbance took place in 102 (76.6%) patients in Group 1 and 140 (83.8%) patients in Group 2. Tinnitus occurred in 89 (66.9%) patients in Group 1 and 125 (74.8%) patients in Group 2. As can be seen from the presented data, the highest frequency of complaints of a cerebral nature was observed in Group 2 patients with MT-MCI compared to Group 1 patients with AT-MCI. It should be noted that memory impairment occurred in all patients in Group 1.

Table 2.

Semiological features of symptoms of cerebral nature

Subjective symptoms	Group 1 (n=133)		Group 2 (n=167)		P
	Abs.	%	Abs.	%	
Headache	79	59.4±4.2	135	80.8±3.0	<0.001
Dizziness	46	34.6±4.1	129	77.2±3.2	<0.001
Decrease of memory	133	100	145	86.8±2.6	<0.01
Fatigue	130	97.7±1.3	134	80.2±3.1	<0.001
Decreased performance	100	75.2±3.7	141	84.4±2.8	<0.05
Decreased attention	123	92.4±2.3	142	85.0±2.8	<0.05
Sleep disturbance	102	76.7±3.7	140	83.8±2.8	>0.05
Tinnitus	89	66.9±4.1	125	74.8±3.4	>0.05

We also conducted an analysis of the focal neurological symptoms. As can be seen from Table 3, the central paresis of the cranial nerve VII was detected in 124 (93.2%) patients in Group 1 and 146 (87.4%) in Group 2. The central paresis of the cranial nerve XII occurred in 86 (64.6%) patients in Group 1 and 123 (73.6%) patients in Group 2. Reduced convergence and weakness of accommodation were identified in 80 (60.0%) patients in Group 1 and 101 (60.4%) patients in Group 2. Reflexes of oral automatism were noted in 96 (72.1%) patients in Group 1 and 129 (77.2%) patients in Group 2. Aniso-reflection was diagnosed in 83 (62.4%) patients in Group 1 and 112 (67%) patients in Group 2. Symptoms of the carotid region took place more frequently in the Group 2 patients, but the focal symptoms of the vertebrobasilar region were more frequent in the Group 1 patients. Thus, instability

in the Romberg pose was observed in 87 (65.4%) patients in Group 1 and 102 (61%) patients in Group 2. Many patients had violations when performing the tests for coordination. In Group 1, an intention tremor in the finger-nose test was observed in 69 (51.8%) patients and an abnormality in the heel-knee-shin tests occurred in 39 (29.3%) patients. These disturbances were identified in 82(49.1%) patients and 41(24.5%) patients in Group 2. At the same time, differences between the two groups were not significant.

Table 3.

Features of focal neurological symptoms

Symptoms	Group 1 (n=133)		Group 2 (n=167)		P
	abs.	%	abs.	%	
Central paresis of the cranial nerve VII	124	93.2±2.2	146	87.4±2.6	>0.05
Central paresis of the cranial nerve XII	86	64.6±4.1	123	73.6±3.4	>0.05
Reduced convergence and weakness of accommodation	80	60.0±4.2	121	72.4±3.5	>0.05
Reflexes of oral automatism	96	72.1±3.9	129	77.2±3.2	<0.05
Aniso-reflection	83	62.4±4.2	112	67±3.6	>0.05
Instability in the Romberg pose	87	65.4±4.1	102	61±3.8	>0.05
Intention tremor in the finger-nose test	69	51.8±4.3	82	49.1±3.9	>0.05
Abnormality in the heel-knee-shin tests	39	29.3±3.9	41	24.5±3.3	>0.05

The clinical-neurological examination revealed that the subjective complaints of a cerebral nature occurred significantly more frequently in Group 2 patients compared with Group 1 patients, except for the memory disorders, which prevailed in Group 1 patients with AT-MCI. With regard to the objective symptoms, the focal neurological symptoms occurred with equal frequency in both groups. It should be noted that the symptoms of the carotid region were more frequent in Group 2 patients and the symptoms of the vertebrobasilar region in Group 1 patients.

We analyzed the results of the psychological tests regarding the cognitive sphere in the CCI patients and the correlations between these parameters and the indicators of neurological status. The MMSE score was 24.8±0.1 points in Group 1 patients versus 23.4±0.15 in Group 2 patients that correspond to MCI in both groups (Table 4). The analysis of the correlations between the severity of cognitive impairment on the MMSE and the objective focal symptoms revealed the following features: An inverse correlation was found between the severity of cognitive impairment and the central paresis of cranial nerves VII and XII ($r = -0.565$), as well as with the reflexes of oral automatism ($r = -0.455$).

Table 4.

Mini-Mental State Examination

Parameter	Control (n=30)	All patients (n=302)	Group 1 (n=133)	Group 2 (n=169)
MMSE score (Norm - 30)	29.5±0.1	23.6 ±0.8*	24.8±0.1*	23.4±0.15*^

* - $P<0.001$ vs Control group; ^ - $P<0.05$ between Group 1 and Group 2

The Bourdon test revealed a decline in the concentration and stability of attention in both groups. In the studied patients, the level of the concentration of attention was 144.6±1.34 points and the sustained attention - 3.5±0.01 points; these values were significantly lower in comparison with the control values. In Group 2 patients, the concentration of attention was 124.2±1.18 points, and the sustained attention 3.4±0.03 points; these indexes were significantly lower compared with indexes of the control group and Group 1 (Table 5).

Table 5.

Concentration and stability of attention in the Bourdon test

Parameters	Control (n=30)	All patients (n=302)	Group 1 (n=133)	Group 2 (n=169)
Concentration of attention	516.0±20.1	144.6±1.34*	170.5±0.27*	124.2±0.18*^^
Stability of attention	4.4±0.05	3.5±0.01	3.7±0.04*	3.4±0.03*^

* - $P<0.001$ vs Control group; ^ - $P<0.05$ and ^^ - $P<0.01$ between Group 1 and Group 2

Correlations were also found with the central paresis of the cranial nerves VII and XII, the reflexes of oral automatism, and the aniso-reflection. In Group 2 patients, there were also correlations with the decreased convergence and the weakness of accommodation.

Thus, the parameters of the cognitive function related to the concentration and stability of attention were less disturbed in patients with AT-MCI compared with the patients having the MT-MCI, and those parameters correlated with the parameters of the neurological focal symptoms.

Conclusion

In conclusion, it should be noted that the development of cognitive impairment in patients with CCI is caused by the phenomena of cortical-subcortical and cortical-cortical dissociation (disconnection syndrome), which are often detected in CCI. In the disconnection syndrome, lesions of the association pathways between the various parts of the brain are observed, which lead to the delay and reduction of intellectual-mental functions.

We revealed that cognitive deficits are predominant in patients with MT-MCI compared with patients having AT-MCI. This is proved by a number of psychological studies, including classical and modern tests, and allows us to differentiate the *dementia* of the *Alzheimer type* from vascular type. Carrying out these tests in clinical practice will allow diagnosis of the pre-dementia disorders in patients with CCI.

Competing interests

The authors declare that they have no competing interests.

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