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Cognitive impairment and quality of life in patients with migraine-associated vertigo

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Abstract. – OBJECTIVE: To study the impact of migraine-associated vertigo (MV) on the cognitive state of patients and their quality of life.

PATIENTS AND METHODS: A total of 120 patients were enrolled in the study, including 40 diagnosed with MV, forty with a simple migraine and 40 healthy volunteers. Cognitive assessments were done using the mini-mental state examination (MMSE), and a battery of tests for cognitive functions in performance, memory, language, space and attention during interictal periods. Also, MRI was used to detect brain white matter lesions and SF-36 for quality of life.

RESULTS: The scores of cognitive tests (MMSE, tracing, memory and VFT scores) in MV cases were significantly lower than those in the simple migraine group. TMT-A and TMT-B scores in the MV group were the highest followed by those in the simple migraine group. The incidence of deep brain, peripheral lateral ventricle and total white matter lesions in the MV group was higher than that in the simple migraine group. Finally, the deep lesion and peripheral lateral ventricle scores in the MV group were significantly higher than those in the simple migraine group. The physical, social, mental and total health scores in the MV group were significantly lower than those in the simple migraine group. All the differences found between groups had statistical significance, and all the variables examined fared best in the healthy control group.

CONCLUSIONS: MV patients show a more pronounced cognitive impairment than patients with a simple migraine or healthy volunteers, the incidence of brain white matter lesions is increased in them, and their quality of life is severely compromised.

Key Words:
Migraine-associated vertigo (MV), Vestibular migraine, Cognitive function, Quality of life.

Introduction

A migraine is a disorder characterized by moderate-to-severe headaches usually associated with sensitivity to external stimuli, nausea and/or vomiting, it has a hereditary basis. Its incidence is highest among those between the ages of 25-55 years. The pain can be severe during an attack and it is often repetitive. The treatment is symptomatic at best, and migraine seriously reduces a patient's quality of life[1]. Some studies[2] have discovered notable cognitive function changes in patients during migraine episodes. The neuropsychological defects in patients who present migraine aura are more severe than in others. They may be accompanied by face agnosia, expression disorders, visual space skill disorders, dysmnesia and persistent attention defects[3]. Some studies[4] even point to migraine as being a risk factor for Alzheimer's disease. Moreover, epidemic studies[5] have found that migraine is closely related to vertigo. Approximately 25% of migraine sufferers have got attack history of vertigo. Episodes of vertigo in migraine sufferers during interictal periods are more frequent than those of non-migraine sufferers. The pathophysiology of MV is not clear but it appears the trigeminal nerve's vascular access and the vestibular system interact in migraine sufferers[6]. MV aggravates the clinical symptoms and cognitive impairment of a migraine and further decreases the quality of life[7]. Meta-analyses demonstrate that the risk of white matter lesions in migraine sufferers is 3.9-fold that of healthy controls[8]. When excluding other risk factors of cerebrovascular disease, the ratio goes up to 4.1. The white matter damages in migraine can be evidence as white matter's asymptomatic ischemic or non-ischemic demyelination lesions[9]. This study aims at analyzing the impacts of cognitive impairment and quality of life in patients with MV and provides reference data for clinical diagnosis and treatment.

Patients and Methods

Patients

Forty patients diagnosed with MV in our hospital between January 2014 and January 2016 were continuously selected and participated in the

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study. Additionally, forty patients with a simple migraine and 40 healthy volunteers were matched, 1:1 according to age, sex and education and were enrolled too. The diagnosis of migraine was consistent with the Diagnostic Criteria of International Migraine Association version 2, including the classification of migraines with aura or without aura. MV was diagnosed according to the Neuhauser criteria, including medical history of migraine; moderate to severe paroxysmal vestibular symptoms (rotatory vertigo, other self motion illusion, location vertigo, poor sport tolerance); and appearance of migraine-related symptoms such as a migraine headache, and photo- or phono-phobia. The severity of vestibule symptoms is classified into 3 levels: mild (does not interfere with daily routines); moderate (interferes but does not limit daily routines; and severe (limits daily routines). The exclusion criteria for the study included: Age <18 years old or >60 years old; presence of anxiety, depression or other emotional disorders; brain trauma, brain tumor, encephalitis or other primary brain lesions and headache secondary to them; otogenic disorders and secondary vestibular dysfunction; recent use of pain killers such as morphine, etc.; previous cognitive impairment and mental illnesses; recent experience of major life or working stimuli; poor cooperation, inability to complete scale scores, etc.

The hospital Ethics Committee approved this study and patients and relatives provided their informed consents. The MV group comprised 16 males and 24 females, aged between 28 and 56 years old (on average 42.7 ± 13.3 years of age). The course of disease ranged from 1-10 months (on average 4.2 ± 2.3 months); the schooling time spanned 13-34 years (24.7 ± 6.6 on average); there were 16 patients with mild symptoms, 19 with moderate symptoms and 5 with severe symptoms. The simple migraine group included 17 males and 23 females, aged between 26-53 years old (on average 42.2 ± 15.4 years). The course of disease ranged from 2-16 months (on average 4.7 ± 2.5 months); the schooling time spanned 10-32 years, (23.6 ± 5.8 on average); there were 24 patients with aura and 16 without aura. Finally, the volunteering group had 18 males and 22 females with, ages between 23-58 years old (43.5 ± 16.2 years on average); and the schooling time spanned 12-33 years, (23.5 ± 7.2 on average).

Study Methods

The cognitive examinations were conducted during the interictal periods, using the mini-mental state examination (MMSE), and a battery of tests for cognitive functions assessing performance in memory, language, space and attention. Additionally, MRI was used to detect brain white matter lesions and the SF-36 for assessing the quality of life in the MV and simple migraine groups.

MMSE is divided into sections including orientation (maximum 10 points), memory (maximum 3 points), attention and calculation (maximum 5 points), recall (maximum 3 points) and language competence (maximum 9 points). The maximum score is 30 points; cognitive impairment begins at <27 points. The Rey-Osterrieth complex figure test (CFT) and the tracing score reflect the accuracy and visuospatial abilities and the recall score reflects the mnemonic ability. The Trail Making Test (TMT) consists of two parts: TMT-A and TMT-B. Analysis indexes evaluate the perception and motion rates (processing speed), and the attention. The Verbal Fluency Test (VFT) evaluates language competence.

The Siemens Verio VB17 3.OT MR imager was employed in head MRI plain scan + FLAIR images. The scanner program defined a layer thickness of 5 mm, layer spacing 1.1mm, cross section spin echo sequences, and sagital and coronal plane scans. The Fazekcas semi-quantitative rating scale was used to score the site and severity of cerebral white matter lesions (WMLs) on T2 weighted imaging, lesions were divided into deep brain and peripheral lateral ventricular white matter lesions. A score of 0 reflected no signal changes; 1 point meant there were peripheral lateral ventricle cap-like or thread-like high signals; 2 points indicated smooth lunar halo-like signals; and 3 points irregular prominent high signals. Points were also assigned for dotted (1 point), fusing (2 points), and mixed patchy high (3 points) signals in the deep white matter. Points were assigned for each brain side, the scale used had 10 grades with 0 being the lowest and 9 the highest.

The SF-36 consists of three parts: physical, social and mental health. A higher score points to a better life quality.

Statistical Analysis

The SPSS20.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The measurement data were expressed by mean ± standard deviation. Comparisons among groups were analyzed by ANOVA. Pairwise comparisons were tested by LSD. Enumeration data were shown by case number or (%) and comparisons among groups by χ^2-test. $p<0.05$ means a given difference has statistical significance.

Table I. Cognitive function evaluation.

Groups	MMSE	Tracing Score	Memory Score	TMT-A Score	TMT-B Score	WET Score
MV group	23.5 ± 3.6	30.5 ± 4.2	14.6 ± 5.5	46.8 ± 6.7	86.7 ± 14.2	13.6 ± 3.2
Simple migraine group	25.2 ± 2.7	32.7 ± 4.3	16.8 ± 5.3	43.7 ± 6.2	83.2 ± 13.5	14.7 ± 3.4
Volunteering group	28.7 ± 3.5	36.6 ± 4.0	19.3 ± 5.0	36.9 ± 5.3	76.5 ± 10.2	16.3 ± 2.6
F	6.534	6.230	5.867	6.858	7.203	6.634
p	0.017	0.019	0.022	0.010	0.009	0.013

Results

Cognitive Function Evaluation

The MMSE, tracing, memory and WFT scores in the MV group were significantly lower than those in the simple migraine group, and highest in the volunteering group. TMT-A and TMT-B scores in the MV group were significantly higher than those in the simple migraine group, while they were lowest in the volunteering group. The differences had statistical significance ($p<0.05$) (Table I).

Evaluation of WMLs

The incidence of deep brain, peripheral lateral ventricular and total white matter lesions in the MV group was significantly higher than that in the simple migraine group, and least in the volunteering group. The differences had statistical significance ($p<0.05$). Similarly, the scores of the deep brain and peripheral lateral ventricle lesions in the MV group were significantly higher than those in the simple migraine group, and least in the volunteering group. The differences had statistical significance ($p<0.05$) (Table II).

Comparisons of SF-36 Scores

The physical, social, and mental health total scores in the MV group were significantly lower than those in the simple migraine group, and highest in the volunteering group. The differences had statistical significance ($p<0.05$) (Table III).

Discussion

Migraine-related cognitive dysfunction mechanisms may be associated with vasomotor disturbances resulting from chronic ischemia during recurring headaches[10]. The frequently used cognitive functional examination scale, MMSE, is extremely sensitive for identifying severe cognitive impairment but displays poor sensitivity to mild cognitive impairment[11-13]. The MMSE is mainly used to evaluate the cognitive function state in the elderly (60 years old or above), and may lead to a "Glass Ceiling Effect" if it is used in young and middle-aged patients. Therefore, this study has combined many cognitive functional tests to carry out a comprehensive, accurate evaluation.

Migraine patients suffer from long-term vasomotor dysfunction. Cerebral vasospasms lead to decreasing blood flow volumes in perforating arterial branches, resulting in brain white matter degeneration[14], especially in deep white matter. Moreover, a neurovascular inflammatory response may be involved in the occurrence of migraine[15]. Vascular endothelial cell changes during migraine attacks may lead to platelet aggregation, thrombosis and micro-infarctions[16]. Imaging stud-

Table II. WMLs evaluation.

Groups	Number of Cases	Deep Brain Lesions [n (%)]	Peripheral Lateral Ventricle Lesions [n (%)]	Incidence [n (%)]	Score of Deep Brain Lesions	Score of Peripheral Lateral Ventricle Lesions
MV group	40	18 (45.0)	12 (30.0)	30 (75.0)	1.9 ± 0.6	1.5 ± 0.7
Simple migraine group	40	15 (37.5)	5 (12.5)	20 (50.0)	1.3 ± 0.4	1.0 ± 0.3
Volunteering group	40	2 (5.0)	1 (2.5)	3 (7.5)	0.2 ± 0.1	0.2 ± 0.1
F (χ^2)		39.420	37.781	10.326	12.534	
p		0.000	0.000	0.000	0.000	

Table III. Comparisons of SF-36 scores.

Groups	Physical Health	Social Health	Mental Health	Total Score
MV group	45.6 ± 6.5	47.2 ± 4.5	36.6 ± 4.6	72.5 ± 8.2
Simple migraine group	49.2 ± 6.3	50.3 ± 4.7	42.2 ± 4.8	78.3 ± 8.6
Volunteering group	63.5 ± 5.7	59.7 ± 5.0	57.8 ± 5.0	92.6 ± 10.3
F	7.231	7.425	7.768	7.935
p	0.000	0.000	0.000	0.000

ies[17] have found that cognitive impairment may correlate with white matter lesions, micro-infarction and micro-hemorrhage, etc. The pathogenic mechanism for MV proposed by Baloh et al[18] states that vertigo and migraine may share an alteration of excitability in the neurons that lead to both the central and peripheral symptoms of an attack. Other aural phenomena may also be caused in a similar fashion. All kinds of effective stimuli may cause transient waves of inhibitory stimuli from central neurons and spread in all directions from there. Neuron inhibition causes massive ion flows, extracellular K^+ increases while Ca^{2+} concentrations decrease. Such changes lead to a decline in cerebral blood flow around the spread inhibition area. Attacks may be associated with the release of neuropeptides such as P substance, neurokinin A and calcitonin gene-related peptides[19]. Patients may encounter problems while performing physical activities due to the rise in the vestibule's discharge rate when the head is moving. Neuropeptides may produce hormone-like effects lasting a long time because they can spread to extracellular fluids. Furthermore, 5-HT also directly influences the discharge rate of vestibular nucleus and neurons[20]. Thus, 5-HT and neuropeptide pathways may play roles in MV's short-term and long-term vertigo[21].

This study showed that MMSE, tracing, memory and VFT scores in the MV group were significantly lower than those in the simple migraine group, and highest in the volunteering group. TMT-A and TMT-B scores in the MV group were significantly higher than those in the simple migraine group, and lowest in the volunteering group. Consequently, results show that the level of cognitive impairment in MV was significantly greater than that in a simple migraine. Likewise, the incidence of deep brain, peripheral lateral ventricle and total white matter lesions in the MV group was significantly higher than that in the simple migraine group, and least in the volunteering group. And the scores of deep brain lesions and peripheral lateral ventricle lesions in the MV group were higher than those in the simple migraine group, and least in the volunteering group.

Conclusions

Taken together, these results indicate that the level of white matter lesions of MV is more severe than that of a simple migraine. The physical, social, mental health and total scores in the MV group were significantly lower than those in the simple migraine group, and highest in the volunteering group. It indicates that the quality of life of MV is significantly lower than that of simple migraine sufferers and normal volunteers, highlighting the need for basic studies to elucidate the pathogenesis of this debilitating disease.

Conflicts of interest

The authors declare no conflicts of interest.

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