Study of the features of systemic dizziness in patients with chronic and recurrent migraine

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Abstract. Migraine and vertigo are the most common disorders in the population, often a combination of them is observed in one patient Despite numerous epidemiological studies showing a close relationship between migraine and vertigo, there are a number of contentious issues in relation to the migraine as a separate disease in the first place the question of terminology and the possibility of dealing with vertigo as the main and often the only manifestation of a migraine attack. The aim of our study was to determine the type of vertigo in patients with chronic migraine (CM) and episodic migraine (EM) and the possible pathophysiological mechanisms of the relationship between them. The study involved 113 patients with an established diagnosis of migraine at Tam Anh Hospital and National Otolaryngology Hospital of Vietnam from Oct. 2018 to Dec 2019. (according to the International Classification of Headache ,3rd edition (ICHD-3), a beta version. All patients underwent clinical and neurological examination, videonystagmography, video head impulse test. It was found that with an increase in the duration of the headache (days), the number of patients with both systemic vertigo (SV) and non-systemic vertigo (NSV) increases. According to the results of the neurological examination, it was found that most patients with SV noted an increase in symptoms with a change in head position - 61.5% (16) vs 29.7% (11), most had a history of hearing problems: 57.7% (15) vs 10 (38.5%). Analysis of the remaining indicators of subjective otoneurological research did not reveal significant differences. It was found that SV is more characteristic of patients with CM. The relationshipbetweenincreasedvertigoandachangeinheadpositionand a history of hearing loss was also identified. This may indicate a pathology of the structures of the inner ear in such patients. Thus, as a result of our study, we can assume a mixed nature of SV, the pathophysiological mechanisms of which probably include central sensitization and peripheral vascular mechanisms.

Key words: chronic migraine, episodic migraine, systemic vertigo, non-systemic vertigo, vestibular migraine

INTRODUCTION

Migraines and vertigo are the most common disorders in the population, often a combination of them is observed in one patient. However, recent epidemiological studies have shown that a combination of migraine and vertigo is more common than might be expected from the coincidence of two very common symptoms (Akdal et al., 2015; Muncie et al., 2017; Mohan et al., 2016).

In the medical literature, vertigo is understood to mean a wide range of disorders from the sensation of imaginary rotation or movement of surrounding objects (true or systemic vertigo (SV)) to disturbance of equilibrium (non-systemic vertigo (NSV)). Moreover, numerous studies have shown that migraine sufferers often experience certain vestibular disorders during a migraine headache, which has led to a discussion of a particular form of migraine - vestibular migraine or migraine-associated dizziness (Muncie et al., 2017; Sugaya et al., 2017; Vanni et al., 2015; Fife and Kalra, 2015).

Accurate diagnosis of vertigo in migraine is complicated by the similarity and combination of groups of symptoms. In accordance with the provisions of the International Classification of Headache, 3rd edition (ICHD-3) published criteria for migraine-associated vertigo (migrainous vertigo, migraine-associated dizziness), developed jointly with the International society for the study of headache and the Barani Society (O'Connell Ferster et al., 2017; Luzeiro et al., 2016; Furman and Balaban, 2015).

Migranous vertigo

- At least 5 seizures meeting criteria C andD.
- Migraine attacks without aura or migraine with aura currently or in history.
- Vestibular symptoms of moderate or severe intensity lasting from 5 minutes to 72hours.
- At least 50% of seizures are accompanied by at least one of the following 3 migrainesymptoms:
- Other causes excluded.

Probable vestibular migraine

- At least 5 episodes of vestibular symptoms of moderate or severe intensity, lasting from 5 minutes to 72hours.
- Compliance with only one of the criteria B and D for vestibular migraine (a history of migraine or migraine symptoms at the time of theattack).
- Other reasons excluded.

According to the classification of vestibular symptoms of the Barani Society, vestibular symptoms that meet the criteria for the diagnosis of "vestibular migraine" are:

- spontaneous dizziness (internal dizziness (false sense of own movement) and external dizziness (false sense of rotation or displacement of theenvironment));
- positional dizziness (occurs after a change in the position of thehead);
- visual-induced dizziness (caused by one large or a complex of moving stimuli);
- dizziness caused by movement of the head (occurs when the headmoves);
- imbalance, instability (sensation of spatial orientation disorder) with nausea caused by movement of the head (other forms of instability are not included in the classification of vestibular migraine (VM))(Lempert et al., 2012).

It should be noted that the combination of various subtypes of non-vestibular vertigo under the term "non-systemic" complicates the diagnostic search and sometimes leads to the idea about the mandatory presence of the disease, whether discirculatory encephalopathy, psychogenic state, etc. In this case, very often at first the plan includes such reasons as side effects of drugs, visual impairment (myopia, astigmatism, etc.) that cause difficulty in visual control of function equilibrium (Liu et al., 2017; Beh and Friedman, 2019).

These diagnostic criteria have been developed in order to further the study of VM, including therapeutic approaches to its treatment. According to somestudies, the prevalence of VM in the General population is 1%, and the disease takes the 1st place among other types of CM and EM. Women are affected more often than men (Formeister et al., 2017; Murdin et al., 2015).Despite numerous studies showing a close relationshipbetween migraine and vertigo, there are a number of contentious issues in relation to the migraine asa separatedisease in the first place the question of terminology and the possibility of dealing with vertigo as the main and often the only manifestation of a migraine attack. VMoften begins several years after the appearance of EM and has a varied clinical picture. In patients with VM when carrying out neurological andotoneurological examination in the majority of cases the pathology is not detected, and the diagnosis is based on history of the disease. Despite the fact that, according to statistics, patients with migraine account for 7% of the total number of calls to the clinic vertigo and 9% in the headache clinic, the disease is still rarely diagnosed. To date, there are nocertain ideas about the clinical and pathophysiological relationship between migraine and vertigo, as well as specific approaches to the treatment of vestibular symptoms of migraine (Goadsby et al., 2017; Dieterich et al., 2016).

To determine the type of vertigo in patients with chronic and episodic migraine and the possible pathophysiological mechanisms of the relationship between them

MATERIAL AND METHODS

The study involved 113 patients with an established diagnosis of migraine at Tam Anh Hospital and National Otolaryngology Hospital of Vietnam from Oct. 2018 to Dec 2019. (according to the International Classification of Headache,3rd edition (ICHD-3), a beta version.

All patients underwent clinical and neurological examination, videonystagmography, video head impulse test.

When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in2000.

All patients agreed to participate in the study and use their data in this article.

Statistical methods included: parametric criteria (Student's T-test), nonparametric criteria (contingency tables, Chi-square test).

Patient exclusion criteria were:

- age over 70years
- the presence ofvestibulopathy
- pregnancy,lactation
- the presence of malignantneoplasms
- the presence of neurological pathology or other chronic diseases that are accompanied bydizziness
- mental illness.

RESULTS

A total of 113 patients with CM and EM were examined. The average age of the patients is 44,2±8.7 years, the number of women was 59, men -54.

During a clinical neurological study, 17 patients (15.0%) revealed complaints and signs of rotational dizziness both during exacerbation and in the interictal period. These patients constituted the main group.

The comparison group was represented by 49 (43.36%) patients in whom a migraine with unsystematic dizziness was detected. 47 patients showed no signs of dizziness (Table 1).

Table 1. Types of migraine in patients

Type of migraine	Type of vertigo, n (%)			p
	Non-systemic	Systemic	Lack of dizziness	
Chronic n=67	25 (37,3)	19 (28,4)	23 (34,32)	<0,01
Episodic n=46	12 (26)	7 (15,2)	27 (58,7)	<0,01

Thus, it was found that with an increase in the duration of the headache (days), the number of patients with both systemic and non-systemic dizziness increases.

When comparing groups of patients with SV and NSV, we did not find significant differences in clinical and demographic indicators (Table 2).

Table 2. Types of dizziness in patients with migraine

Type of dizziness	Sex	Age, years	Headache debut age,years	Headache frequency	Headache duration
Systemic	m.-9 f-17	42,3±11,2	22,1±7,4	12,1±7,1	14,7±6,1
Non-systemic	m.-12 f.-25	42,5±10,8	20,5±6,8	12,2±6,7	14,9±6,8
p	>0,05	>0,05	>0,05	>0,05	>0,05

According to the results of the neurological examination, it was found that most patients with SV noted an increase in symptoms with a change in head position - 61.5% (16) vs 29.7% (11), most had a history of hearing problems: 57.7% (15) vs 10 (38.5%).

Analysis of the remaining indicators of subjective otoneurological research did not reveal significant differences.

Observation of eye movements during seizures and in the interactial period in patients of the main group suggests the presence of central vestibular disorders, which does not exclude the presence of peripheral vestibular disorders. That is, vertigo with migraine is a heterogeneous disorder due to a number of pathophysiological mechanisms.

Currently, the most widespread hypothesis of the origin of the vestibular symptoms of migraine, in which migraine headache is seen as migraine aura is due to spreading depression (a wave of inhibition) in the cerebral cortex from the primary tumor. This wave is accompanied by a narrowing of the blood vessels, changing their file extension. In cases when a vertigo spell not accompanied by headache, vestibular disorders can be due to the release of neuropeptides (substance P, neurokininand,callconomy peptide). Neuropeptides have a stimulating effect on background impulse activity of the sensory epithelium inner ear and vestibular nuclei of the brainstem. Asymmetric key parameter neuropeptides leads to vertigo. Asymmetric release neuropeptides the patient experiences discomfort during movement due to the increased background impulse activity of the vestibular structures (Akerman and Goadsby, 2015; Andreou et al., 2015). Positional vertigo, occurs at the end of an attack of vestibular migraine, explain the hormone-like action calcitonine peptide and other neuropeptides that penetrate into the extracellular fluid. Part stem mechanisms generating the phenomenon of cortical spreading depression when the VM is also discussed. According to this version, the basis migrainous vertigo are functional disorders between the vestibular nuclei, trigeminal system and thalamocortical connections, and migrainous vertigo in these cases can be the equivalent of allodynia and Central sensitization (Bhola et al., 2015; Dieterich et al., 2016; Lampl et al., 2015).

Genetic hypothesis of the origin of headaches in migraine suggests that mutations in the gene CACNA1A, which encodes the Central pore-forming subunit CaV2.1-(P/Q-type) calcium channels, cause at least three neurological syndrome in which there is pathology of calcium channels: episodic ataxia 2-type, familial hemiplegic migraine 1 and spinocerebellar type ataxia 6 type. Accumulated evidence

suggests that the pathogenesis of vestibular symptoms in migraine may be involved pathology subunit CaV2.1 calcium channel. Therefore, the head Belpre migraine can be considered the result of pathology of the channels in which the pathology of the cerebral cortex is the result of different mutations in a gene increases sensitivity of calcium channels in cells of the cerebral cortex by acting on multiple ion channels, involved mainly in the glutamate homeostasis. Thus, the end result will lead to increased concentrations of glutamate and K+ ions in the extracellular space of the synaptic gap, which may contribute to Central sensitization and the initiation of the excessive activity of the cerebral cortex . The studied familial cases of occurrence of a combination of migraines and headaches, which, as mentioned above, confirms the genetic origin of occurrence of combined pathology. In one family may be the presence of several relatives suffering from vestibular symptoms and headache in migraine, some family members may have a simple headache, and some suffer from childhood benign paroxysmal vertigo, which suggests the existence of phenotypic heterogeneity of this disease (Khaiboullina et al., 2017; Ferrari et al., 2015; Gormley et al., 2016; Jacobs and Dussor, 2016).

CONCLUSIONS

It was found that systemic vertigo is more characteristic of patients with CM. Our data on the relationship between migraine and vertigo confirm the hypothesis about the leading role of central sensitization as the main pathophysiological mechanism of the coexistence of these pathologies. The relationship between increased vertigo and a change in head position and a history of hearing loss was also identified. This may indicate a pathology of the structures of the inner ear in such patients.Thus,asaresultofourstudy,wecanassumeamixednatureofSV,thepathophysiological mechanisms of which probably include central sensitization and peripheral vascular mechanisms.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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