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EDITORIAL

Migrainous vertigo – A new diagnostic entithy

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ABSTRACT

Vertigo and dizziness are frequently reported by patients with migraine. There is a high co-morbidity between migraine and balance disturbance, but clinical observations suggest that vertigo can be an independent migrainous symptom.

Vertigo and dizziness can be related to migraine in various ways: causally (migrainous vertigo), statistically (vertigo syndrome are not caused by migraine, but show a statistical association, possibly as a result of on association of both condition with a third factor) or just by chance (co-existence by coincidence).

*The recent term of **migrainous vertigo (MV)** is more precise in defining migraine and balance symptoms occur as a part of a single phenomenon, differentiating from simply co-morbid symptoms.*

Because MV is not presently included in the IHS classification of migraine, Neuhauser et al. proposed operational clinical criteria modelled on IHS headaches classification.

Key words: migrainous vertigo, dizziness, vertigo, migraine

INTRODUCTION

Vertigo and dizziness are frequently reported by patients with migraine. There is a high co-morbidity between migraine and balance disturbance, but also vertigo can be an independent migrainous symptom.

Because many clinicians (neurologists, ENT doctors, general physicians, etc) are dealing with patients with complaints of migraine and dizziness it is of interest to review some aspects about the current knowledge in this respect.

Migraineurs suffer from motion sickness more than controls and persistent cerebellar symptoms may develop during familial hemiplegic migraine.

Vertigo and dizziness can be related to migraine in various ways:

- causally (migrainous vertigo),
- statistically (vertigo syndrome are not caused by migraine, but show a statistical association, possibly as a result of on association of both condition with a third factor) or

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- just by chance (co-existence by coincidence) (1).

For describing the vestibular syndrome caused by migraine some clinicians use the new term of **migrainous vertigo (MV)** in order to highlight the causal relation that exist between migraine and dizziness, suggesting possible pathogenetic links between migraine and vertigo.

Although it is not yet included in the International Headache Classification (IHS), MV is increasingly recognised as a new and different clinical entity, especially by Neuhauser's group and represents one of the most common causes of episodic vertigo. ❑

DEFINITION OF MIGRAINOUS VERTIGO (MV)

We have to distinguish between vertigo which is a vestibular symptom and non-vestibular dizziness (that may be due to orthostatic hypotension, anxiety disorders, major depression, excessive toredness, etc), because MV and non-vestibular dizziness can co-exist in the same patient.

The terms migraine-associated vertigo and migraine-related vertigo may describe symptoms that occur co-morbidly (migraine and vertigo are separate phenomena that occur in the same patient), as well as migraine in which vestibular abnormalities are integral part of migraine symptomatology

For adults, vertigo is present in the IHS (International Headache Society) classification only in the framework of basilar migraine which may include vertigo as an aura symptom (2).

Basilar-type migraine is defined as migraine with aura – with at least 2 attacks with symptoms originating from the brainstem and/or from both hemispheres simultaneously affected. The aura consists of at least two of the following, fully reversible symptoms but no motor weakness: dysarthria, vertigo, tinnitus, hypacusia, diplopia, visual symptoms simultaneously in both temporal and nasal fields of eyes, ataxia, decreased level of consciousness, simultaneously bilateral paraesthesias (2).

Marianne Dieterich considers that if the attacks of vertigo are associated with other brainstem symptoms (disturbances of consciousness, psychomotor deficits, and changes of mood) we can speak about basilar migraine described by Bickerstaff. There are also some particular forms of basilar migraine that are monosymptomatic (manifesting only with vertigo and hearing disorder) that are called *vestibular migraine* (3).

Benign paroxysmal vertigo of childhood characterised by recurrent brief episodic attacks of vertigo occurring without warning and resolving spontaneously (2) – could be an early manifestation of migrainous vertigo.

The recent term of **migrainous vertigo (MV)** is more precise in defining migraine and balance symptoms occur as a part of a single phenomenon, differentiating from simply co morbid symptoms (1). ❑

DIAGNOSIS OF MIGRAINOUS VERTIGO

Migrainous vertigo (MV) is a vestibular syndrome caused by migraine and manifests with attacks of spontaneous or positional vertigo lasting seconds to days and migrainous symptoms during attacks. Spontaneous rotational vertigo was reported by 67% of the patients and positional vertigo in 24% of patients with migrainous vertigo participating in Neuhauser HK study (2006). (4)

Case series with a high number of patients (up to 100 patients) highlighted clinical features of migrainous vertigo that provide evidence for migrainous origin: the co-occurence with visual auras, photophobia and phonophobia, relief by sleep and effectiveness of antimigraine therapy.

Because MV is not presently included in the IHS classification of migraine, Neuhauser et al. proposed operational clinical criteria modelled on IHS headaches classification.

According to H Neuhauser & T Lempert, for the diagnosis of a **definite MV**, it is necessary that *recurrent episodic vestibular symptoms* (such as rotational vertigo or illusory self or object motion; spontaneous, positional or provoked/aggravated by head motion) *of at least moderate intensity* (interfering with daily activities) to be present in a patient with current or a previous history of migraine diagnosed according to IHS criteria.

Also, in at least two of vertiginous attacks migraine symptoms (headache, photophobia, and phonophobia, visual or other auras) occur and as in the IHS classification, other causes of these symptoms are ruled out by appropriate investigations.

The same authors consider that for the diagnosis of a **probable MV** a patient with recurrent episodic vestibular symptoms of at least moderate severity should have:

- current or previous history of migraine according to IHS criteria, or
- migrainous symptoms occurring during ³ 2 attacks of vertigo, or
- presence of migraine precipitants (food triggers, sleep irregularities, hormonal changes) before vertigo in ³ 50% of attacks, or
- response to migraine medications in ³ 50% of attacks.

Also, other causes of these symptoms are ruled out by appropriate investigations.

In both definite and probable MV the general and neurological clinical examination are unremarkable in the symptom-free period.

Differential diagnosis of MV should be made with: Menière's disease – the vestibular form, BPPV (benign paroxysmal positioning vertigo), episodic ataxia type 2, transient ischemic attacks in vertebrobasilar system, basilar artery thrombosis, and brainstem/cerebellum haemorrhage, vertebral artery dissection (3). ❑

EPIDEMIOLOGY OF MV

Using these criteria, Neuhauser et al. identified migrainous vertigo in 9% of migraine patients (5).

MV is a frequent cause of recurrent vertigo in patients presenting to specialized dizziness clinics (5, 7) and is also frequent in headache clinics (5).

MV is relatively common, but under-diagnosed in the general population and has considerable personal and healthcare impact.

In a German nationally representative general-population setting, Neuhauser HK (7, 8) found a lifetime prevalence of MV of about 1%. This is a frequent condition at the general population level, in line with the high prevalence of MV in specialized dizziness and migraine clinics (1, 7, 8, and 9).

The same study found that migraine headaches and vestibular vertigo occurr in general population about three times more often than expected by chance: at a lifetime migraine prevalence of 16% and vestibular vertigo of 7%, chance co-occurrence is expected in 1,1% of the population, but in Neuhauser HK study was found 3,2%, suggesting the existence of common pathophysiological mechanisms between migraine and vestibular vertigo (7, 8).

Female preponderance among patients with MV reflects the female preponderance among migraineurs in general (7, 8).

Benign paroxysmal vertigo of childhood is characterized by brief attacks of vertigo or disequilibrium, anxiety, and often nystagmus or vomiting that occur recurrently for months or years in otherwise healthy young children (11). Many of these children later develop migraine, often year after vertigo attacks have ceased (12). In a population-based study, the prevalence of recurrent vertigo probably related to migraine was estimated at 2.8% in children between 6 and 12 years (13). ❑

PATHOPHYSIOLOGY OF MV

Most authors conceptualized MV as a vestibular disorder. The pathophysiology of MV is unclear, but might have links with migraine pathophysiology.

Migraine is a primary headache, with no underlying structural brain changes. The current knowledge about migraine pathophysiology is that migraine is a neurovascular disorder, wherein cranial vascular changes are driven neurogenetically. Central nervous system (CNS) dysfunction might play a key role in its pathogenesis (14).

Aura is due to cortical involvement during cortical spreading depression – in migraine aura regional blood flow reduction that begins from occipital lobe and extends to frontal lobe is secondary to the reduction in neuronal metabolism. Also, spreading depression may play a role in MV when cortical areas who process vestibular information are involved (15)

Neuronal deficits in the brainstem could be the pathogenetic link between migraine and vertigo. Migraine is likely due to a disturbance in the brainstem, PET studies during migraine attack demonstrate activation of the rostral brainstem – locus coeruleus (the main central noradrenergic nucleus), midbrain dorsal raphe (the main serotonin-containing nucleus in the brainstem nuclei) (Weiller 1995, Bahra 2001).

The presence of subclinical vestibular involvement in migraine in symptom-free interval suggests that MV could be due to a neuronal disorder of the brainstem. Harno H et al. found subclinical vestibulocerebellar

dysfunction interictally in migraine with and without aura. Comprehensive neurotological tests were performed between attacks in 36 migraine patients (12 patients with migraine with aura and 24 patients with migraine without aura): video-oculography, electronystagmography, static posturography, and audiometry. Despite the absence of clinical neurotologic symptoms most of the migraineurs (83%) showed abnormalities in the last one of these tests that suggested subclinical vestibulocerebellar dysfunction (15). Vestibulo-ocular reflex abnormalities were also reported in migraineurs (Helm). Optoelectronic 3D movement analysis may be abnormal interictally in migraine patients, even in the absence of vestibular symptoms, suggesting subclinical vestibular and cerebellar dysfunction in migraine (Sandor).

Trigeminovascular system and the neurogenic inflammation play a key role in migraine headache. Trigeminal fibres innervating the brain vessels arise from trigeminal ganglion; when trigeminal ganglion is stimulated the trigeminal fibres release substance P and calcitonin-gene-related-peptid (CGRP) involved in the sterile inflammation of cranial vessels that leads to pain (Goadsby, 1988). Neurotransmitters like CGRP (calcitonin-gene related peptide), serotonin, noradrenaline, dopamine – involved in migraine pathogenesis, are also known to modulate the activity of vestibular neurons, and thus could contribute also to MV pathogenesis (15, 22).

Genetic defects of ion channels have been identified as the cause of several paroxysmal neurological disorders. Migraine is considered a brainstem channelopathy, since Ophoff (23) identified abnormal voltage-gated P/Q type calcium, channel 1A subunit gene (CACNA1A) on chromosome 19 in the in familial hemiplegic migraine (FHM type1). Other FMM cases are linked to other 2 mutations in other 2v genes ATP1A2, encoding a catalytic subunit of a Na+/K+ + ATPase and SCN1A - the voltage gated sodium channel.

Also, episodic ataxia type 2 (EA2) is due to the same mutation on chromosome 19 as FHM1, both diseases – FHM1 and EA2 – having vertigo and migraine as proeminent clinical features.

Migrainous vertigo displays clinical similarities with FHM and EA-2. By now, for MV no genetic defect could be identified in the same region as for FHM and EA-2 (25, 26). M. von Breven explored the hypothesis that mutations in CACNA1A, ATP1A2, and SCN1A and in the calcium channel b4 confer susceptibility to MV and found that is no evidence that genes causing FHM and EA-2 are susceptibility loci for MV (24).

The syndrome of MV needs further research activity as it is common and is clinically relevant. In addition, it may help to clarify pathomechanisms of migraine itself, by elucidating which brain pathways account for the link between migraine and vertigo (27). ❑

TREATMENT OF MV

Treatment of MV currently parallels that of migraine headache, as proper studies of optimal MV management are just beginning (28).

In MV attacks it is effective the early administration of antiemetics (metoclopromide, domperidone) in combination with non-steroidal anti-inflammatory and analgesic drugs (ibuprofen, diclofenac, aspirin, paracetamol). Ergotamine tartrate could also be used.

Tryptanes that are relatively contraindicated for the treatment of migraine with aura due to risks of cerebral and cardiac infarction as a result of vasoconstriction.

In MV prophylaxis the drug of choice is the beta-blocker metoprolol retard (100 mg/day, for at least 6 months). Alternatives are:

- flunarizin (calcium antagonist 10-20 mg/day)
- anticonvulsants: valproic acid (600-1200 mg/day), lamotrigine (50-100 mg/day), topiramate (100 mg/day) (3).
- acetazolamide – which is not normally used for migraine prophylaxis, was applied in MV prevention successfully (1). ❑

CONCLUSION

Dizziness-free migraine and migrainous vertigo could be entities of the same migrainous spectrum, we postulate that could be a continuum of dizziness-free migraine – migraine with subclinical vestibular abnormalities – migrainous vertigo. These entities might have several common pathogenetic links.

These could be a support for migrainous vertigo response to the repertoire of acute and prophylactic medications that are used for migrainous headache.

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