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IAN Reviews in Neurology 2023

Stroke and Headache

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CHAPTER 11

Non-headache Symptoms in Migraine: What do They Mean?

Farsana MK, Thomas Mathew, Girish Baburao Kulkarni

ABSTRACT

Migraine is one of the most common primary headache disorders, characterized by recurrent episodes of disabling headaches, which are the defining features of this disease. Apart from headache other symptoms and associated comorbidities have a bearing in diagnosis disability and management of migraine, and frequently make migraine patients more incapacitated. Despite reports of fatigue associated with migraine dating back to the 19th century, the broader phenotype of an adult migraine attack has only recently been described non-headache symptoms may precede the headache phase by up to 72 hours and persist for a day after the headache resolution in the postdrome. The highest occurrence of non-headache symptoms is during the headache phase compared to the prodrome and postdrome. The most commonly reported non-headache symptom in the prodromal phase is neck stiffness, as compared to the difficulty in concentration during the headache phase and fatigue during the postdrome. The highest co-occurring symptoms were neck stiffness, thirst, and abdominal pain. Another important aspect of migraine heterogeneity is comorbidity with other neurological diseases (stroke or seizures), cardiovascular disorders, and psychiatric illnesses (anxiety and depression). The potential effect of acute and preventive treatments on non-headache symptoms has been poorly investigated. Given the clinical consequences, further research must be directed to specifically study these issues from a therapeutic point of view, to improve the quality of migraine patient care.

Keywords: Migraine, Non-headache symptoms, Variants, Comorbidities, Treatment.

INTRODUCTION

Migraine is one of the most common primary headache disorders characterized by recurrent episodes of disabling headaches.[1] Many epidemiological studies have demonstrated its higher incidence and the effects on socioeconomic and personal aspects of life. Migraine was listed one among the highest global causes of disability under 50 years of age in the Global Burden of Disease (GBD) 2019, and affects around 1 billion people worldwide.[2] A migraine attack classically has four phases, namely the prodromal (premonitory), aura, headache, and postdrome, which often overlap.[3] Along with severe headaches, non-headache symptoms associated with migraine attacks and comorbid diseases frequently make migraine patients more incapacitated.[4] Better recognition of the evolution of non-headache symptoms through the different phases of migraine can improve our understanding of migraine pathophysiology and help in the management of the disease.[5,6]

NON-HEADACHE SYMPTOMS IN MIGRAINE

Although the cardinal symptom of migraine is recurrent episodes of disabling headaches, it may not necessarily be always the most bothersome for all patients.[7] Non-headache symptoms may precede the headache phase by up to 72 hours and persist for a day after the

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headache resolution in the postdrome phase.[8-10] Despite reports of fatigue linked to migraine dating back to the 19th century, the broader phenotype of an adult migraine attack has only recently emerged in the past 30–40 years through several prevalence and phenotypic studies in which these symptoms were assessed.[11,12] Non-headache symptoms such as nausea, vomiting, photophobia, and phonophobia are an established part of the International Headache Society (IHS) criteria for migraine, and the recent International Classification of Headache Disorders-3 (ICHD-3) **(Box 1)** lists variants of migraine with non-headache symptomatology as well.[13]

According to a recent study by Messina et al., 99% of patients reported at least one non-headache symptom in one phase of the migraine attack, and 54% had at least one non-headache symptom occurring across the phases of the migraine.[6] Non-headache symptoms were higher during the headache phase compared to the prodrome and postdrome. Most symptoms occurred throughout all three phases, implying ongoing brain events with headache as just one feature of the attack. The highest co-occurring symptoms were neck stiffness, thirst, and abdominal pain. Patients with non-headache symptoms during all three phases of migraine were more likely to be female, had chronic migraine with higher levels of disability, and experienced drug overuse headaches more frequently. In addition, there were no discernible differences in the frequency of non-headache symptoms between patients with and without aura, those on prophylactic medication, or those with episodic and chronic headaches.[6] **Table 1** lists the various non-headache symptoms across the four phases of migraine.

BOX 1: The International Classification of Headache Disorders (ICHD-3) classification of migraine.

1. Migraine
  - 1.1 Migraine without aura
  - 1.2 Migraine with aura
    - 1.2.1 Migraine with typical aura
      - 1.2.1.1 Typical aura with headache
      - 1.2.1.2 Typical aura without headache
    - 1.2.2 Migraine with brainstem aura
    - 1.2.3 Hemiplegic migraine
      - 1.2.3.1 Familial hemiplegic migraine (FHM)
        - 1.2.3.1.1 Familial hemiplegic migraine type 1 (FHM1)
        - 1.2.3.1.2 Familial hemiplegic migraine type 2 (FHM2)
        - 1.2.3.1.3 Familial hemiplegic migraine type 3 (FHM3)
        - 1.2.3.1.4 Familial hemiplegic migraine, other loci
      - 1.2.3.2 Sporadic hemiplegic migraine (SHM)
    - 1.2.4 Retinal migraine
  - 1.3 Chronic migraine
  - 1.4 Complications of migraine
    - 1.4.1 Status migrainosus
    - 1.4.2 Persistent aura without infarction
    - 1.4.3 Migrainous infarction
    - 1.4.4 Migraine aura-triggered seizure
  - 1.5 Probable migraine
    - 1.5.1 Probable migraine without aura
    - 1.5.2 Probable migraine with aura
  - 1.6 Episodic syndromes that may be associated with migraine
    - 1.6.1 Recurrent gastrointestinal disturbance
      - 1.6.1.1 Cyclical vomiting syndrome
      - 1.6.1.2 Abdominal migraine
    - 1.6.2 Benign paroxysmal vertigo
    - 1.6.3 Benign paroxysmal torticollis

PATHOPHYSIOLOGY OF NON-HEADACHE SYMPTOMS

Susceptibility for migraine is genetically inherited, but several additional factors also influence symptomatology and disease activity. The complex biology of migraine remains unsolved and involves a series of central and peripheral nervous system areas and networks. More recently, migraine was considered a disorder of sensory brain processing, where impairment of the filtering of sensory and nociceptive inputs causes ordinarily unbothersome sensations to be perceived as disturbing.[14]

Functional neuroimaging of non-headache symptoms across migraine phases reveals a substantial involvement in numerous subcortical and cortical areas. Sensory afferents from the head and neck region, along with the nociceptive input from the cranial vasculature and dura, converge in the trigeminocervical complex (TCC) located in the brainstem through the trigeminal (TG) and cervical ganglia (CG). Numerous ascending and descending connections project to the rostroventral medulla (RVM), locus coeruleus (LC), periaqueductal grey (PAG), hypothalamus, thalamus, and cerebral cortex.[14]

Cortical spreading depression (CSD) is thought to be the neurophysiological correlate of migraine, characterized by a slow (2–6 mm/min) propagating depolarization wave in neuronal and glial cell membranes followed by cortical suppression lasting up to 30 minutes. This pattern of activity coincides with the initiation and progression of aura symptoms and is associated with a wave of hyperemia, followed by a prolonged phase of cortical oligemia.[3] **Table 2** and **Figure 1** summarize the brain areas and neuro-chemical systems implicated in non-headache symptoms of migraine.

Symptoms during the Prodromal Phase

The migraine prodrome is defined in ICHD-3 beta as symptoms preceding and forewarning a migraine attack by 2–48 hours, occurring before the aura in migraine with

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TABLE 1: Non-headache symptoms across various phases of migraine.

Prodromal phase			
Increased sensitivity to external stimuli: • Photophobia • Phonophobia • Osmophobia • Allodynia • Neck stiffness	*Cognitive/Behavioral symptoms*: • Fatigue/Lethargy • Difficulty in concentration • Mood changes • Irritability • Confusion • Disorientation • Speech difficulty	*Homeostatic and hormonal alterations*: • Yawning • Food craving/aversion • Thirst • Polyuria • Altered sleep–wake cycle	*Cranial autonomic symptoms*: • Lacrimation • Nasal stuffiness • Rhinorrhea • Aural fullness • Abnormal taste • Sensation of throat swelling
Aura phase			
Visual aura: • Flashes of light • Brightly colored spots • Zigzag lines • Foggy vision • Blind spots	*Brainstem aura*: • Dysarthria • Vertigo • Tinnitus • Hypoacusis • Diplopia • Ataxia • Decreased level of consciousness	*Sensory-motor aura*: • Tingling • Numbness • Paresthesia • Weakness	*Speech and language*: • Word-finding difficulty *Retinal*: • Monocular positive, or negative visual symptoms
Headache phase			
Gastrointestinal symptoms: • Nausea • Vomiting • Abdominal pain	*Sensory hypersensitivity*: • Phonophobia • Photophobia • Osmophobia • Allodynia • Neck stiffness	*Vestibular symptoms*: • Vertigo • Dizziness • Imbalance	*Cranial autonomic symptoms*: • Dizziness • Visual blurring • Conjunctival injection • Conjunctival tearing • Ptosis • Eyelid swelling • Nasal stuffiness • Rhinorrhea • Aural fullness • Pupillary change • Facial flushing • Facial sweating • Taste disturbance
Postdromal phase			
Cognitive/Mood/Energy: • Fatigue • Intolerant/Irritable • Yawning • Emotional • Difficulty with thoughts • Difficulty reading or writing • Difficulty with speech • Concentration difficulties • Mood changes	*Autonomic*: • Dizziness • Pale face • Constipation/Diarrhea • Frequent urination • Hunger/Food craving • Thirst	*Gastrointestinal symptoms*: • Nausea/Vomiting • Flatulence • Abdominal pain • Anorexia	*Sensory hypersensitivity*: • Neck stiffness • Phonophobia • Photophobia • Head discomfort • Movement sensitivity

aura and before the onset of pain in migraine without aura. Previous studies report its occurrence in 8–87% of adults and 67% of pediatric patients with migraine.[15]

Prodromal symptoms can be broadly divided into increased sensitivity to sensory stimuli, cognitive and behavioral changes, homeostatic and hormonal alterations, and cranial autonomic symptoms.[14] Neck discomfort was the most commonly reported symptom in a recent study by Messina et al., and 39% of patients experienced the neck discomfort early in the premonitory stage. Early activation of

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TABLE 2: Brain areas and neurochemical systems implicated in non-headache symptoms of migraine.

Non-headache symptoms	Brain areas implicated	Neurochemicals implicated
Fatigue	Several cortical regions, hypothalamus, and LC	NA, orexins, and DA
Neck discomfort	PAG, TCC, hypothalamus, and thalamus	CGRP, neuronal NOS, NA, DA, and glutamate
Photophobia	Occipital cortex and thalamus	CGRP, neuronal NOS, NA, DA, and glutamate
Nausea	Rostral dorsal medulla and PAG	DA, serotonin, Ach, histamine, and substance P
Yawning	Hypothalamus	DA
Thirst, polyuria	Hypothalamus	ADH and orexins
Food cravings	Hypothalamus, BG, and limbic system	NPY, orexins, and CCK
Cranial autonomic symptoms	Superior salivatory nucleus	VIP and PACAP
Mood change	Limbic system (CC, insula, amygdala) and caudate nucleus	Serotonin, DA, and NA
Difficulty in concentration and memory disturbances	Frontal cortex, caudate nucleus, anterior temporal lobe, and hippocampus	DA, NA, and serotonin

(Ach: acetylcholine; ADH: antidiuretic hormone; BG: basal ganglia; CGRP: calcitonin gene-related peptide; CC: cingulate cortex; CCK: cholecystokinin; DA: dopamine; LC: locus coeruleus; NA: noradrenaline; NOS: nitric oxide synthase; NPY: neuropeptide Y; PAG: periaqueductal grey; PACAP: pituitary adenylate cyclase-activating peptide; TCC: trigeminocervical complex; VIP: vasoactive intestinal peptide)

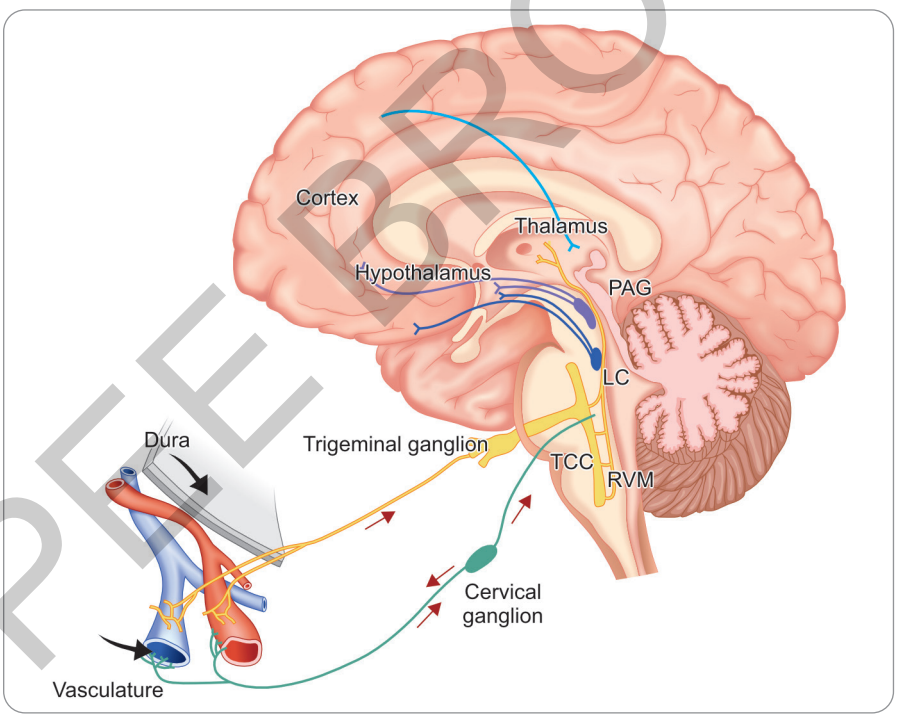

FIG. 1: Pathophysiology of migraine symptomatology. Sensory afferents from the head and neck region, along with the nociceptive input from the cranial vasculature and dura, converge in the trigeminocervical complex (TCC) located in the brainstem through the trigeminal and cervical ganglia. Numerous ascending and descending connections project to the rostroventral medulla (RVM), locus coeruleus (LC), periaqueductal grey (PAG), hypothalamus, thalamus, and cerebral cortex.

the TCC before the ascending input to the thalamus, where the headache presumably arises, explains its occurrence before the headache.[6] Previous studies also reported yawning, mood changes, lethargy, and light sensitivity in the order of decreasing frequency.[15] According to Giffin et al., tiredness or fatigue was the most common, reported in 72% of patients, followed by difficulty with concentration (51%) and stiff neck (50%). A high number of patients experience photophobia (49%), phonophobia (38%), and nausea (24%) as well, in the premonitory period continuing through the headache phase to the postdrome.[11]

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Photo- and phonophobia showed the highest co-occurrence, which might represent their common origin, whereas yawning had a high co-occurrence with many other symptoms such as lethargy, craving, and mood changes. Prodrome was more common in females. 72% of the patients could correctly predict headache onset within 72 hours based on premonitory symptoms; yawning had the highest predictability.[11,15]

Symptoms during the Aura Phase

A migraine aura is a transient and reversible visual, sensory, or other neurological symptom that classically precedes a migraine headache, occurring in about 30% of patients. Aura can be visual, sensory, speech/language, motor, brainstem, or retinal. Individual symptoms can last 5–60 minutes and >60 minutes if there is more than one aura symptom.[16]

Visual aura accounts for 98–99% of all migraine auras, whereas sensory and language disturbances occur respectively in 36% and 10% of cases. Visual auras are usually seen in isolation, whereas the other symptoms co-occur.[17]

In a systematic review of clinical features of visual aura by Michele Viana et al., commonly reported visual aura included foggy, blurred vision or dimness (25–54%), zigzag or jagged lines (24–81%), scotoma (23–77%), phosphenes (small bright dots 19–70%), flashes of bright light or star-shaped figures (16–38%), flickering light (12–91%), hemianopia (7–22%), black dots (3–17%), and visual snow (7%).[18]

A Brazilian study on 122 migraines with aura patients showed blurred vision (54.1%) and small bright dots (47.5%) more common, whereas the frequencies of classic zigzag or jagged lines (41.8%) and the typical "C" crescentic shape were low (16.4%).[19]

Visual snow is a rare phenomenon characterized by alterations in the visual field, which persists even when the eyes are closed. Hypermetabolism of the right lingual gyrus and the anterior lobe of the left cerebellum was found in patients with visual snow in a [18F]-fluorodeoxyglucose positron emission tomography (PET) study.[20]

An auditory aura includes tinnitus, music, or noises; a sensory aura as tingling, numbness, or paresthesias; and a motor aura can present as hemiparesis. Language aura is rare and can occur as word-finding difficulty or trouble understanding words. The prevalence of these less common auras varies widely in different studies.

Most frequently reported brainstem aura includes dysarthria, vertigo, tinnitus, hyperacusis, diplopia, ataxia, and decreased level of consciousness. A recent review has suggested cortical localization of brainstem aura to vestibular cortex, temporo-parieto-occipital junction, posterior and superior parietal lobe, and temporal-insular regions. Retinal aura can be repeated, with monocular, positive, or negative visual symptoms, and is considered rare. The pathophysiology is reversible retinal vasospasm, retinal spreading depression, or both. Recent reports include alien hand syndrome, gelastic aura, and auditory or olfactory hallucinations.[16]

SYMPTOMS DURING THE HEADACHE PHASE

In 99% of cases, the headache phase coexists with non-headache symptoms. Most premonitory symptoms became more prevalent during the headache phase, except yawning, hunger or food cravings, and increased energy. In a recent study by Messina et al., difficulty concentrating was the most frequently reported non-headache symptom during the headache phase (87%).[6]

About 70–80% of migraine sufferers have nausea, and 30% experience vomiting, followed by anorexia and delayed gastric emptying.[21] Patients with gastrointestinal symptoms from migraines may have autonomic nervous system dysfunction. Patients with frequent nausea during migraines are twice as likely to develop chronic migraines than those with less frequent nausea.[22,23]

Around 70–90% of migrants have sensory hypersensitivity, including photophobia, phonophobia, osmophobia, and allodynia, in conjunction with the headache phase. At least one cranial autonomic symptom may be present in 74% of the population, with 70% having two or more. Lacrimation (45.5%), conjunctival injection (34.5%), eyelid edema (34%), aural fullness (27.5%), facial sweating (25%), facial flushing (17.5%), nasal congestion (9%), rhinorrhea (5%), and ptosis (4%) were the symptoms most frequently observed. About 30–50% of migraine patients report associated vertigo, dizziness, or imbalance. The vertigo can be spontaneous or positional.[24,25]

Symptoms during the Postdrome

The migraine postdrome is a constellation of symptoms occurring after the acute headache has subsided. This entity is yet to be defined in the ICHD. In a cohort of 827 individuals, studied by Kelman, 68% of the patients reported postdrome symptoms. The average duration of the postdrome was 25.2 hours. Tiredness (71.8%), headache (33.1%), cognitive difficulties (11.7%), hangover (10.7%), gastrointestinal symptoms (8.4%), mood changes (6.8%), and weakness (6.2%) were the most prevalent symptoms.[26]

The most prevalent individual postdrome symptoms were asthenia (55%), tiredness (46%), somnolence (29%), concentration difficulties (28%), phonophobia (27%), photophobia (26%), unhappiness (26%), and yawning (24%). Giffin et al., in a recent study, found that 97 individuals (81%) had at least one non-headache symptom during the postdrome, including fatigue/weariness (88%) and difficulty concentrating (56%) in that order, as well as stiff neck

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(42%).[9] Postdrome effects disappear in 93% of attacks within 24 hours following headache relief. There was no connection between the duration of the postdrome and the intensity of the migraine or the use of medication.[27]

MIGRAINE VARIANTS

Episodic syndromes that may be associated with migraine, also called migraine variants, are recurrent, periodic, paroxysmal disorders in children and adolescents. These episodic syndromes are diagnosed after excluding other conditions and are characterized by sudden onset, spontaneous resolution without permanent sequel, and may or may not be associated with headaches. In a pediatric migraine cohort, 9.8% had migraine variants, of which 10–70% had coexisting migraine. The most common types were benign paroxysmal vertigo (BPV) (38%), acephalgic migraine (29%), abdominal migraine/cyclic vomiting syndrome (CVS) (19%), benign paroxysmal torticollis (BPT) (10%), and confusional migraine (5%).[28,29] **Table 3** summarizes the salient features of important migraine variants.

TABLE 3: Salient features of important migraine variants.

Migraine variant	Important clinical characteristics
Benign paroxysmal vertigo	• Less than 4 years, equal in boys and girls • Disabling vertigo without provocation or prodrome • Lasts for seconds to minutes • Pallor and sweating, vomiting, and nystagmus • Electroencephalography shows no epileptiform activity
Benign paroxysmal torticollis	• Without premonitory symptoms • Head tilt with rotation • Pallor, agitation, irritability, and vomiting • Lasts hours to days, 2–3 times/month • Spontaneous and stereotypic • Attacks may remain one sided or alternate sides • The attacks frequently cease by age 3 or 4
Cyclic vomiting syndrome	• Age of onset is 5 years. Male–female ratio is equal • Recurrent episodes of severe vomiting usually beginning in the early morning, stereotypical recurring intervals • Self-limited and often ends at puberty • Premonitory abdominal pain, anorexia, or nausea the night before • Episodes may last hours to days (24–40 hours), average 12 episodes/year • Characteristic for each patient nausea, anorexia, abdominal pain, headache, phonophobia, photophobia, lethargy, pallor, and less frequently, diarrhea, and fever
Abdominal migraine	• Children with a positive family history of migraine • Stereotypical recurrent paroxysmal bouts of abdominal pain, separated by periods of wellness • Pain is sore, dull, and periumbilical in location • Severe enough to interfere with normal activity, lasts at least an hour • Associated pallor, anorexia, and nausea and vomiting
Hemiplegic migraine	• Familial or sporadic • Fully reversible motor weakness or fully reversible visual, sensory and/or speech/language symptoms • Associated other neurological features such as ataxia, epilepsy, periodic paralysis, retinitis pigmentosa, sensorineural deafness, essential tremor, and nystagmus • History of the more usual forms of migraine • Family history of migraine

COMORBIDITIES IN MIGRAINE

An important aspect of migraine heterogeneity is comorbidity with other neurological diseases, cardiovascular disorders, and psychiatric illnesses.

Psychiatric Illness

Psychiatric comorbidities are more common in migraine with aura than without aura, depressive disorders being the most common. Patients with psychiatric comorbidities are at high risk of transformation into chronic migraine. Identification of comorbidity will help in improved patient management. Migraineurs are two to four times more likely to experience severe depression in their lifetime. The pathophysiology of this comorbid association remains unknown, but genetic factors, serotonergic dysfunction, ovarian hormone influences, and hypothalamic–pituitary–adrenal axis dysregulation are implicated.[30]

Migraine patients are reported to have a higher risk of comorbid bipolar disorder and seem to more likely to have a rapid cycling illness course. Anxiety is more prevalent in chronic migraine patients than in those with episodic migraine, and it is two to five times as common in migraine patients overall. The risk of developing generalized anxiety disorder was higher in migraine patients, increased with headache frequency.[4]

Other Neurological and Cardiovascular Diseases

Sleep disruptions are linked to migraine type and intensity, indicating their strong and significant association.

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Insomnia, sleep-related breathing disorders (such as obstructive sleep apnea), sleep-related movement disorders (such as restless leg syndrome), central disorders of hypersomnolence (such as narcolepsy), circadian rhythm-related sleep-wake disorders, and parasomnia are all linked to migraine.

Both migraines and epilepsy share several systemic symptoms, including olfactory dysfunction, nausea, vomiting, and visual and other sensory problems. CSD, the pathophysiological hallmark of aura, further suggests that excessive neuronal activity causes the recruitment of larger populations of rhythmically firing neurons, which in turn causes epileptic seizures.

Migraine is thought to increase the risk of cardiovascular disease as well. People with migraine with aura are more likely to experience ischemic, hemorrhagic, and subclinical ischemic strokes. Oral contraceptive use, smoking, female, and older age are all possible risk factors for ischemic stroke among migraineurs.[31]

DIFFERENTIAL DIAGNOSIS

Non-headache symptoms of migraine, especially aura, should be differentiated from other causes of transient neurological symptoms such as transient ischemic attack (TIA), seizures, and syncope. The main differentiating features are listed in **Table 4**.

MANAGEMENT OF NON-HEADACHE SYMPTOMS IN MIGRAINE

Patients with vascular risk factors should be evaluated along the lines of TIA, including MRI of the brain with angiography, when non-headache symptoms in form of aura occur abruptly. If there is a seizure suspicion, electroencephalography (EEG) can be performed and a thorough cardiac workup for syncope.

Non-headache symptoms can be challenging to treat since they resolve spontaneously before the drugs have a chance to start working. Many patients may not require treatment if their symptoms are short-lasting. The potential effect of acute and preventive treatments on non-headache symptoms has been poorly investigated. The adverse effects of several acute migraine treatments, such as acetaminophen, nonsteroidal anti-inflammatory drugs, and triptans, might be similar to the non-headache symptoms such as nausea, dizziness, paresthesia, and somnolence. Only one study looked at whether acute migraine treatments could reduce non-headache symptoms, it found that triptans had no effects on such symptomatology during the postdromal phase.[9] Another recent study found that patients who received treatment with monoclonal antibodies targeting the calcitonin gene-related peptide (CGRP) pathway experienced relief in non-headache symptoms, like irritability and mood swings as well. Additionally, this study

TABLE 4: Differential diagnosis of non-headache symptoms in migraine.

Characteristics	Non-headache aura symptoms of migraine	Transient ischemic attack	Seizure	Syncope
Age and gender	More common in younger age and females	More common in older age and males	No age or gender predilection	Any age
Clinical presentation	• Both positive and negative symptoms • Visual the most common • May evolve into other modality (spreading character) visual to somatosensory • No complete loss of consciousness • Mental slowing and confusion	• Predominantly negative symptoms • Maximum at onset • No spreading character • Loss of consciousness is rare	• Predominantly positive symptoms • Loss of consciousness and amnesia for event common • Postictal negative symptoms may persist for hours to days	• Light-headedness, darkening of vision, or muffled hearing • Brief period of impaired awareness
Onset and duration	• Gradual on set progressive over 5 minutes • Last for 20–60 minutes • Can be prolonged and recur anytime	• Abrupt onset and gradual recovery (minutes) • Last for minutes to <1 hour • Recur over days or weeks	• Brief <2 minutes • Can recur anytime	• Brief seconds to less than a minute • Can recur anytime
Other features	Headache can precede, co-occur, or follow the non-headache symptoms	Headaches may occur, usually during the attacks	• Tongue bite, incontinence • Postictal-myalgia, confusion, and headache	Sweating, pallor, nausea, and rapid and complete recovery

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demonstrated that anti-CGRP monoclonal antibodies could delay the onset of non-headache symptoms in addition to pain.[32] The use of acute and prophylactic medications for migraine management can be planned so as to help treating the non-headache symptoms and comorbidities. For example, use of antiemetics for nausea and vomiting, avoiding ergots in patients with aura, and use of parenteral medications when patient has vomiting. With respect to prophylactic drugs presence of comorbidities in a given patient can be considered for appropriate selection of drugs (e.g., depression, obesity, asthma, etc.).

CONCLUSION

Many non-headache symptoms and comorbidities of migraine have a significant negative impact on the quality of life. Early recognition and management of non-headache symptoms is important. Given the clinical consequences, further research must be done to specifically study these issues from a therapeutic point of view, to improve the quality of migraine patient care.

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