MIGRAINE- THE PREVENTABLE KILL JOY HEADACHE

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INTRODUCTION

Headache is any pain or discomfort in the head and face, but strictly it is any pain above the orbitomeatal line. [1,2] Headache is described as primary when it is the disease whereas it is described as secondary when it is the symptom of another disease. The majority of headaches (over 90%) are primary.

Migraine is derived from the Greek word *hemicranium,* meaning 'unilateral' because it presents as unilateral headaches about 60% of the time. It has no known direct cause and so it is a primary headache syndrome and only second to tension headache in terms of prevalence. [1]

WHO global burden of disease, injuries and risk factors (GBD) in 2016 listed migraine among the five leading causes of disability with 45.12 million years lost to disability (YLD) and earlier in 2015 it was listed among the three leading causes of disability in under 50s. [3,4]

Prevalence is as high as 20% in adult population of 20 to 40 years of age; less common in children under 15 years and adults after 40 years of age. However, the proportion of those with auras (focal cortical symptoms that precede headache) is found to be relatively higher with advancing age after 40 years. Migraine is more prevalent than diabetes and bronchial asthma combined with a female to male ratio of 3:1. Not less than 13 variants of migraine are described in the international classification of headache disorders third edition (ICHD-3).

Migraine may be disabling but like other primary headaches, it however lends itself to treatment with excellent prognosis if diagnosed and properly characterized.

This review looks at migraine with the tenor of increasing awareness to its burden and increasingly excellent prognosis with better understanding of its biology and available pharmacologic arsenal.

CLASSIFICATION

The International Classification of Headache Disorder third edition (ICHD-3) of the International Headache Society is used. It is a 14 part classification system and migraine is described in part 1 of it.

Broadly migraine could be episodic or chronic

Episodic headache occur for less than 15 days in a month.

Chronic headache occur for at least 15 days in a month for at least 3 consecutive months or up to 180 days in a year.

1. Migraine

1.1 Migraine without aura

1.2 Migraine with aura

1.2.1 Migraine with typical aura

1.2.1.1 Typical with headache

1.2.1.2 Typical 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, otherloci

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1.2.3.2 Sporadic hemiplegic migraine (SHM)
1.2.4 Retinal migraine
1.3 Chromic 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 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
16.2 Benign paraoxysmal vertigo
1.6.3 Benign paraoxysmal torticollis

https://ichd-3.org/1-migraine

· from the international headache society (www.ih-s.org)

PATHOPHYSIOLOGY

Migraine is a multiphasic syndrome with headache as its most prominent phase and it has increasingly become known from functional and structural neuroimaging that the brain of the migraineur is functionally and structurally different from the normal which is believed to have a strong genetic basis from current originator and translational research.

Premonitory phase: This heralds the spectrum of migraine attack with food cravings or yawning or disturbed sleep, all pointing to the hypothalamus as the neuronal substrate. It may last up to 24 hours or more before the auras begin.

Aura Phase: This presents with visual symptoms of scintillating light flashes of zig-zig lines that appears episodically and described as fortification lines or teichopsia that last about 20 to 30 minutes. The neuronal substrate is the occipital cortex with cortical spreading depression as the underlying mechanism.

Headache phase: This is described as unilateral in 60% and severe in 80% of cases with pulsatile or throbbing quality and lasts for at least 4 hours and may be up to 72 hours. It is mediated by branches of the trigeminal, greater and lesser occipital nerves from C1, C2 , C3 upper cervical nerves from the nociceptors in the pain bearing structures of the cranium and pericranium. These nerves are believed to be activated centrally from the hypothalamus in response to triggers with the release of Calcitonin Gene Related Peptide(CGRP) peripherally which in turn leads to the release of inflammatory pain mediators like substance P, bradykinin and prostaglandins. The associated activation of the parasympathetic nervous system as evidenced by the release of Vasoactive Intestinal Polypeptide (VIP) causes vasodilation which together with the inflammation described above underpin the neuronal substrate for the headache phase of migraine. The demonstration of increased CGRP, a marker of trigeminal nerve stimulation and VIP, a marker of parasympathetic nervous system in blood during the attacks of headache has corroborated the mechanisms described above.

Postdrome phase: This usually follows the headache phase and may present with fatigue, lack of concentration and last for a few days.

SEMIOLOGY

Migraine attacks may begin with exposure to triggers. Common triggers are stress and poor sleep. Less common triggers include menstruation, chocolates, red wines and nitrate containing drugs. Premonitory symptoms like yawning, poor concentration and food cravings may precede the headache phase for a few days. The association of sleep, stress, menstruation and near predictable onset of symptoms make the hypothalamus a central substrate in migraine. With the exposure to a trigger, the attack is set on in the hypothalamus which in turn activates a peripheral trigeminovascular stimulation that cascades the pain pathway

centrally through the thalamus to the sensory cortex.

Headache usually begins on waking up in the morning, described as throbbing or pulsatile in nature and of severe intensity in 80% of cases, unilateral or hemicranial in 60% and bilateral in 40%. It is preceded by auras in about 20% of cases, which are focal cortical symptoms that are usually visual, like light flashes (also called zig-zag lines or fortification spectrum or teichopsia). Less commonly auras could also be sensory symptoms or speech abnormalities like dysarthria, brain stem symptoms and rarely motor weakness and usually they last for 20-30 minutes. The transient nature of auras could confuse them with vascular transient ischaemic attacks (TIA) but the gradual buildup of auras may help to differentiate them from TIA which are sudden and abrupt in onset and equally brief.

A third of patients have gastrointestinal symptoms like nausea and or vomiting and when there is associated photophobia and or phonophobia the diagnostic certainty that the headache is migraine is shored up to as high as 90%.

Headache of migraine usually last at least 4 hours and may be as long as 72 hours and are characteristically disabling being aggravated by routine physical activity of walking, talking and climbing of staircase which force the patient to sit or lie still in a quiet and light subdued environment. These features differentiate migraine from cluster headaches and other disabling primary headaches. There could be associated allodynia (pain provoked by a harmless stimulus) in the upper part of the torso from the dress worn with patients preferring to be clothes bare. Headache is followed by postdromal symptoms like fatigue, yawning and poor concentration for few days which are similar to the early premonitory symptoms, all pointing to the hypothalamus as the neuronal substrate (vide supra)

DIAGNOSIS

This is purely clinical. Neuroimaging is done to exclude a secondary headache when there is a possibility of another diagnosis. [1,2]

The ICHD-3 of the International Headache Society criteria is used in the diagnosis.

MIGRAINE WITHOUT AURA

Diagnostic criteria

A. At least five attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following four features:
    1. unilateral location
    2. pulsating or throbbing quality
    3. moderate or severe pain intensity
    4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
D. During headache at least one of the following:
    1. nausea and or vomiting
    2. photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis

MIGRAINE WITH AURA

Diagnostic criteria:

A. At least two attacks fulfilling criteria B and C

B. One or more of the following fully reversible aura symptoms:

1. visual
2. sensory
3. speech and or language
4. motor
5. brainstem
6. retinal

C. At least three of the following six characteristics:

1. at least one aura symptom spreads gradually over 5 or more minutes

2. two or more aura symptoms occur in succession
3. each individual aura symptom lasts 5-60 minutes
4. at least one aura symptom is unilateral
5. at least one aura symptom is positive
6. the aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for by another ICHD-3 diagnosis

https://ichd-3.org/1-migraine

from the international headache society (www.ih-s.org)

TREATMENT

The drug treatment of migraine could be abortive or prophylactic

1. Abortive- Drug options include in order of preference:
   - i. Triptans like Sumatriptan, Frovratriptan, Zolmitriptan which are available as either tablets or as subcutaneous injections or as nasal insufflation plus a NSAID like ibuprofen or naproxen OR
   - ii. ergotamine tatrate/caffeine tablets (Cafergot®) or as injectable dihydroergotamine

2. Prophylactic- This is needed in chronic forms of migraine (more than 15 headache days in a month or 180days in a year). There are pharmacologic and non-pharmacologic approaches to prophylaxis in migraine.
   - a) Pharmacologic options include: Choice depends on tolerability, availability, side effect profile, co-morbidities and affordability.
   - i. Propranolol
   - ii. Verapamil
   - iii. Gabapentin
   - iv. Topiramate
   - v. Leveracetam
   - vi. Pizotifen
   - vii. Amitriptyline
   - viii. Botulinum toxin as subcut injection
   - ix. CGRP antibody, Erenumab as subcut injection

   - b) Non-Pharmacologic measures include cognitive and biofeedback mechanisms where the patient is taught behavioural measures to prevent an attack

PROGNOSIS

Migraine may be disabling enough to warrant prophylaxis, it however does not leave the sufferer with permanent injury. Attacks become less frequent and less severe as patient advances in years and spontaneous remission and conversion of chronic to episodic forms is known. Familial Hemiplegic migraine, a rare variant is associated with weakness that may last for days before full recovery and brainstem migraine is associated with paroxysmal vertigo, vomiting and altered sensorium transiently which can all simulate a more sinister diagnosis but a thorough history and evaluation by a neurologist can unravel such a diagnostic dilemma. [2]

CONCLUSION

Migraine is a primary headache syndrome with a huge level of disability which can both be prevented and treated if properly characterized and where this is difficult at the primary and secondary levels of care, consult to a neurologist is advised to differentiate it from other disabling and life threatening headaches. [7,8]

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