CHAPTER

80

Primary Headache Disorders - An Update

Anup Kr Bhattacharya, Agnibha Maity

Headache is nearly universal symptom with a complex & heterogeneous set of causes. Nearly half of the world's population has an active headache disorders.[1] In the second edition of ICHD -2, headache is divided into secondary disorders, attributable to a specific aetiology and primary disorders without an underlying cause.[2] Primary headache classification is split into three sections: migraine, tension type headache & trigeminal autonomic cephalgia.

MIGRAINE

Migraine is a common disabling primary headache disorder. Epidemiological studies have documented its high prevalence and high socioeconomic and personal ssimpacts. In the global burden of disease survey 2010, it was ranked as the third most prevalent disorder and seventh highest specific cause of disability worldwide. Its prevalence in women far exceeds that of men in adulthood, with female: male ratio 2.8:1, peaking at 3.3:1 between age 40 & 45 years. The female predominance is maintained in the postmenopausal age group.[3-6] Prior to puberty, migraine prevalence is higher in boys than in girls.[7,8] Migraine has two major subtypes. 1.1 Migraine without aura is a clinical syndrome characterised by headache with specific features and associated symptoms. 1.2 Migraine with aura is primarily characterised by the transient focal neurological symptoms that usually precede or sometimes accompany the headache.

Migraine Without Aura: In a population based series up to 12% of individuals with migraine without aura experienced premonitory symptoms.[9] Premonitory symptoms were reported by prospective electronic diary documentation. The most common symptoms were tiredness (72%), difficulty with concentration (51%), and a stiff neck(50%).[10] The most reliable predictors of an attack were yawning, difficulties with speech, difficulties with reading & increased emotion. Premonitory symptoms accurately predicted the onset of migraine headache within 72 hours in 72% of the time. In about 60% of patients the headache is unilateral.[11] Whether unilateral or bilateral, the pain is predominately in the distribution of the first division of the trigeminal nerve. Most commonly the pain tends to be frontotemporal and periorbital, often spreading to parietal and occipital areas. A quarter to a third of patients experience pain in one or both regions of the occiput and neck.[12,13] The relevance of this is paramount. It is not infrequent that the cervical spine is erroneously implicated in generating the pain in primary headache disorders. However involvement of regions of the occiput and neck are consistent with the physiological nociceptive connections which sub serve the head & neck.[14,15] Functionally the trigeminal nucleus extends beyond the traditional nucleus caudalis to the dorsal horn of the high cervical region. The sensory innervations of the superior sagittal sinus are mainly from the ophthalmic i.e. first division of trigeminal. In human volunteers local anaesthetic block of the greater occipital nerve results in modulation of the ipsilateral nociceptive blink response.[16] This is the basis for the therapeutic success of occipital nerve blockade[17] and neurostimulation[18] in headache.

MIGRAINE WITH AURA[19-23]

Recurrent attacks, lasting minutes, unilateral, fully reversible visual, sensory or other CNS symptoms that usually develop gradually and are usually followed by headache and associated migraine symptom.

Diagnostic criteria

A. At least two attacks fulfilling criteria B & C

B. 1 or more of the following fully reversible aura symptoms: 1.Visual 2.Sensory 3.Speech. 4. Motor 5.Brainstem. 6. Retinal.

C. At least two of the following four characteristics:1. At least one aura symptom spreads gradually over >=5 min, and/or two or more symptoms occur in succession.2.Each individual aura symptom lasts 5-60 minutes.3.At least one aura symptom is unilateral.4.Aura is accompanied, or followed within 60 min, by headache.

D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded.

The aura is a complex neurological symptom that occurs usually before the headache, but it may begin after the pain phase has commenced, or continue into the headache phase. Visual aura is the most common type of aura, occurring in over 90% of patients. It often presents as a fortification spectrum: a zigzag figure near the point of fixation that may gradually spread right or left and assume a laterally convex shape with an angulated scintillating edge, leaving absolute or variable degrees of relative scotoma in its wake. Next in frequency are sensory disturbances, in the form of pins & needles moving slowly from the point of origin and affecting a greater or smaller part of one side of the body, face and/or tongue. Less frequent are speech disturbances, usually aphasic but often hard to categorise. When aura includes

motor weakness, disorder should be coded as hemiplegic migraine or one of its sub forms.

MIGRAINE WITH TYPICAL AURA[24-25]

Migraine with typical aura in which aura consists of visual and/or sensory and/or speech/language symptoms, but no motor weakness, and is characterised by gradual development, duration of each symptom no longer than 1 hour, a mix of positive & negative features and complete reversibility.

Diagonistic Criteria

A. At least two attacks fulfilling criteria B & C.

B. Aura consisting of visual, sensory, and/or speech/language symptoms, each fully reversible, but no motor, brainstem or retinal symptoms.

C. At least two of the following four characteristics:

1. At least one aura symptom spreads gradually over >=5 minutes, and/or two or more symptoms occur in succession.
2. Each individual aura symptom lasts 5-60 minutes.
3. At least one aura symptom is unilateral.
4. Aura is accompanied or followed within 60 min by headache.

D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded.

TYPICAL AURA WITH HEADACHE

Migraine with typical aura -- aura is accompanied or followed within 60 min by headache with or without migraine characteristics.

Diagnostic Criteria

A. Fulfils criteria for migraine with typical aura.

B. Headache, with or without migraine characteristics, accompanies or follows aura within 60 min.

TYPICAL AURA WITHOUT HEADACHE

Migraine with typical aura - not associated with headache during next 60 min.

MIGRAINE WITH BRAINSTEM AURA[26-29]

Migraine aura suggestive of originating from the brainstem but no motor weakness.

Diagnostic Criteria

A. At least two attacks fulfilling criteria B-D

B. Aura consisting of visual, sensory and/or speech/language symptoms, each fully reversible, but no motor or retinal symptoms

C. At least two of the following brainstem symptoms:

1. Dysarthia
2. Vertigo
3. Tinnitus
4. Hypacusis
5. Diplopia
6. Ataxia
7. Decreased level of consciousness

D. At least two of the following four characteristics:

1. At least one aura symptom spreads gradually over >= 5 minutes, and/or two or more symptoms occur in succession
2. Each individual aura symptom lasts 5-60 minutes
3. At least one aura symptom is unilateral
4. The aura is accompanied, or followed within 60 minutes, by headache

E. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded.

HEMIPLEGIC MIGRAINE [30-39]

Migraine with aura associated with motor weakness.

Diagnostic Criteria

A. At least two attacks fulfilling criteria B and C

B. Aura consisting of both of the following:

1. Fully reversible motor weakness.
2. Fully reversible visual, sensory and/or speech/language symptoms

C. At least two of the following four characteristics:

1. At least one aura symptom spreads gradually over>=5 minutes, and/or two or more symptoms occur in succession
2. Each individual non-motor aura symptom lasts 5-60 minutes and symptoms last <72 hours
3. At least one aura symptom is unilateral
4. The aura is not accounted for by another ICHD-3 diagnosis and transient ischemic attack and stroke have been excluded

FAMILIAL HEMIPLEGIC MIGRAINE

Migraine with aura including motor weakness, and at least one first-or second-degree relative has migraine aura associated with motor weakness.

Diagnostic Criteria

A. Fulfils criteria for hemiplegic migraine

B. At least one first-or second-degree relative has had attacks fulfilling criteria for hemiplegic migraine.

FAMILIAL HEMIPLEGIC MIGRAINE TYPE 1(F H M 1)

A. Fulfils criteria for familial hemiplegic

B. A causative mutation on the CACNA1A gene has been demonstrated.

FAMILIAL HEMIPLEGIC MIGRAINE TYPE 2(F H M 2)

A. Fulfils criteria for familial hemiplegic migraine

B. A causative mutation on the ATP1A2 gene has been demonstrated.

STATUS MIGRAINOSUS[41]

A debilitating migraine attack lasting for more than 72 hours.

Diagnostic Criteria

A. A headache attack fulfilling criteria B and C

B. Occurring in a patient with migraine without aura and/or migraine with aura, and typical of previous attacks except for its duration and severity

C. Both of the following characteristics:

1. Unremitting for >72 hours

2. Pain and/or associated symptoms are debilitating.

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

MIGRAINOUS INFARCTION[42]

One or more migraine aura symptoms associated with an ischemic brain lesion in the appropriate territory demonstrated by neuroimaging.

Diagnostic Criteria:

A. A migraine attack fulfilling criteria B and C

B. Occurring in a patient with Migraine with aura and typical of previous attack except that one or more aura symptoms persists for >60 minutes.

C. Neuroimaging demonstrates ischemic information in a relevant area

D. Not better accounted for by another diagnosis.

MIGRAINE TRIGGERED SEIZURE

A seizure triggered by an attack of migraine with aura.

Diagnostic Criteria

A. A seizure fulfilling diagnostic criteria for one type of epileptic attack, and criterion B below

B. Occurring in a patient with migraine with aura, and during, or within 1 hour after, an attack of migraine with aura

C. Not better accounted for by another diagnosis.

CYCLIC VOMITING SYNDROME

Recurrent episodic attack of intense nausea and vomiting, usually stereotypical in the individual and with predictable with timing of episodes. Attacks may be associated with pallor and lethargy. There is complete resolution of symptoms between attacks.

Diagnostic Criteria

A. At least five attacks of intense nausea and vomiting, fulfilling criteria B and C

B. Stereotyped in the individual patient and recurring with predictable periodicity.

C. All of the following:

1. Nausea and vomiting occur at least four times per hour

2. Attacks last>=1 hour and up to 10 days

3. Attacks occur >=1 week apart

D. Complete freedom from symptoms between attacks

E. Not attributed to another disorder.

ABDOMINAL MIGRAINE

An idiopathic disorder seen mainly in children as recurrent attacks of moderate to severe midline abdominal pain, associated with vasomotor symptoms, nausea and vomiting, lasting 2-72 hours and with no symptom in between episodes. Headache does not occur during these episodes.

Diagnostic Criteria

A. At least five attacks of abdominal pain, fulfilling criteria B-D

B. Pain has at least two of the following three characteristic:

1. Midline location, periumbilical or poorly localized

2. Dull or 'just sore' quality

3. Moderate or severe intensity

C. During attacks, at least two of the following:

a. Anorexia

b. Nausea

c. Vomiting

d. Pallor

RETINAL MIGRAINE[43]

Repeated attacks of monocular visual disturbances, including scintillations, scotoma or blindness, associated with migraine headache.

Diagnostic criteria

A. At least two attack fulfilling criteria B and C

B. Aura consisting of fully reversible monocular positive and/or negative visual phenomena (e.g. scintillations, scotoma or blindness) confirmed during an attack by either or both of the following:

1. Clinical visual field examination

2. The patient's drawing (made after clear instruction) of a monocular field defect.

C. At least two of the following three characteristics

1. The aura spreads gradually over>5 minutes

2. Aura symptoms last 5-60 minutes

3. The aura is accompanied or followed within 60 minutes by headache.

D. Not better accounted for by another ICHD-3 diagnosis and other causes of amaurosis fugax have been excluded.

PATHOPHYSIOLOGY OF MIGRAINE[44]

Based on clinical symptoms, pathophysiology of migraine can be divided into three phases:

1. The trigger phase characterised by neuronal

hyperexcitibility.

2. The aura phase possibly involving cortical spreading depression and finally

3. The headache phase due to cranial vasodilatation precipitated by activation and sensitization of the trigeminal system at the peripheral and central levels.

Exploring each phase of migraine reveals unique mechanisms and divulges novel therapeutic targets. Sensory fibres innervate the cranial vessels arising from trigeminal ganglion which contain neuropeptides. Trigeminovascular inputs from dural meninges have reflex connections between neurons in the pons in the superior salivatory nucleus and are a part of cranial parasympathetic outflow that in part is mediated through the pterygopalatine ganglion. In addition certain genetic abnormalities may be responsible for altering the threshold to migraine specific triggers in the brain, e.g. mutations of the P/Q type calcium channel gene that plays an important role in familial hemiplegic migraine. The subsequent events following the trigger phase lead to the symptoms observed during the aura and headache phases can be explained on the basis of neurovascular involvement. Clinical & experimental considerations suggest that the pathogenesis of the migraine headache is intimately linked to the trigeminal innervations. When activated following cortical spreading depression causes dilatation of cranial vessels, including arteriovenous shunts. Thus, migraine pain is due to activation of the nociceptors in intracranial structures, in concert with a reduction in the function of endogenous pain control pathways. This nociceptive information from cranial blood vessels is conveyed to central neurons in the trigeminal sensory nucleus that in turn relay the pain signals to higher centres and headache is perceived. In addition trigeminal pathway may get sensitized and release CGRP, this reinforces vasodilatation and enhances the relay of nociceptive impulses to the central nervous system.

MANAGEMENT OF MIGRAINE [45-47]

Managing Aggravating factors:

1. Anxiety & Emotion=Most migraineurs cope well with stresses but many have attacks when they relax. Stress may induce other triggers such as missed meals, poor sleep and muscle tension.

2. Hormonal Triggers=About 50% of female migraine sufferers experience troublesome migraine headaches associated with menstruation. Migraine can worsen in first trimester of pregnancy but improve thereafter. The menopause, oral contraception and hormone replacement therapy can be associated with worsening, improvement or no change in the disorder.

3. Missed meals=May trigger attacks. Regular meals should be encouraged.

4. Specific foods=Less commonly implicated in triggering migraine than is widely believed. A food is a trigger when: A>Migraine onset occurs within 6 hours of intake. B. The effect is reasonably reproducible. C. Withdrawal leads to improvement. Most migraineurs can eat whatever they like as long as they keep up with their energy demands. A few susceptible individuals note a definite relationship between consumption of certain foods, particularly alcohol, and the onset of migraine. The foods may not always trigger an attack but tip the balance when the person is vulnerable.

5. Too much and too little sleep= can both play a role. Sleepless nights results in overtiredness which triggers migraine. Conversely, sleeping in for even half an hour longer than usual, often at the weekend, can trigger migraine. In both cases, the cause of the altered sleep pattern may be the true trigger.

6. Strenuous exercise=Can precipitate an attack in a person unaccustomed to it. This puts many people off exercise when in fact regular exercise may help prevent migraine attacks. This is because it improves blood sugar balance, helps breathing, stimulates the body to release its own natural pain killers and promotes a general sense of wellbeing.

DRUG INTERVENTION (ACUTE)

The evidence base for many acute antimigraine drug is poor. For aspirin/metoclopramide combination the evidence is better and for the triptans it is generally good. Whilst, logically, drug treatment should be selected for each patient according to his or her need. Consequently there is a treatment ladder which begins with drugs chosen because they are safest and cheapest whilst being known to have efficacy. All patients should start on the first step of this ladder. As a general rule all acute drug therapy should be combined with rest and sleep.

STEP ONE: Simple Oral Analgesic ± antiemetic. Recommended analgesic doses for acute migraine are typically greater than standard doses to achieve rapid therapeutic levels against a background of gastric stasis. NSAID + a prokinetic antiemetic: Aspirin 600-900mg up to 4 doses in 24 hours. or Ibuprofen 400-600 mg up to 4 doses in 24 hours or Tolfenamic Acid rapid release 200 mg repeated once if necessary after 1-2 hours or Naproxen 750-825mg with a further 250-275mg up to twice in 24 hours or Diclofenac-potassium 50-100mg repeated up to a total of 200 mg in 24 hours. There is a little evidence for the efficacy of paracetamol alone. For nausea & vomiting :-Prochlorperazine 3-6mg buccal tablet, dissolved between gum & cheek up to twice in 24 hrs OR Domperidone 10 mg up to 4 times in 24 hours. MIGRAMAX (Lysine Acetylsalicylate 1620 mg plus metoclopramide 10 mg per sachet up to three sachets in 24 hours) is a convenient preparation. An alternative to those who cannot tolerate aspirin is Paramax sachets (paracetamol 500 mg plus metoclopramide 5 mg per sachet, up to 3 doses in 24 hours.

Step Two: Rectal Analgesic ± Antiemetic=Diclofenac suppositories 100 mg (upto 200 mg in 24 hours) for pain plus Domperidone suppositories 30-60 mg when needed for nausea or vomiting. Peptic ulcer or lower bowel disease is contraindication to step two. The occurance of diarrhoea during acute migraine may prevent effective use.

Step Three: Specific anti-migraine drugs=The marketed triptans differ in ways that might rationally suggest one rather than another for a particular patient. Clinical trials indicate that they range in comparative efficacy. About 30% of patients fail to respond to any particular one, with nonresponsive attributable to a variety of factors including low and inconsistent absorption, use of medication at wrong time(too early or too late in an attack), inadequate dose and individual biological variability. Triptans should be taken at the start of headache phase. There is increasing evidence of greater efficacy when taken whilst pain is still mild, but triptans appear to be ineffective if administered during aura. SUMATRIPTAN was first launched, and clinical experience of its use is greatest. The 50mg tablet and the rapidly dispersing RADIS 50mg tablet are equally appropriate for first use of triptan. When response to these is inadequate, RADIS 100 mg tablet or 20 mg nasal spray may be used according to preference. Total dosage in 24 hours should not exceed 300 mg orally or 40 mg intranasally. If a rapid response is expected then 6 mg subcutaneously, is the triptan of choice. ZOLMITRIPTAN 2.5mg are also equally effective for first use of triptan. A second dose may be taken for lack of effect after two hours if needed. Total dose in 24 hrs should not exceed 10 mg. Zolmitriptan 5mg nasal spray produces a rapid response and may be useful if vomiting is already occurring since upto 30% is absorbed through the nasal mucosa. Rizatriptan 10 mg are alternative to Sumatriptan 100 mg. The total dose in 24 hrs should not exceed 20 mg. NARATRIPTAN, ALMOTRIPTAN, . ELETRIPTAN, FROVITRIPTAN are other triptans being used in the treatment of migraine.

Ergotamine Tartrate 1-2 mg has shown significantly lower relapse rate which may be due to its prolonged duration of action. STEP 3 is contraindicated if there is uncontrolled hypertension, risk factors for CAD or cerebrovascular disease, advanced age and in children below12 yrs.

Step Four: There is some evidence that the combination of sumitriptan 50 mg and Naproxen 500 mg is superior to either drug alone. Other combinations of STEP ONE+THREE may be worth trying, followed by steps TWO+THREE. In all cases NARCOTICS are not recommended for the emergency treatment of migraine and their use can be associated with delayed recovery. Patient in whom there is potential contraindication to take triptan may benefit from Sumatriptan 6mg S/C or Diclofenac 75 mg I/M which can be given alone or in combination with chlorpromazine 25-50 mg I/M or I/V. Metoclopropamide 10-20 mg or Prochlorperazine 12.5 mg are alternative options but can cause acute dystonia including oculogyric crisis, which can be reversed by Procyclidine 5-10 mg I/M or I/V.

PATIENT WHO PERSISTENTLY EXPERIENCE RELAPSE

There is some evidence that this occurs more in those whose untreated attacks last longer than 24 hrs. Naratriptan, Eletriptan, Frovatriptan are associated with relatively low recurrence rates. Ergomatrine is associated with significantly less relapse. Naproxen or tolfenamic acid may be used pre-emptively if relapse is anticipated.

LONG DURATION MIGRAINE

Migraine lasting longer than 3 days is uncommon (status migrainous). Apparently long duration attacks may be migraine with a superseding tension type headache for which Naproxen or Diclofenac preferable to specific antimigraine drugs.

PROPHYLACTIC TREATMENT OF MIGRAINE

Unfortunately at present there is no cure for migraine. Thus who suffer from frequent migraine attacks may require preventive therapy.

First Line: Beta adrenergic blocker without partial agonism is first line if not contraindicated by asthma, heart failure, peripheral vascular disease or depression. Atenolol 25-100 mg bid is to preferred over metoprolol 50-100 mg and Propanolol LA 80 mg-160 mg bd. Bisoprolol 5-10 mg od may be the choice but evidence of its efficacy is needed. Amitriptyline 10-150 mg daily, at 1-2 hours before bedtime is first line when migraine coexists with : troublesome tension type headache, another chronic pain condition, disturbed sleep or depression. Common adverse effect is dry mouth, sedation, dizziness, nausea.

Second Line: Topiramate 25 mg-50 mg bid and Sodium valproate 300-1000 mg bd are second line. Adverse effect reported for sodium valproate include nausea, asthenia, somnolence, weight gain, alopecia. Liver dysfunction is reported rarely. About 50% patient taking topiramate for migraine experience tingling sensation which usually resolve with continued use.

Third Line: There is some clinical justification for considering other antiepileptics such as Gabapentin 300 mg od -800 mg tds, although evidence of efficacy is far from robust. The most common adverse effect reported are dizziness & sedation. Methylsergide 1-2 mg tds is generally considered to be most effective prophylactic, but is held in reserve. This is partly because of its association with retroperitoneal fibrosis although it is said not to have this side effect in courses of less than 6 month. Beta blockers and Amitriptyline can be used together, and a synergistic effect is claimed for this combination.

Other Drugs Used in Prophylaxis but with Limited or Uncertain Efficacy: Pizotifen and Clonidine widely used for many years but with little clinical trial. Verapamil MR 120-240mg bid also had limited clinical trial evidence of efficacy. SSRI like Fluoxetine 20-40 mg are of uncertain value. Other drugs including lisinopril, montelukast, candesartan, riboflavin and Co-enzyme Q10 show potential benefit but further research is necessary. Onabotulinumtoxin A is licensed for prophylaxis of patients with more than 15 headache days per month, of which at least eight days are with migraine.

Hormone Related Migraine: An effect of hormones on migraine is common, and greater for migraine without aura. Evidence suggests estrogen withdrawal triggers migraine in some women. More than 50% women report an association between migraine & menstruation. Depending on need for contraception, several options can be tried in whatever orders seems appropriate. Prophylaxis should be tried for a minimum of three cycles at maximum dose before it is deemed ineffective.

A. Nonhormonal prophylaxis does not depend on regular menstruation. Mefenamic acid 500 mg tds or qds can be given from the onset of menstruation until last day of bleeding. It is recommended as first line in migraine occurring with menorrhagia and/or dysmenorrhoea.

B. Triptans have been studied in clinical trials of short term prophylaxis of menstrual attack of migraine. The greatest evidence of efficacy is for Frovatriptan for 6 days (5mg bd on day 1, 2.5 mg bd on day 2-6) starting 2 days before the expected onset of migraine.

C. Hormones for menstrual migraine are supplements, if the woman has an intact uterus and is menstruating regularly, no progesterones are necessary. Transdermal estrogen 100 microgram is used from 3 days before onset of mens for 7 days.

D. Combined hormonal contraceptive and the progesterone only oral desogestrel, subdermally implanted etonogestrel and injectable depot progestogens inhibit natural ovarian cycle, which can benefit menstrual migraine.

ADVANCES IN MIGRAINE PREVENTION[48]

While there have been a number of target receptors and molecules identified as potentially related to migraine there is not much progress in relation to therapy..The latest foray in migraine prevention is antibodies either to calcitonin gene related peptide (CGRP) or to its receptor. It is suggested that antimigraine site should reside in areas not limited by the BBB such as intra & extra cranial vessels, dural mast cells and the trigeminal system.

NONDRUG INTERVENTION

1. Improving physical fitness may reduce susceptibility.
2. Relaxation therapy, stress reduction, coping strategies are first line treatments where a specific indication exists.
3. Yoga and medication are said to enhance stress management and appeal to some people.

TRIGENIMAL AUTONOMIC CEPHALGIAS[49-51]

It is now an accepted clinical term, first proposed by Goadsby and Lipton, for a group of primary headaches with pain and autonomic involvement in the facial area of the trigeminal nerve.All these headache syndrome have 2 features in common: short lasting,unilateral,extremely severe headache attacks accompanied by typical autonomic symptoms.

CLUSTER HEADACHE

Cluster headache is a relatively common condition by neurological standards, probably affecting about 1 in 1000 people, although compared to other more common primary headaches, such as migraine, it is clearly rare in clinical practice. Cluster headache is certainly the most prominent and most common of the TACs and is considered one of the most severe pain syndromes in humans—in fact, women have described the headache worse than childbirth.

Diagonistic Criteria

A. At least five headache attacks fulfilling criteria B–D:

B. Severe or very severe unilateral orbital, supraorbital and/or temporal headache attacks, which last untreated for 15–180 minutes. During part (but less than half) of the time course of the cluster headache, attacks may be less severe, less frequent, or of shorter or longer duration.

C. The headache is accompanied by at least one of the following symptoms ipsilateral to the pain:

1. Conjunctival Injection or lacrimation
2. Nasal congestion and/or rhinorrhea
3. Eyelid edema
4. Forehead and facial sweating
5. Miosis and/or ptosis
6. A sense of restlessness and agitation

D. The attacks have a frequency from one every other day to 8 per day

E. History or physical and neurological examination do not suggest any other disorder, and/or they are ruled out by appropriate investigations.

Episodic cluster headache: At least two cluster periods lasting 7 days to 1 year separated by pain-free periods lasting ≥1 month.

Chronic cluster headache: Attacks occur for more than one year without remission or with remission of <1 month.

Probable cluster headache: Attacks fulfilling all but one of the criteria for cluster headache.

Treatment: Many patients with acute cluster headache respond very well to oxygen inhalation. This should be given as 100% oxygen at 10-12L/min for 15-20 min. It appears that high flow and high oxygen content are important. Sumatriptan 6mg S/C is rapid in onset and will usually shorten an attack to 10-15 min.Sumatriptan 20 mg and Zolmitriptan 5mg nasal spray are both effective in acute cluster headache. The choice of preventive treatment in chronic cluster headache depends in part on the length of the bout. A 10 day course of prednisolone,beginning at 60 mg daily for 7 days and followed by a rapid tapper may interrupt pain bout for many patients. Lithium 400-800mg appears to be particularly useful for the chronic form of the disorder. Many experts favor verapamil as first line preventive treatment. Initial dose range 40-

80mg twice daily.Effective dose may be as high as 960 mg/day. Methylsergide 3-12 mg, Topiramate 100-400 mg, Gabapentin 1200-3600mg, Melatonin 9-12 mg are also used for long term prevention of episodic and prolonged chronic cluster headache.

Paroxysmal hemicranias was first described by Sjaastad and Dale and is characterized by relatively short bouts of severe unilateral pain in the orbital and temporal area. The typical attack duration is 10–20 minutes, and the typical frequency is more than 5 attacks per day, but there are reports of between 1 and 40 attacks per day. The age of onset is usually in the twenties, with a 3:1 female to male ratio.

A. At least 20 attacks fulfilling criteria B–D

B. Attacks of severe unilateral orbital, supraorbital or temporal pain lasting 2–30 minutes

C. Headache is accompanied by at least one of the following:

1. ipsilateral conjunctival injection and/or lacrimation
2. ipsilateral nasal congestion and/or rhinorrhea
3. ipsilateral eyelid edema
4. ipsilateral forehead and facial sweating
5. ipsilateral miosis and/or ptosis

D. Attacks have a frequency above 5 per day for more than half the time, although periods with lower frequency may occur

E. Attacks are prevented completely by therapeutic doses of indomethac

F. Attacks are not attributed to another disorder

Treatment: Indomethacin (25-75mg tid) can completely suppress attacks of PH,is treatment of choice.Verapamil an effective treatment for cluster headache,does not appears to be effective for PH.Topiramate useful in some cases. Piroxicam has been used although not effective as indomethacin. Secondary PH has been reported with lesions in the region of sella turcica, including AV malformation, cavernous sinus meningioma, pituitary pathology, epidermoid tumors. Secondary PH patients requires high dose of indomethacin(200mg/day).

SUNCT/SUNA (Short lasting unilateral neuralgiform headache attacks with conjunctival injection & tearing): It is rare primary headache syndrome characterized by severe,unilateral orbital or temporal pain that is stabbing or throbbing in quality.

Diagnostic Criteria: A. At least 5 attacks fulfilling criteria B-D.

B. Attacks of unilateral orbital, supraorbital or temporal stabbing or pulsating pain lasting 5-240 seconds.

C. Pain is accompanied by ipsilateral conjunctival injection & lacrimation.

D. Attacks occur with a frequency 3-200 per day.

E. Attacks are not attributed to another disorder.

Treatment: Therapy of acute attack is not a useful concept bcoz attack is of short duration. However IV Lidocaine which arrest the symptom can be used in hospitalized patients. Long term prevention to minimize disability and hospitalization is goal of treatment. The most effective treatment for prevention is Lamotrigine 200-400mg/day. Topiramate and Gabapentin may also be effective. Carbamazepine, 400-500 mg/day has been reported by patients to offer modest benefit.

Hemicrania Continua: The essential features of hemicrania continua are moderate and continuous unilateral pain associated with fluctuation of severe pain,complete resolution of pain with indomethacin and exacerbation that may be associated with autonomic features, including conjunctival injection, lacrimation and photophobia on affected side.The age of onset ranges from 11-58 years. Women are affected twice as often as men.The cause is unknown.

CHRONIC TENSION TYPE HEADACHE[52]

A disorder evolving from frequent episodic tension – type headache, with daily or very frequent episodes of headache, typically bilateral, pressing or tightening in quality and of mild to moderate intensity, lasting hours to days, or unremitting. The pain does not worsen with routine physical activity, but may be associated with mild nausea, photophobia or photophobia.

Diagnostic Criteria

A. headache occurring on ≥ 15 days per month on average for more than three months (≥ 180 days per year) and fulfilling criteria B through D.

B. Lasting hours to days, or unremitting

C. At least two of the following characteristics:

1. Bilateral Location
2. Pressing or tightening (non-pulsating) quality
3. Mild or moderate intensity
4. Not aggravated by routine physical activity such as walking or climbing stairs.

D. Both of the following:

1. No more than one of photophobia, or mild nausea.
2. Neither moderate or severe nausea nor vomiting

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

Treatment: The pain in TTH can be managed by simple analgesics such as acetaminophen,aspirin,or NSAIDs. Behavioral approaches including relaxation can also be effective. For chronic TTH amitriptyline is the only proven treatment.

MEDICATION OVERUSE HEADACHE[52]

Headache occurring on 15 or more days per months developing as a consequence of regular overuse of acute or symptomatic headache medication (on 10 or more, or

15 or more days per month, depending on the medication) for more than 3 months. It usually, but not invariably, resolves after the overuse is stopped.

A. Headache occurring on 15 or more days per month in a patient with a pre-existing headache disorder.

B. Regular overuse for more than three months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache:

Regular intake for > 10 days per month for > 3 months of ergotamines, triptans, opioids, or combination analgesics, **or** any combination of ergotamines, triptans, simple analgesics, NSAIDs and opioids without overuse of any single drug or drug class alone or when the pattern of overuse cannot be reliably established.

Regular intake for > 15 days per month for > 3 months of simple analgesics (ie, acetaminophen, aspirin, or NSAID).

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

ICHD-3: International Classification of Headache Disorders, 3rd edition; NSAID: nonsteroidal anti-inflammatory drug.

PRIMARY COUGH HEADACHE

It is a generalised headache that begins suddenly, lasts for several minutes, sometimes up to few hours and precipitated by coughing and it is preventable by avoiding coughing. Indomethacin 25-50 mg two to three times daily is treatment of choice.

There are reports cough headache has got a increased propensity for development of cerebrovascular diseases.

PRIMARY EXERCISE HEADACHE

It has features resembling both cough headache & migraine.It may be precipitated by any form of exercise. Often has the pulsatile quality of migraine.Exercise regimen should begin modestly and progress gradually to higher levels of intensity. Indomethacin at daily doses from 25-150 mg is generally effective.

PRIMARY HEADACHE ASSOCIATED WITH SEXUAL ACTIVITY

3 types of sex headache are reported: A dull bilateral ache in head & neck that intensifies as sexual excitement increases; a sudden severe, explosive headache occurring at orgasm; a postural headache developing after coitus that resembles the headache of low CSF pressure. Management can often be limited to reassurance. Propanolol is used, dose varies from 40-200mg/day. An alternative is CCB like Diltiazem 60 mg tid.

CONCLUSION

Our current understanding regarding the primary headache disorder has greatly accelerated in recent years. Clarity in population prevalence of the most common primary headache disorders, TTH & migraine has been restored by eloquent and well designed epidemiological studies like AMPP. Migraine comorbidity, and in particular, its relationship with CVD, has become an intense area of investigation, thanks to large cohort studies of the WHS and PHS increasing clinical and radiologic observations have led to great strides in comprehending mechanisms underlying uncommon primary headache disorders. Finally conceptualising primary headache has led to important reasarch questions addressing disease progression and transformation in multiple realms: clinically, physiologically and anatomically.

REFERENCES

1. Stovner Lj, Hagen K, Jensen R, et al. The Global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalagia* 2007; 27: 193-210.
2. Headache Classification Subcommittee of the International Headache Society. The International classification of headache disorders, 2nd edition. *Cephalagia* 2004; 24:9-160.
3. Stewart WF, Lipton RB, Celentano DD, Reed MI, Prevalence of migraine headache in the United States, Relation to age, income, race, and other sociodemographic factors. *JAMA* 1992; 267:64-69.
4. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalance and burden of migraine in the United States: data from the American Migraine Study II. *Headache* 2001; 41:646-657.
5. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF; AMPP Advisory Group. Migraine prevalence.
6. Abu-Arfeh I, Russell G. Prevalence of headache and migraine in school children. *BJM* 1994; 309:765-769.
7. Mortimer MJ, Kay J, Jaron A. Epidemiology of headache and childhood migraine in an urban general practice using ad hoc, Vahlquist and HIS criteria. *Dev Med Child Neurol* 1992; 34:1095-1101.
8. Blau NJ.Adult migraine:London:Chapman and Hall;1987:3-30.
9. Russell MB,Andersson PG,Iselius L.*Cluster headache* 1996; 36:608.
10. Giffin NJ, Ruggiero L, Lipton RB, Silberstein SD, Tvedkov JF, et al. Premonitory symptoms in migraine: An electronic diary study. *Neurology* 2003; 60:935-40. [Pub Med]
11. Rasmussen BK, Jensen R,Olesen J. Ppulation-based analysis of the diagnostic criteria of the International Headache Society. *Cephalagia* 1991; 11:129-34. [Pub Med]
12. Kalman L. Migraine pain location: A tertiary care study of 1283 migraineures. *Headache* 2005; 45:1038-47. .[Pub Med]
13. Chakravarty A, Mukherjee A, Roy D. Migraine pain location in adult patients from eastern India. *Annals Indian Acad of Neurol* 2008; 11:98-102. [PMC free article] [Pub Med]
14. Kaube H, Keay KA, Hoskin KL, Bandler R, Goadsby PJ. Expression of c-Fos-like immunoreactivity in the caudal medulla and upper cervical spinal cord following stimulation of the superior sagittal sinus in the cat. *Brain Res* 1993; 629:95-102 [Pub Med]
15. Couch JR, Diamond S. Status migraineosus: Causative and therapeutic aspects. *Headache* 1983; 23:94-101. [Pub Med]
16. Busch V, Jakob W, Juergens T, Schulte-Mattler W, Kaube H, May A. Occipital nerve blockade in chronic cluster headache patients and functional connectivity between trigeminal and occipital nerves. *Cephalalgia* 2007; 27:126-14 [Pub Med].
17. Afridi SK, Shields KG, Bhola R, Goadsby PJ. Greater occipital nerve injections in primary headache syndromes-prolonged effects from a single injection. *Pain* 2006; 122:126-9. [Pub Med]

18. Saper JR, Dodick DW, Silberstein SD, McCarville S, Sun M et al. Occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. *Cephalalgia* 2010; 31:271-85. [PMC free article] [Pub Med]
19. Cao Y. Weich KM. Aurora S. et al. Fundamental MRI-BOLD of visually trigerred headache in patients with migraine. *Arch Neurol* 1999; 56:548-554.
20. Charles A and Brennan K. Cortical spreading depression –new insights and persistent questions. *Cephalagia* 2009; 29:1115-1124.
21. Cologno D. Torelli P and Manzoni GC, Migraine with aura: A review of 81 patients at 10-20 years' follow-up. *Cephalagia* 1998; 18:690-696.
22. Cutrer FM Sorensen AG, Weisskoff R.M. et al. Perfusion weighted imaging defects during spontaneous aura *Ann Neurol* 1998; 43:25-31.
23. Eriksen MK Thomsen LL. Andersen I. et al. Clinical characteristics of 362 patients with familial migraine with aura. *Cephalagia* 2004; 24:564-575.
24. Eriksen MK, Thomsen LL and Olesen J. Implications of clinical subtypes of migraine with aura. Headache 2006:46:286-297. Matharu MJ and Goadsby PJ. Post-traumatic chronic paroxysmal hemicranias (CPH) with aura. Neurology 2001:56:273-275.
Morrison DP, Abnormal perceptual experiences in migraine *Cephalagia* 1990; 10:273-277.
25. Silberstein SD. Niknam R. Rozen TD et al. Cluster headache with aura. Neurology 2004; 54219-221. Wijinan CA. Wolf PA. Kase CS. et al. Migraines visual accompaniments are not rare in late life: The Framingham Study. *Stroke* 1998; 29:1539-1543.
26. Ambrosini A. D'Onofrio M, Greco GS et al, Famillial basilar migraine associated with a new mutation in the ATPIA2 gene. *Neurology* 2005; 65:1826-1828.
27. Bickerstaff E. R. Basilar artery migraine Lancet 1961;1:15 Caplan LR. Migraine and vertebrobasilar ischemia. *Neurology* 1991; 4155:61.
28. Enksen MK. Thomsen LL and Olesen. J Implecations of clinical subryptes of migraine with aura. *Headache* 2006; 46:286-297.
29. Kirchman M. Thomsen LL and Olesen J. Basilar-type migraine: Clined epidomlogic and genetic features. *Neurology* 2006; 66:880-886.
30. Ambrosini A, D' Onofrio M, Grieco GS, et al Familial basilar migraine associated with a new mutation in the ATPIA2 gene. *Neurology* 2005; 65:1826-1828.
31. De Fusco M, Marconi R, Silvestri L, et al. haploinusfficiency of ATPIA2 encoding the NA+/K+ pump alpha2 subunit associated with familial hemiplegic migraine type2. *Nat Genet* 2003; 33:192-196.
32. Discharge M, Freilinger T, Eskstein G, et al. Mutation in the neuronal voltage-gated sodium channel SCNIA in familial hemiplegic migraine. *Lancet* 2005; 366:371-377.
33. Dreier JP, Jurkat-Rott K, Petzoid GC, et al. Opening of the blood brain barrier proceeding cortical edema in a severe attack of FHM type II. *Neurology* 2005; 64:2145-2147.
34. Eriksen MK, Thomsen LL and Olesen J. Implications of clinical subtypes of migraine with aura. *Headache* 2006; 46:286-297.
35. Plansen JM, Schytz HW, Larsen VA et al. Hemiplegic migraine aura begins with cerebral hypoperfusion : imaging in the acute phase. *Headache* 2011; 51:1289-1296.
36. Hansen JM, Thomsen LL, Olesen J, et al. Coexisting typical migraine in familial hemiplegic migraine. *Neurology* 2010; 74:594-600.
37. Lizuka T, Takhahashi Y, Sato M, et al. Neurovascular changes in prolonged migraine aura in FHM with a novel ATPIA2 gene mutation *J Neurol Neurosurg Psychiat* 2012; 83:205-212.
38. Jurkat-Rott K, Freilinger T, Dreier JP, et al. Variability of familial hemiplegic migraine with novel AIA2 Na + /K+ATPase variants. *Neurology* 2004; 62:1857-1861. Kirchmann M, Thomsen LL, and Olesen J. Basilar –type migraine: clinical, epidemiologic and genetic features. *Neurology* 2006; 66:880-886.
39. Leo L, Gherardini L, Barone V, et al, Increased susceptibility to cortical spreading depression in the mouse model of familial hemiplegic migraine type-2. *PloS Genet* 2011; 7:el002129.
40. Carroll D. Retinal migraine Headache 1970;10:9-13, Chronicle EP and Mulleners WM. Visual system dysfunction in migraine: A review of clinical and psychological findings *Cephalalgia* 1996; 16: 525-535.
41. Akhtar ND, Murray MA and Rothner AD. Status migrainosus in children and adolescents. *Semin pediatr Neurol* 2001; 8:27-33.
42. Bono G, Minonzio G, Mauri M and Clerrici AM. Complications of migraine: Migrainous infarction *Clin Exp Hyper tens* 2006; 28:233-242.
43. Carroll D. Retinal migraine Headache 1970;10:9-13, Chronicle EP and Mulleners WM. Visual system dysfunction in migraine: A review of clinical and psychological findings *Cephalalgia* 1996; 16:525-535.
44. Prameela B et al., *Sch Acad J Pharm* 2014; 3:285-289.
45. Wikinson M,Williams K,Leyton M.Observations on treatment of an acte attack of migraine.*Res Clin Stud Headache* 1978; 6:141-146.
46. Johnson ES,Ratcliffe DM,Wilkinson M.Naproxen sodium in treatment of migraine. *Cephalagia* 1985; 5:5-10.
47. Bates D,Ashford E,Dawson R,et al.Subcutaneous sumatriptan during migraine aura.Sumatriptan Aura Study Group. *Neurology* 1994; 44:1587-1592.
48. Walter S,Bigal ME CGRP receptor antagonist and antibodies against CGRP and its receptor in migraine treatment.*Br J Clin Pharmacol* 2015; 80:193-19.
49. May A. Cluster headache: pathogenesis, diagnosis & management. *Lancet* 2005; 366:843-855.
50. Drummond PD. Dysfunction of the sympathetic nervous system in cluster headache. *Cephalgia* 1988; 8:181-186.
51. Sjaastad O, Editor. Cluster headache syndrome. London: W.B. Saunder; 1992.
52. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013; 33:629.