Headache – Clinical approach to headache and management of migraine

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Summary

- The majority of headaches are primary headaches with no identifiable cause. Tension type headache is the most common type of primary headache followed by migraine.
- The first step in the diagnosis of headache is the exclusion of a secondary cause. This involves clinical history and examination particularly looking for 'red flags' followed by appropriate investigations.
- Migraine is characterized by attacks of moderate to severe throbbing headaches that are often unilateral in location, worsened by physical activity, and associated with nausea and/or vomiting, photophobia, and phonophobia.
- The degree of impact on daily activities in migraine is significant and is a useful to differentiate it from tension type headaches which does not have a similar significant impact.
- The treatment of migraine includes acute/abortive therapy and preventive therapy. Analgesics and Triptans form the mainstay of acute therapy.

Introduction

Headache is a common and often disabling symptom that affects both sexes and almost all age groups. There are a multitude of causes for headache and a physician, whether in a General practice or a specialist Neurology outpatient, is often faced with the daunting task of correctly identifying the type of headache and treating it appropriately. Fortunately the vast majority of headaches are primary headaches which are often benign in nature and can be successfully managed with analgesics and other medications. It is important however, to be aware of secondary causes of headache because these are often life-threatening and need to be identified promptly and treated optimally.

This review will look at the clinical approach to a person presenting with headache, making a diagnosis and treatment with an emphasis on diagnosis and management of migraine.

Classification of headache

Headaches may be broadly classified into primary and secondary headache (ICHD 3).

Primary headache

Primary headaches are those that do not have an identifiable cause from the clinical examination and subsequent investigation. The majority of headaches (around 90%) fall into this category. A study on the prevalence of headache in the general population found that tension type headache was the most common type of primary headache (78% of patients) followed by migraine (16% of patients).¹ Migraine however is the most common type that presents to the Emergency department of a hospital.²

Secondary headaches

Secondary headaches are those which arise secondary to a cause that can be identified from the clinical history and examination and investigations. There are several identifiable causes – the common causes include sinusitis or ear infections, refractive error, fasting, head trauma and intracranial tumour/infection, subarachnoid hemorrhage etc.

Clinical approach to headache

The first step in the clinical approach to headache is the exclusion of a secondary cause. This involves clinical history and examination particularly looking for 'red flags' followed by appropriate investigations.

The approach to recognizing a secondary cause of headache in a clinical setting involves:

1. History: A careful history that asks relevant

questions is invaluable in detecting a secondary cause.

- 2. Examination: This includes
- i. **Neurological examination** looking for neurological deficits, features of raised intracranial pressure (papilloedema), meningeal signs. Examination of the fundus to look for papilloedema is vital in the evaluation of headache.
- ii. Systemic examination Eg. General build and nutritional status, blood pressure, pulse, fever, skin lesions suggestive of autoimmune disease etc.

Points to note:

• It is useful to have a pathophysiological approach to clinical history and examination where an attempt is made to recognize the structure

involved that causes the headache (intracranial structures like meninges, blood vessel,pericranial structures like sinuses, eyes, temporo-mandibular joint etc.).

• If 'red flags' are detected in the history, these remain red flags even if the examination is normal. This is because many of the secondary causes (subarachnoid hemorrhage, intracranial tumour, cerebral venous thrombosis) may not have any significant clinical finding on examination.

3. Investigations

The decision to investigate a person presenting with headache depends on the clinical setting (if a secondary cause is suspected) and the hospital setting (primary vs. Tertiary care hospital). Investigations are done based on the most likely diagnosis considered after clinical examination (pre-test probability).

The investigations include

- 1. Systemic screen
- Imaging of the brain: The radiological imaging based on the pre-test probability is given in Table 3.
- 3. **CSF study :** It is important to rule out raised intracranial pressure (no papilloedema, no intracranial space-occupying lesion) before doing a lumbar puncture for a CSF study. The decision to do a CSF study is again based on the diagnosis being condidered (pre-test probability). The different aspects of CSF study with relation to the possible diagnosis are given in Table 2.

Table 2: CSF study in evaluation of headache

CSF Study	Diagnosis considered	Features
Pressure	Idiopathic intracranial hypertension	Raised pressure (lateral decubitus position)
RBC	Subarachnoid hemorrhage	Raised RBC count, uniform xanthochromia
WBC	Infections/ inflammatory	Raised WBC count
Glucose	Infections/ malignancy	Decreased in meningitis
Protein	Inflammatory/ infections/ malignancy	Raised protein
Cytology	Malignancy	Atypical cells
Cultures	Infections	

Box 1: Red flags for secondary headache

Red flags are clinical features (history and examination) that are indicative of a secondary cause for the headache. It is important to actively look for and rule out these 'red flags' before a headache can be termed a primary headache.

The important 'red flags' to look for may be summarised using the 'SSNOOP' mnemonic developed by Dr. David Dodick, Mayo Clinic³ (Table 1)

Red flags suggest a secondary cause for headache				
Systemic symptoms	Fever, weight loss			
S econdary risk factors	HIV, Cancer, autoimmune disease			
N eurological symptoms or abnormal signs	Confusion, papilledema, focal neurological signs			
O nset	First or worst headache, sudden/abrupt onset			
O lder age	New onset and progressive headache, especially in middle age >50 yr			
P attern change from previous headaches	Change in attack frequency, severity, clinical features			

Table 3:	Radiological	investigation	based	on	diagnosis
consider	ed				

Diagnosis considered (Pre-test probability)	Radiological investigation	
Migraine?	None	
Tension headache?	None	
Subarachnoid hemorrhage?	CT Brain(P)	
Intracranial hemorrhage?	CT Brain (P)	
Meningitis?	CT (P+C) or MRI (P+C)	
"Space occupying lesion"?	CT (P+C) or MRI (P+C)	
Cerebral venous sinus thrombosis?	MRI (P+C) preferred over CT	
Abbreviations: CT – Computerised tomography, P – Plain, C - Contrast, MRI – Magnetic Resonance Imaging		

PRIMARY HEADACHE

Primary headache is the most common type of headache in the general population. It is essentially headache that does not have an identifiable cause.

Types of primary headache

There are four conditions that are classified under primary headaches (according to the ICHD-3 classification).

- 1) Migraine
- 2) Tension type headaches

3) Cluster headache and other Trigeminal Autonomic Cephalgias (TAC)

4) Other primary headaches

Other primary headaches

- 1) Primary cough headache
- 2) Primary exercise headache
- 3) Primary headache associated with sexual activity
- 4) Primary thunderclap headache
- 5) Cold stimulus headache
- 6) External pressure headache
- 7) Primary stabbing headache
- 8) Nummular headache
- 9) Hypnic headache
- 10) New Daily persistent headache

Migraine

Migraine is a common primary headache disorder characterized by attacks of moderate to severe throbbing headaches that are often unilateral in location, worsened by physical activity, and associated with nausea and/or vomiting, photophobia, and phonophobia. There are two subtypes – migraine with aura and migraine without aura. The diagnostic criteria to identify the type of migraine and treatment are discussed below.

Migraine without aura

This is known as common migraine. It is typically unilateral and lasts 4-72 hours.

Diagnostic criteria

The diagnosis of migraine without aura is made if it fulfils all the following 4 criteria (ICHD-3)

- 1. At least 5 attacks
- 2. Headache lasting 4-72 hours (without treatment)
- 3. Headache with any two of the following:

Unilateral/ moderate to severe intensity/ throbbing quality/ aggravated with physical activity

- 4. Any one of following associated features:
 - Nausea, photophobia or phonophobia

Probable migraine – If any one of the 4 criteria is unfulfilled, it is termed 'probable migraine'.

Secondary causes should be necessarily excluded (examination, imaging when needed) as in all cases of primary headache.

The diagnosis of migraine is not always easy. It should be understood that migraine has a spectrum of attacks – not all attacks may fit into one pattern or meet the criteria for migraine. These headaches may be called probable migraine or episodic tension type headache (ETTH). Such headaches are often lower in intensity and may respond to Triptans. A person suffering from such headaches often does not come to a clinic for medical care.

Box 2: The ID Migraine screen

This is a useful test to screening tool for migraine. If two out of the three questions are answered in the affirmative, the person is likely to have migraine. This test is best for ruling out migraine rather than confirming a diagnosis.⁴

ID Migraine

Yes or no answers to the following questions (If the answers to 2 out of the 3 questions is 'yes', it suggests migraine)

- With your headaches
- 1. Do you have dislike of light?
- 2. Do you have nausea?
- 3. Do your headaches have impact on work, school, recreational activities?

Migraine with aura

Migraine with aura is also known as classical migraine. An aura is a complex of neurological symptoms which usually occur before the start of the headache. It may occasionally continue into the headache phase or even start after onset of headache. The aura is a reversible neurological event. It is often unilateral and spreads slowly.

Auras are of 4 types

- 1) Visual
- 2) Sensory Typical aura
- 3) Speech/ language —
- 4) Others- Motor (hemiplegic), Brainstem (basilar), Retinal (ocular)

Box 3: Diagnostic pearls (migraine without aura)			
These are features that are useful but not necessary for diagnosis of migraine			
Presence of trigger	Menstrual, red wine, weather, stress etc.		
factors			
Location	Headache usually unilateral but may be bilateral in 40%,		
	unilateral pain may shift sides. Neck pain is common,		
Impact on daily activities	Yes, migraine impacts daily activities unlike TTH		
Pattern recognition	Episodic headache with a stable pattern, of more than 6		
	months duration, which is disabling is migraine until proven		
	otherwise		
Stereotyped pattern of	Same pattern of headache, but may vary in same patient across		
headache	time		
Response to triptans	Not necessary, even to ergots		
Family history	Often yes, including motion sickness		
4			

The degree of impact on daily activities in migraine is significant and is a useful to differentiate it from tension type headaches which do not have a similar significant impact.

Tension type headache (TTH) vs. Migraine			
TTH	Migraine		
'Featureless' – does not have the defining features of migraine	Has defining features		
No or minimum impact on daily activities usually	Significant impact		
May be episodic or chronic	Episodic		

Diagnostic features - migraine with typical aura

- 1. One of the three types of typical aura is present visual, sensory, speech with/or language aura
- 2. Two of the following 4 features should be present
- i. At least one aura symptom spreads over 5 minutes, and/or two or more symptoms occur in succession
- ii. Aura lasts 5 to 60 minutes
- iii. At least one aura must be unilateral
- iv. Headache comes along with the aura or follows within an hour

It should be kept in mind that a typical aura as described above occurs only in about 20% of migraineurs and may not occur with every attack.

Visual aura is the most common type of typical aura. The most characteristic is the 'fortification spectrum' where zig-zag lines of lightoccur near the point of fixation which may gradually spread to the right or left. Scotomas or dark spots are also seen.

Diagnostic criteria of other kinds of migraine with aura

Migraine with brainstem aura

- Features of migraine with typical aura *plus* the following
- At least TWO of the following brainstem symptoms Dysarthria, Vertigo, Tinnitus, Hyperacusis, Diplopia, Ataxia, Altered sensorium

Migraine with hemiplegic aura

- Features of migraine with typical aura *plus* the following
- Fully reversible motor weakness lasting <72 hours

Retinal migraine

- Features of migraine with typical aura *plus* the following
- Monocular visual phenomena (positive phenomena scintillations , Negative

phenomena – blindness), which is fully reversible over 5-60 minutes

- Aura spreads over > 5 minutes
- Headache occurs along with aura or within 1 hour

Other types of episodic headache

Menstrual migraine

This is a type of migraine without aura, triggered by menstruation. It is seen in up to $2/3^{rd}$ of women with migraine. They typically usually occur on day -2 to +3 of the menstrual period (where day 1 is the first day of the menstrual period) and occurs in 2 out of 3 menstrual periods. They last longer and are often more severe than other types of typical migraine. Because of its long duration, it must be differentiated from status migrainosus.

Vestibular migraine

This was previously known as migraineassociated vertigo. The patient has vertigo (lasting 5-72 hours) associated with current or past history of migraine headache (+/- aura). 50% of vertigo episodes are associated with headache, photo/phonophobia, and visual aura. The vertigo could be spontaneous or induced by change in position, visual stimuli (large moving visual stimulus like watching a moving car), head motion induced (during head movement).

Complications of migraine

- Status migrainosus Migraine (with or without aura) lasting continuously for more than 72 hours is called status migrainosus. This is by definition a debilitating condition.
- 2. *Migrainous infarction* An ischemic stroke may occur along with an attack of migraine (usually migraine with aura). There is neuroimaging evidence of an ischemic brain lesion in the appropriate territory and other causes of a stroke must be excluded. This is a rare condition.
- 3. *Migraine aura triggered seizure (migralepsy)* Migraine with aura may trigger an attack of seizure during or within 1 hour after the aura. This is also very rare.

TREATMENT OF MIGRAINE

Principles of treatment

Pharmacological therapy is frequently required for treating acute migraine attacks.Treatment of migraine may be divided into:

Acute therapy – Symptomatic/ abortive treatment given at the time or just before onset of headache, to relieve symptoms or to abort a migraine attack.

Preventive therapy – Prophylactic therapy aimed at reducing the frequency and severity of migraine attacks, as well as acute therapy used to abort a migraine attack.

ACUTE THERAPY FOR MIGRAINE

Treatment of the acute attack is aimed at aborting the migraine attack and relieving the symptoms (headache, nausea etc.). In the Indian context and drug availability patterns, we can divide treatment options into 3 levels. Choice of level would depend on severity of attack, nature of occupation, and comorbidities. The 3 levels of treatment are:

First level for non-disabling headaches could be just Paracetamol 1000mg with or without an antiemetic (preparations of Paracetamol with Domperidone 10mg are easily available).

The second level for more severe headaches would be a nonsteroidal anti-inflammatory drug (NSAID). The most commonly used in migraine are Naproxen and Ketorolac. Naproxen is freely available as 250, 275 and 500mg tablets, of which the former is most often used. Ketorolac is available as 10mg tablets. An anti-emetic like Domperidone can be added.

The third level would be triptans (See Box 4-Triptans). Ergots are also effective, but have tendency to be overused. Both ergots and triptans are avoided if the possibility of basilar migraine is being considered. Various triptans are available now. Preparations are available for oral use, nasal spray, skin patch and injectable. Finally if the acute treatments are required regularly more than two times a week, we would recommend re-assessing the patient to consider the possibilities of secondary headaches, tension type headaches and medication overuse headaches.

Category	Medication (with adult dose)	Remarks	Evidence level for effectiveness ⁵
Analgesics	Paracetamol 1000 mg (for non- incapacitating attacks)		A (Definitely effective)
Ergots	DHE nasal spray 2 mg and pulmonary inhaler 1 mg DHE IV, IM, SC - 1mg Ergotamine/caffeine- 1/100 mg	 Contraindicated in Coronary artery disease (CAD) Past stroke Uncontrolled hypertension Pregnancy 	A B (Probably effective)
NSAIDs	Aspirin 500 mg Diclofenac - 50, 100 mg Ibuprofen - 200, 400 mg Naproxen - 250, 275, 500mg Ketorolac - 10, 20mg		A
Triptans	Sumatriptan oral - 25, 50, 100 mg; nasal spray - 10, 20 mg; patch - 6.5 mg; subcutaneous injection- 4, 6 mg Zolmitriptan nasal spray - 2.5, 5 mg; Naratriptan - 1, 2.5 mg Rizatriptan - 5, 10 mg oral 2.5, 5 mg	 Contraindicated in Coronary artery disease (CAD) Past stroke Uncontrolled hypertension Pregnancy 	A
Antiemetics	Domperidone 10mg at onset of symptoms	Usually combined with Paracetamol or NSAID	В

Table:4 Acute	treatment	options	for	migraine	- medications
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PREVENTIVE THERAPY FOR MIGRAINE

Medications for preventive therapy are given in regular doses even when the individual does not have a migraine attack. Preventive therapy is aimed at reducing the frequency and severity of migraine attacks, thus improving the quality of life. A full therapeutic trial may take two to six months.⁶ Table 5 gives a list of the commonly used medications for preventive therapy.

The choice of medication will depend on the acceptable side effect profile and the efficacy in the individual. If a drug from a particular class does not provide relief, a trial of another medication may prove efficacious. Beta blockers, Calcium channel blockers and anticonvulsants like Topiramate are commonly used. Cyproheptadine is useful for preventive therapy in children and adolescents.

When to initiate preventive therapy?

Not every person with migraine requires to be on preventive therapy. Some of the indications to start prophylactic medication are as follows:

- Interference with daily routine despite acute therapy
- More than 3 episodes per month
- Severe, disabling attacks in high functioning individual (even if there is less than 3 episodes per month).
- 10-14 headache days per month
- Adverse effects from abortive therapy
- Motor, brainstem aura or any prolonged aura
- Patient preference
- Overuse of abortive therapy medication

Box 4: TRIPTANS

- Triptans are specific for the treatment of migraine.
- **Timing:** They need to be administered during the aura preceding the headache or immediately after the onset of headache.
- **Mechanism of action:** selective agonists of Serotonin (5-HT) receptors (1B/1D), Block release of Calcitonin Gene Related Peptide (CGRP) which is a vasodilator.
- There is not much to choose between the various triptans in terms of overall efficacy, however some patients who do not respond to one may respond to another.
- Sumatriptan has the advantage of multiple forms of availability including nasal spray. Tablets are available as 25 and 50mg, and Sumatriptan is deemed ineffective if a dose taken immediately does not help.
 Rizatriptan 10mg is also freely available, however if a patient is on Propranolol as prophylaxis then dose of Rizatriptan needs to be reduced by half or more.
- Triptans are contraindicated in
 - Coronary artery disease (CAD)
 - Past stroke
 - Uncontrolled hypertension
 - Pregnancy
- Side-effects: Triptan may be associated with sensations of tightening of throat, chest, jaw, neck, limbs and paresthesia of limbs & mouth, hot/cold sensations. These are attributed to esophageal narrowing due to muscular contraction. If the possibility of an underlying cardiac illness is ruled out, these are usually harmless and reassurance is helpful.

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Category	Adult dose	Main adverse effects
Betablockers Propranolol	Start with 30 to 40mg/ day in divided doses, up to 80 to 160 mg/day	Fatigue, exercise intolerance
Calcium channel blockers Flunarizine	5- 10mg once daily at night	Weight gain
Antiepileptics Divalproate	Start with 125mg once daily night, usual maintenance dose - 250 to 500mg once daily at night	Adverse effects: Liver toxicity, sedation, nausea, weight gain, tremor, teratogenicity, possible drug toxicity
Topiramate	Start with 25mg daily night, usual maintenance dose - 25 to 50mg twice daily	Paresthesia, fatigue, nausea
Antidepressants Amitriptyline	10 to 150 mg per day	Weight gain, dry mouth, sedation
Serotonin		
antagonist Cyproheptadine	0.25 to 1.5 mg per kg (2 to 8 mg daily) Used in children and adolescents	
Botulinum toxin	To be used only by experienced personnel	

Table 5: Some common medications used for preventive therapy of migraine.

Non-pharmacological measures to treat migraine

- Education, identification and avoidance of triggers,
- Adequate hydration
- Regular meals
- Regular sleep, good sleep hygiene
- Stress management, meditation and relaxation
- Holistic approach headache clinics

Illustrative Case Scenarios

The following case scenarios illustrate the approach to a diagnosis and treatment of migraine.

Case Scenario A:

A 32 year old teacher with no known comorbidities, comes with complaints of 8 years duration of intermittent moderately severe headaches, once in about 2 to 3 months, lasting four to five hours, during which she has throbbing on either side, along with significant nausea, occasional vomiting and is unable to tolerate light and sound. She has noticed that this happens most often after missing a meal or sleep deprivation. She does not usually take any medications, but gets relief with one or two tablets of paracetamol which she takes if headache comes when she is working. She has not taken leave due to the headache till now. She has two children, and has completed her family. Her children are 9 and 5 years old, and she has been gaining weight since the first delivery. She is otherwise well adjusted, and has no obvious stressors at home or at work. Her mother and one sister also have intermittent headaches. Her BMI is 34, fundus is normal, there are no cranial nerve deficits, nor any long tract signs.

Questions:

- 1. Is this migraine? What type is it?
- 2. Does she need any investigations?
- 3. Does she need abortive medications?
- 4. Does she need prophylactic medications?
- 5. Does she need to be explained non pharmacological measures? If so, what?

Answers:

- 1. Yes, this is migraine without aura.
- 2. She will not require investigations for the migraine per se, but rather for the weight gain. She will need further questioning and systemic examination for thyroid and other endocrine disorders, and investigations accordingly. She will also need to be asked if there is history suggestive of excessive day time somnolence and snoring, and if yes, we will need to plan a polysomnogram (PSG) to assess if she may have obstructive sleep apnea (OSA).
- 3. She reports relief with paracetamol itself. We can recommend that she takes Paracetamol 1000mg along with Domperidone 10mg at the time of headache. We would not need to consider second or third line at this moment.
- 4. Since her headaches are occasional, and responding to first line abortive treatment, and she has never missed work due to the headaches, it is not necessary to start her on prophylactic therapy.
- 5. All patients should be explained non pharmacological measures. These would include sleep hygiene (improving sleep habits), taking meals on time, adequate hydration (taking enough water) and finding time for meditation, relaxation and exercise. In her case, special emphasis would be on exercise and reduction, and treating any underlying endocrine problems. If she does have history suggestive of OSA, then she would need to be seen by a Pulmonologist who looks after sleep lab. If PSG confirms OSA, then she would be taken up for trial of nocturnal noninvasive positive airway pressure ventilation (CPAP or BiPAP).

Case Scenario B:

A 20 year old college student comes with 3 year history of headaches on the second or third day of the menstrual cycles about once in two to three months. The headaches are throbbing on either side, occasionally bifrontal, along with nausea, phono and photophobia. She takes a tablet of Paracetamol every time, with which she gets relief in half to one hour on most occasions. She has no history suggestive of dysmenorrhea. She is 157 cms tall and weighs 53 kg.

Discussion:

Here the problem is one of "menstrual migraine". In fact she does not report any headaches other than those associated with menstrual cycles. She has partial response to Paracetamol. Options are to use abortive Paracetamol

1000 mg along with Domperidone 10 mg, or to move to one of the NSAID's like Naproxen 250 mg or Ketorolac 10 mg. She would not need prophylactic therapy at the moment. For those with frequent disabling headaches related to menses, intermittent abortive therapy to cover 2 to 4 days of the menstrual cycles with NSAID's (naproxen or ketorolac) twice daily along with domperidone and ranitidine or long acting triptan (naratriptan or zolmitriptan) taken twice daily. In view of the potential problems with hormonal therapy, the option of estrogen progestin contraceptive pill preparations are not used as often only for menstrual migraine prophylaxis.

Case Scenario C:

A 40 year old man presents with 4 years duration of intermittent giddiness lasting several hours to 2-3 days not associated with vomiting or headache. He had had intermittent headaches since high school days which would a throbbing on either side of head lasting few hours, for which he had not taken any consultation. He does have these intermittent headaches even now, but he is more concerned about the episodes of giddiness which come almost every week. During these episodes, he prefers to go and lie down in a dark quiet room. He had no problems with hearing and does not report any tinnitus. He has never required admission to a hospital for these problems but has had to take leave 8 times over the last four years.

Discussion:

This patient would qualify for probably migraine with vertigo. He would need basic evaluation by an ENT specialist to look for peripheral vestibular dysfunction as well. Betahistine, cinnarazine, promethazine are options for symptomatic abortive therapy besides triptans.

The episodes are interfering with social and occupational functioning. Thus he would be a candidate for prophylactic therapy as well. If he were moderately built or obese, then topiramate is a good choice. We start with 25 mg once daily at night and titrate upwards as per requirements up to 50 mg twice daily as migraine prophylaxis. Topiramate is avoided in those with history of glaucoma and renal stones. Divalproate 250 to 500 mg once daily at night is another choice amongst anticonvulsants, but weight gain, menstrual irregularities (polycystic ovaries), hair loss, tremors can sometimes be limiting factors, especially in women. Flunarazine is a calcium channel blocker, also freely available. Used at 5 to 10 mg once daily at night, the main concern is weight gain. For those with sleep problems and anxiety overlay, amitriptyline is also an option. It can be used at smaller doses of 5 and 10 mg once daily at night, occasionally going up to 25 mg. Propranolol is a good short duration prophylactic. It is a non-selective beta blocker, and is contraindicated in those with history of bronchospasm. The advantage of propranolol lies in its lack of sedation, so it is often used in those with increased frequency of headaches in the run up to examinations or any temporary stressful period when they want to avoid sedation. Non pharmacological measures in migraine with vertigo would include vestibular rehabilitative exercises.

CONCLUSIONS

- Distinguish between primary versus secondary headache Look for red flags e.g. SSNOOP
- Among the four groups of primary headache, migraine is the most important
- Treatment options for migraine are acute and preventive
- Behavioral and lifestyle modification are major non-pharmacological interventions for treating migraine.

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