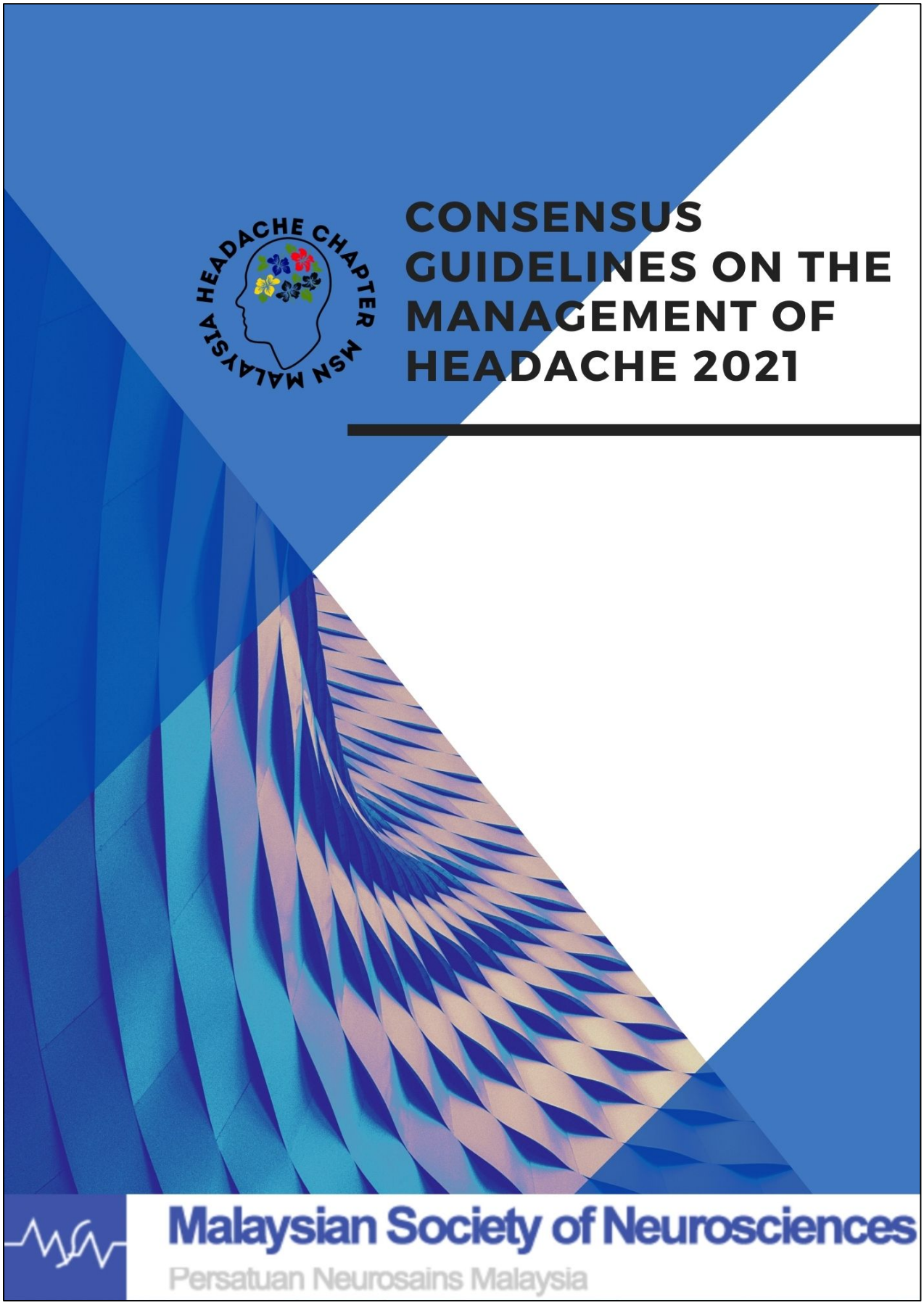
HEADACHE CHAPTER
MSN MALAYSIA
CONSENSUS GUIDELINES ON THE MANAGEMENT OF HEADACHE 2021
Malaysian Society of Neurosciences
Persatuan Neurosains Malaysia

Statement of intent

Standards of medical care are determined on the basis of all clinical data available for an individual case and are subjected to change with the advancements in scientific knowledge, technology and as patterns evolve. These parameters of practice shold be considered as guidelines only and not serve as a standard of medical care. Adherence to these practices will not always guarantee a successful outcome in every case, nor should they be construed as including all proper methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the health care provider in light of all clinical data presented by the patient and the diagnostic and treatment options, available locally.

Foreword

Headaches, as one of the most common neurological disorder encountered and in particular migraine, are among the principal causes of disability worldwide. Therefore, optimal management of headache disorders is important to reduce the burden of disease associated with these disorders.

Since the publication of the first consensus guidelines on the Management of Headache in 2005, major developments have taken place in the available treatment options for headache disorders. In this update of the consensus guidelines, the Headache Chapter of the Malaysian Society of Neurosciences has not only incorporated evidence-based medicine, but also value-based prioritization in the treatment recommendations. The integration of best research evidence with clinical expertise and patient perspectives has made the guidelines practical and useful for all treating clinicians.

I would like to commend and congratulate Dr Shahnaz Merican and the panel of experts for their excellent efforts in producing these updated consensus guidelines. I sincerely hope that the guidelines will help to improve the management of headache disorders and the lives of people living with these conditions.

My best wishes,

Associate Professor Dr. Ai Huey Tan

President

Malaysian Society of Neurosciences

Preface

As President of the Headache Chapter of Malaysian Society of Neurosciences, I am proud to be part of a collaborative team of colleagues, experts in related co-morbid disorders and professionals to produce this update on the first Consensus Guidelines on the Management of Headache 2005.

Ther treatment of people worldwide who experience frequent and disablling headaches has always been challenging and sometimes frustrating as it often requires a lengthy consultation followed by discussion of treatment options and realistic goals to be achieved. In my experience, successful treatment relies on a partnership between the treating physician and the patient. Once the correct diagnosis has been made, the doctor's role to impart knowledge and education is vital, acting as a resource to garner the patient's commitment and empower themselves towards a better quality of life.

Many years of hard work by scientists and researchers have fuelled more understanding in the pathophysiology of migraine headache and has changed treatment options. The molecular era has resulted in novel and exciting treatments, targetted to specific receptors and molecules such as antibodies to CGRP (Calcitonin Gene-Related Peptide) and the CGRP receptor. Neuromodulation therapy with a variety of devices have gained an important role in reducing the burden of headache, although not available in Malaysia.

This document will produce algorithms to aid diagnosis, including codes from the International Classification of Headache (ICHD) 3rd edition. We included as much as possible, treatment options with medication which are available in Malaysia, while also keeping those which have an essential place in treatment guidelines but are unavailable, at this time.

The purpose of the statement, as was in 2005, is to enable informed improved care and treament of people with headache. I want to thank all the members of the panel for their commitment and hard work, and Dr Sonesh Kalra for his invaluable support and enabling the meetings and discussions, especially during times of social distancing in 2020.

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1. GENERAL APPROACH TO A PATIENT WITH HEADACHE

Headache is one of the most common medical complaints reported worldwide. Approximately three billion people have migraine and tension-type headache (TTH). TTH was the third most prevalent and migraine was the sixth most prevalent disorder in 2016[1].

Migraine is a common primary headache disorder affecting more than one billion people in the world[2]. It was the second leading cause of years of living with disability (YLDs) in 2016, contributing 45.1 million of total years of life with disability (YLDs)[1]. Prevalence can vary with age and is at the highest for population under the age of 50 globally. The prevalence for migraine and TTH is 14.4% and 26.1% respectively[1].

Headache and migraine made up 14% of all patient encounters in a survey among neurology practices in Malaysia in 1990. In 2017, headache disorders became the second leading cause of YLDs in Malaysia[3].

The most frequent diagnoses for headache are migraine and tension-type headache (TTH), with the majority of headaches being benign in nature. Headaches caused by intracranial pathology are critically important but less common.

Diagnosis

An accurate diagnosis is essential to plan any necessary investigations and form a management plan.

The first task of a physician is to determine whether the presenting symptoms are part of primary headache disorder or signs of another illness (secondary headache).

A simplified algorithm to rule out the secondary causes is shown below along with a list of red and orange flags in the form of SNNOOP10:

Algorithm 1: Headache diagnosis

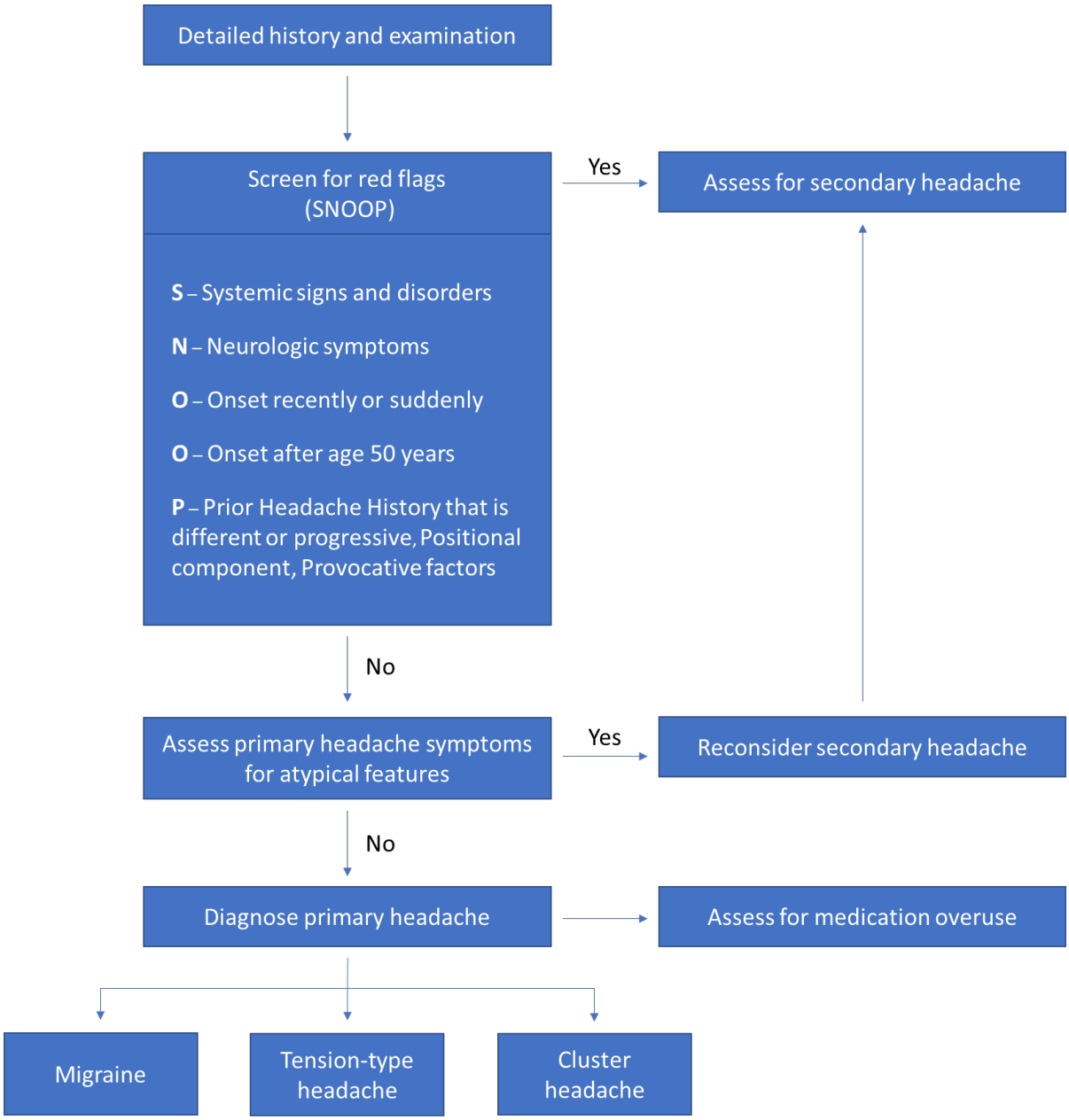


Table 1 SNNOOP10 list of red and orange flags

Sign or symtom	Related secondary headaches (most relevant ICHD-3b categories)	Flag colour
Systemic symptoms including fever	Headache attributed to infection or nonvascular intercranial disorders, carcinoid or pheochromocytoma	Red (orange for isolated fever)
Neoplasm in history	Neoplasms of the brain; metastasis	Red
Onset of headaches is sudden or abrupt	Subarachnoid hemorrhage and other headache attributed to cranial or cervical vascular disorder	Red
Systemic symptoms including fever	Headache attributed to infection or nonvascular intercranial disorders, carcinoid or pheochromocytoma	Red (orange for isolated fever)
Neoplasm in history	Neoplasms of the brain; metastasis	Red
Onset of headaches is sudden or abrupt	Subarachnoid hemorrhage and other headache attributed to cranial or cervical vascular disorder	Red
Older age (after 50 years)	Giant cell arteritis and other headache attributed to cranial or cervical vascular disorders; neoplasm and other nonvascular intracranial disorders	Red
Pattern change or recent onset of headache	Neoplasm, headaches attributed to vascular, nonvascular intercranial disorders	Red
Positional headache	Intracranial hypertension or hypotension	Red
Precipitated by sneezing, coughing or exercise	Posterior fossa malformations; Chiari malformation	Red
Papilledema	Neoplasm and other nonvascular intracranial disorders disorder; intracranial hypertension	Red
Progressive headache and atypical presentation	Neoplasms and other nonvascular intracranial disorders	Red
Pregnancy or puerperium	Headaches attributed to cranial or cervical vascular disorders; postural puncture headache; hypertension-related disorder (e.g. preeclampsia); cerebral sinus thrombosis; hypothyroidism; anemia; diabetes	Red
Painful eye with autonomic features	Pathology in posterior fossa, pituitary region; or cavernous sinus; Tolosa-Hunt syndrome; ophthalmic causes	Red
Posttraumatic onset of headache	Acute and chronic posttraumatic headache; subdural hematoma and other headache attributed to vascular disorders	Red
Pathology of the immune system such as HIV	Opportunistic infections	Red
Painkiller overuse or new drug at onset of headache	Medication overuse headache; drug incompatibility	Red

Abbreviations: ICHD-3b = International Classification of Headache Disorders 3b
An overview of signs and symptoms, their related secondary headache, and distribution in red and orange flags

Table 1: Red flag for headache disorders

A detailed, well-focused history is the most important diagnostic tool. Invest a reasonable amount of time for the history taking of a patient with headache. Patients with 'known' migraine should be carefully reappraised to confirm the accuracy of the diagnosis.

The majority of patients will not volunteer all the symptoms and past history, unless specifically asked for to put all the information together , like pieces of a puzzle, to arrive at a diagnosis, as listed in table 2 below:

Questions	Guide to differentiating features
TIME - Age of onset ***When was the first attack?***	● Migraine frequently begins in childhood, adolescence, or young adulthood. ● TTH can occur at any age. ● Consider another diagnosis if onset is in late adulthood e.g. brain tumours, temporal arteritis, SLE, etc.
- Frequency & patterns ***How often do these headaches occur?*** ***How many attacks do you have in a month?*** ***Do you have more than one type of headache?***	● The longer the headaches have been present in its current form, the more likely they are benign. ● Headaches that become progressively worse or change in character usually indicate possible organic etiology. ● Frequency will help determine degree of severity of migraine and TTH. ● Cluster Headache often occurs during the night, whereas migraine often occurs in the mornings. TTH typically progresses throughout the day.
- Duration ***How long does each attack last?***	● Migraine headaches typically last between 4 - 24 hours but can be present up to 72 hours or longer. ● TTH can be present for days or weeks. ● Secondary headaches due to brain tumours are usually variable in frequency, degree of intensity and occur daily, becoming progressively worse.
CHARACTER - Location ***Where does the pain start?*** ***Where does the pain travel?*** ***Is the pain superficial or deep?***	● Unilateral pain, alternating sides, suggests migraine, but migraine can also be over both temples or is generalised. ● Short lasting, deep and penetrating severe unilateral periorbital pain suggests cluster headache.

	● Bilateral generalised, but sometimes unilateral pain, most severe over the occiput, with neck and shoulder aches suggest TTH. ● Pain from dental, sinus, temporo-mandibular joint (TMJ) or eye disease are usually frontal / facial. Generalised TTH-like headache can occur due to secondary contraction of scalp and facial muscles, causing secondary TTH. ● Pituitary and parasellar tumours frequently cause bitemporal headaches; posterior fossa tumours are often initially posterior but can be generalised. ● Unilateral focal throbbing headache, sometimes with neck pain can be a presenting complaint of carotid artery dissection. There will be associated focal neurological symptoms due to ensuing cerebral ischaemia / infarction. Some may complain of pulsatile tinnitus.
- Intensity ***How severe is the headache?***	● The most severe acute onset headaches are caused by subarachnoid haemorrhage, meningitis, primary thunderclap headache, migraine, cluster headache and malignant hypertension.
- Nature of pain ***Can you describe the pain?***	● Migraine usually throbbing and pulsating. ● TTH usually dull, nagging, tight, constricting or a steady aching pain. ● Cluster headache pain is very severe and is often described as a sharp, burning or piercing sensation on one side of the head. It's often felt around the eye, temple and sometimes face. It tends to affect the same side for each attack. ● Raised intracranial pressure headache is usually described as aching or throbbing in nature.
ASSOCIATED FEATURES ***Do you have any associated symptoms?***	● Visual aura suggests migraine. ● Dizziness and vertigo can be associated with migraine. ● Change in mood or behaviour may be a prodrome associated with migraine, but may also be an associated depression or

	anxiety disorder in migraine or TTH. ● Nausea and vomiting occur with migraine but may also be a feature of raised intracranial pressure from any cause. ● Stiffness of muscles or tender spots suggests TTH or myofascial pain syndrome. ● Restricted neck movements may be a sign of a secondary cervical condition. ● Neck pain and stiffness may be a sign of meningitis. ● Cluster headache is associated with redness, tearing of the eye and runny nose on the affected side.
CAUSES - Predisposing, triggering, aggravating, relieving factors ***What provokes the attack?*** ***What aggravates the pain?*** ***What relieves the pain?***	● Common migraine triggers include fatigue, overwork, relaxation after stress, sleep excess or deprivation, missing meals, menstruation, certain foods and drinks. ● Migraine is aggravated by bright light and sound and physical activity. ● TTH commonly appears during the day or in the evening alone, but can be present all day. ● Both migraine and TTH can be aggravated by stress. ● Headache caused by raised intracranial pressure is commonly worse in the morning and may awaken a person from sleep. It is aggravated by coughing, straining and vomiting. It is commonly associated with vomiting and will progressively lead to further neurological signs and symptoms. ● Headache caused by low intracranial pressure will be aggravated by standing or sitting and relieved by lying down.
- Family history ***Does anyone in the family have similar or recurrent headaches?***	● Migraine is an inherited disorder and frequently a family member is similarly affected.
RESPONSE - Patient's actions and limitations during an attack	● Severe migraine tends to cause irritability and avoidance of company and work responsibilities. An acute, severe attack

How does the pain affect your daily activities?	usually results in the person wanting to be left alone, in a dark quiet room to rest and sleep. ● In TTH, the person is usually able to carry on with daily activities, unless it becomes more chronic and severe.
- Medications used ***Have you responded to any previous treatments?*** ***How often have you needed to take these medications?***	● Ensure that all the medications, including prescribed and over-the-counter drugs are asked about. ● An indication of medication overuse in history is suggested, if pain relief medications are required for more than 2-3 times a week.
INTERVALS - Concerns, anxieties and fears about attacks ***How do you feel between attacks?*** ***Do you have any ideas about your headaches, or any worries?*** ***Why have you come now?***	● Migraine is characterised by headache-free periods between severe attacks. ● Headache secondary to intracranial pathology may not remit and continue to worsen despite use of analgesic medications. ● When headache frequency and severity are worsening, there may be anxiety and worry about the underlying cause.

Table 2: Questions' guide for differentiating features for headache

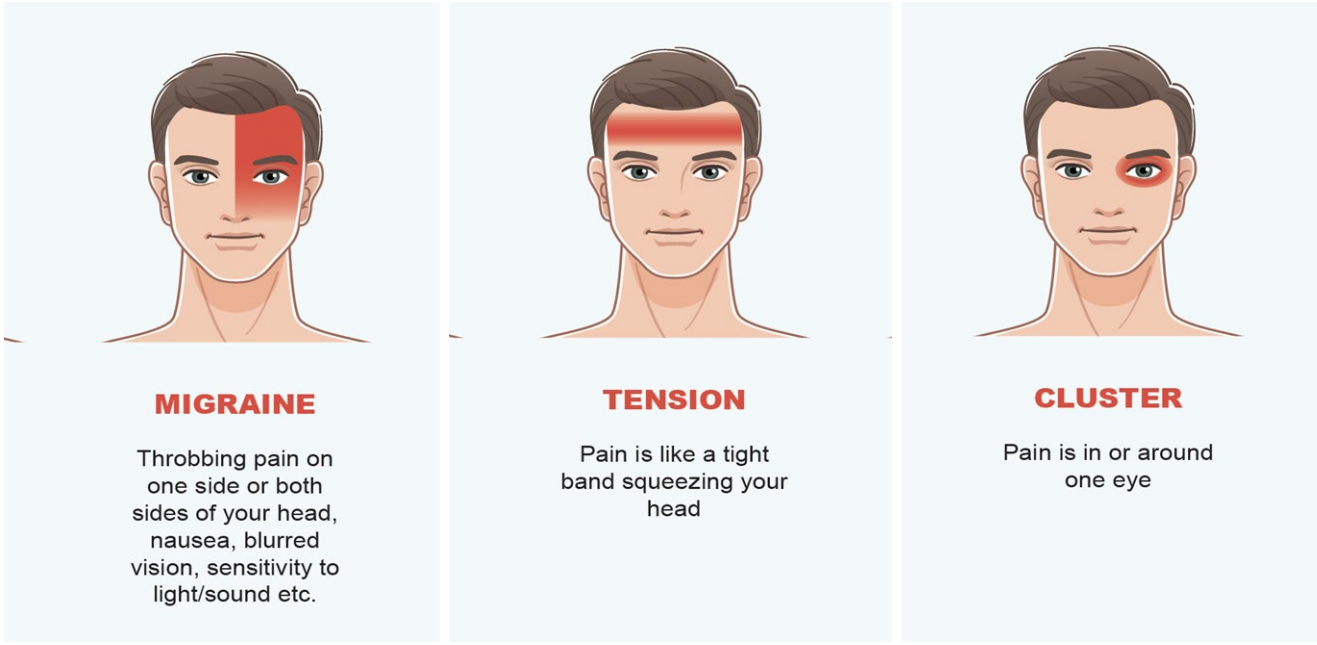
Physical examination

- Observe the patient and note any features that can point to diagnosis. Patient's demeanour may suggest concomitant depression, anxiety or stress.
- If patient is having the headache at time of examination, look for red eye, ptosis, nasal congestion to suggest cluster headache.
- Neurological examination, especially fundoscopy should always be done.
- Blood pressure measurement is recommended.
- Examine head and neck for muscle tenderness, especially in tension-type headache and myofascial pain syndrome.
- Examine jaw and bite and look for signs of teeth grinding.

2. PRIMARY HEADACHES

Three main primary headache disorders are migraine, tension-type headache (TTH) and cluster headache. Some patients can have features of both migraine and TTH.

Patients with medication-overuse headache (MOH) can have variable headache characteristics with features of both migraine and TTH, occurring daily.



MIGRAINE[4]	TENSION-TYPE HEADACHE (TTH)[4]	CLUSTER HEADACHE[4,5]
Moderate-to-severe intensity / pulsating	Mild / moderate intensity / pressing-tightening	Severe intensity
Unilateral	Bilateral	Unilateral, around / behind the eye / temple
4–72 hours	30 mins to 1 week	15–180 mins
Variable frequency	Variable frequency	1–8 times daily during clusters
Nausea, vomiting, phonophobia, photophobia, pain aggravated by activity	±Pericranial tenderness, may be associated with no more than one phonophobia, photophobia or mild nausea, not worsen with activity	Restlessness, ptosis, conjunctival tearing / injection, rhinorrhoea and/or nasal congestion, facial sweating
Affects 2–3 times more women than men[2]	More common in women than men[6]	Affects 3 times more men than women

Figure 1: Summary of type2 of primary headache and its respective features.

General Principles of Treatment of Primary Headache Disorders

- Patient education is of primary importance to ensure compliance to treatment. Time taken to explain and reassure will allay patient anxiety and set realistic goals for treatment.
- Discuss predisposing factors, trigger identification (dietary sensitivities, skipping meals, bright lights) and avoidance, with help of a headache diary (physical or digital). Lifestyle adjustments and medications can modify and control migraine headaches.
- As a general rule, all acute drug therapy should be combined with non-pharmacological treatments.
- Preventive treatment should be started at the lowest possible dose and increased gradually, bearing in mind that most drugs in this category need about 4 weeks to take effect.
- A drug should be optimized as long as it is tolerable. Adding another drug from other drug classes may be useful when there is a suboptimal response or dose limitation due the side effects[7].
- The average duration of treatment of preventive therapy is 3 to 6 months, after which response to treatment should be reviewed for tapering or discontinuation.

3. MIGRAINE

Diagnosis and Classification

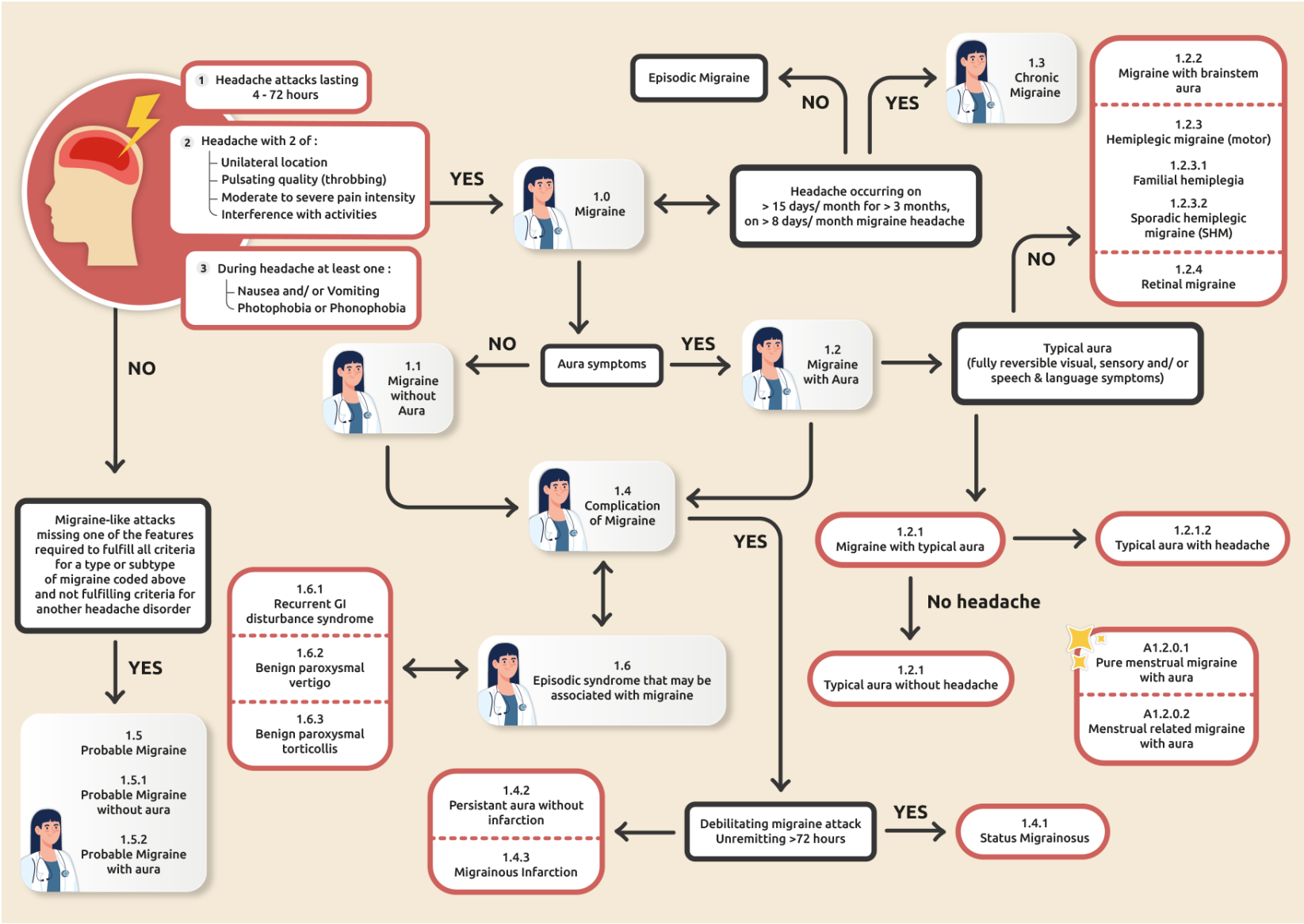
A community-based prevalence study on headache in Malaysia showed that headache is a very common symptom, with a last-year prevalence of migraine of 9.0%. Migraine with aura constituted approximately 10.6% of the migrainous population[8]. Based on headache frequency, Migraine can be divided into[4]:

- Low-frequency episodic migraine (less than 10 headache days per month)
- High-frequency episodic migraine (10-14 headache days per month)
- Chronic migraine (15 or more headache days per month for more than 3 months)

Migraine	Subtypes
Migraine without aura	
Migraine with aura	• Typical aura with headache • Typical aura without headache • Migraine with brainstem aura • Hemiplegic migraine – familial and sporadic • Retinal migraine
Chronic migraine	
Complications of Migraine	• Status migrainosus • Persistent aura without infarction • Migrainous infarction • Migraine aura-triggered seizure

Table 3: Type of migraine and its subtypes

Algorithm 2: Migraine diagnosis



Complications of migraine

1. Status migrainosus

Description:

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.

Remissions of up to 12 hours due to medication or sleep are accepted.

2. Persistent aura without infarction

Aura symptoms persisting for more than one week without evidence of infarction on neuroimaging.

3. Migrainous infarction

Description:

One or more migraine aura symptoms occurring in association with an ischaemic brain lesion in the appropriate territory demonstrated by neuroimaging, with onset during the course of a typical migraine with aura attack.

Diagnostic criteria:

A. A migraine attack fulfilling criteria B and C

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

C. Neuroimaging demonstrates ischaemic infarction in a relevant area

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

Only cerebral infarction occurring during the course of a typical migraine with aura attack fulfils this condition.

4. Migraine aura-triggered seizure

A seizure triggered by an attack of migraine with aura, occurring during or within 1 hour after a migraine attack.

Pathophysiology of Migraine

It is widely accepted that head pain in migraine is caused by stimulation of the trigeminovascular system. There are many theories on the pathophysiology of migraine, the earlier theory being the vascular theory, which was replaced by the neurovascular theory, and further evolved to migraine being the resulting outcome of dysfunction of the brainstem and hypothalamic nuclei[9,10].

The brainstem and hypothalamic nuclei have a role in modulating sensory inputs (touch, lights, sound and smell), and its dysfunction results in the perception of activation of sensory systems under normal circumstances. The same core dysfunction possibly lead to the generation of symptoms via the network of connections between the brainstem and the diencephalic nuclei. The dysfunction can further lead to central desensitization of the trigeminovascular neurons which accounts for the widespread cutaneous allodynia (cephalic and extracephalic).

The thalamus, which acts a meeting point for sensory input that projects to the cortex (via ascending mechanisms) could explain the hypersensitivity to light, sounds and smells. The homeostatic control relating to sleep, feeding and activity by the hypothalamus can be affected by the dysfunction. Genetics also play a role in predisposing patients to migraine susceptibility.

Wnile there is much to be learnt in the understanding of migraine pathophysiology, the progress made since the vascular theory has led to the discovery of several therapeutic classes for migraine treatment; triptans, gepants, ditans, and the calcitonin gene-related peptide (CGRP) receptor antagonists.

Treatment of Migraine

The therapeutic goals of migraine are:

1. Treat the acute attack (rescue or abortive treatment) and
2. Prevent further attacks (prophylactic or preventive treatment)

The patient should be informed of the migraine diagnosis and that it is an inherited tendency to headaches which cannot be cured. Lifestyle adjustments and medications can modify and control migraine headaches. Patient education, usually with the help of a headache diary, and working together with the doctor will lead to a satisfactory outcome.

The doctor can treat the acute attack of head pain in migraine by:

1. Advising avoidance of precipitating factors if present.
2. Nonpharmacologic methods e.g. behaviour feedback, relaxation therapy (See chapter on psychological management)
3. The use of drugs (pharmacologic agents)

PREDISPOSING FACTORS Not always avoidable but may be treatable	**TRIGGER FACTORS** Important in some patients but varies among individuals
Stressful lifestyle	Dietary sensitivities Well recognized - Certain drinks, cheeses, chocolates, citrus fruits, food additives
Depression / anxiety	Relaxation after stress, especially at weekends or on holiday (weekend headache)
Menstruation	Missing meals, too much or too little sleep,

	long distance travel
Menopause	Bright lights, hot sun, heat, loud noise
Head or neck disorders	Strenuous infrequent exercise

Table 4: List of predisposing factors and trigger factors of migraine

Management of acute migraine attack

The treatment options for acute migraine attacks are:

Migraine-specific treatments:

1. Triptans; serotonin 5-HT 1B/1D agonists

Non-specific treatments:

1. Paracetamol and its combination drugs
2. Nonsteroidal anti-inflammatory drugs (NSAIDs)
3. Cyclooxygenase-2 (COX-2) inhibitors
4. Opioids

It is important to emphasise that the overuse of analgesics and migraine-specific medications can be the cause of persisting headache (medication-overuse headache). Other symptoms apart from headache during migraine attack may also warrant treatment.

Drug class	Medication and Dose	Comments
Triptans;	• Sumatriptan 50 – 100 mg PO • Eletriptan 40 mg PO • Naratriptan 2.5 mg PO • Rizatriptan 10 mg PO • Zolmitriptan 2.5 mg PO	- For use in moderate to severe migraine. - Only oral sumatriptan is available in Malaysia. - If headache reduced after first dose but symptoms recur, a second dose can be given within 24 hours but not exceeding 300mg/day.
Paracetamol	• Paracetamol 500 – 4000 mg daily PO	- For mild to moderate migraine.
NSAIDs	• Diclofenac sodium 50 – 75 mg PO or 75 mg IM • Diclofenac potassium 50 – 100 mg daily PO • Ibuprofen 400 – 2400 mg PO • Mefenamic Acid 500 – 1000 mg PO • Naproxen sodium 550 – 1100 mg PO • Dexketorofen 50 mg IV/IM	- For mild to moderate migraine.
COX – 2 inhibitors	• Etoricoxib 120 mg stat PO	- Concerns regarding possible cardiovascular or renal complications

		warrant careful consideration, especially with frequent use and if vascular risk factors are present.

Table 5: Drug therapy for acute migraine attack.

New FDA approved acute migraine drugs: (currently not approved in Malaysia)

- Lasmiditan is a selective 5-HT1F receptor agonist that may play a role in treatment of patients with cardiovascular contraindications to triptans.
- Ubrogepant and Rimegepant are CGRP antagonists that has been proven safe and effective.

Preventive therapy in migraine

Prophylaxis is the mainstay in the treatment of the patient with chronic severe migraine, but it is estimated that preventive therapies are used by only 3 – 13% of migraineurs[11]. Appropriate and adequate use of preventive therapy would improve their quality of life and reduce the hours lost in productivity as well as obviate or reducing the need for acute treatment dugs.

Prophylaxis is indicated when[7]:

1. Attacks significantly interfere with a patient's daily routines despite acute treatment.
2. Frequent attacks (≥ 4 monthly headache days).
3. Contraindication to, failure of, or overuse of acute treatments, with overuse defined as:
    - 10 or more days per month for ergot derivatives, triptans, opioids, combination analgesics, and a combination of drugs from different classes that are not individually overused
    - 15 or more days per month for non-opioid analgesics, paracetamol, and NSAIDs.
4. Side effects with acute treatment.
5. Patient preference.

The choice of preventive medications should be made based on its efficacy and side effects, patient's preference, child-bearing potential in female patients and presence of comorbidities. Preventive treatment can be divided into non-pharmacological and pharmacological and can be used in combination.

Drug class	Medication and Dose	Comments
Beta Blockers	• Propranolol 40 – 120 mg PO • Atenolol 25 – 50 mg PO • Metoprolol 50 – 100 mg PO	- Should not be used in patients with co-existent asthma, severe cardiac insufficiency or Raynaud's phenomenon. - Treatment option in hypertensive patients with migraine.
Angiotensin II-receptor blockers (ARB)	• Candesartan 4 –16 mg PO	- Treatment option in hypertensive patients with

		migraine.
Cyclic Antidepressants (TCA)	● Amitriptyline 10 – 50 mg PO	- Sedating effect of TCA may be beneficial for patients with comorbid insomnia. Common side effects are dry mouth, sedation, blurred vision and constipation.
SNRIs antidepressants	● Venlafaxine XR 75 – 225 mg PO ● Duloxetine 30 – 60 mg PO	- To be taken in the morning. - Patients should be counselled on the possibility of withdrawal. It may be most effective in patients with comorbid depression and migraine.
Calcium Channel Blockers	● Flunarizine 5 – 10 mg PO	- Depression and extra-pyramidal symptoms can occur, usually in elderly.
Anticonvulsants	● Sodium Valproate (immediate release) 200 – 400 mg PO ● Sodium Valproate (modified release) 500 – 1000 mg PO ● Topiramate 25 –100 mg PO	- May cause neural tube defects and teratogenic potential. Do not use in pregnant woman. - Not recommended in patients with liver disease. - Inform patients of side effects of topiramate (tingling of hands, visual blurring, panic attack and depression).
5-HT antagonists	● Pizotifen 0.5 – 2 mg PO	- Avoid abrupt withdrawal.
Botulinum Toxin	● Onabotulinumtoxin A: 155 - 195 units every 12 weeks IM	- For use in chronic migraine. Reduction in headache may only be felt after third treatment.
Monoclonal antibodies targeting calcitonin gene-related peptide (CGRP) receptor	● Erenumab 70 or 140 mg SC monthly	- Favourable tolerability profile, side effect includes injection site reactions and constipation[12.]

Table 6: Drug therapy for prophylaxis in migraine.

Other new CGRP inhibition for prevention of migraine are:

- Fremanezumab 225 mg SC monthly, or 625 mg SC 3-monthly (not available in Malaysia)
- Galcanezumab 240 mg SC once, followed by 120 mg SC monthly
- Eptinezumab IV 100mg every 3 monthly (not available in Malaysia)

Non-pharmacological therapies could play a significant role in migraine treatment for patients who are seeking alternative options for their migraine or patients who are not responding or unable to tolerate pharmacological treatment[13].

Neuromodulation treatments stimulate the nervous system (centrally or peripherally) by modulating the headache pain mechanisms with an electric current or magnetic field. The following non-invasive treatment have been cleared by the US Food and Drug Administration (FDA)[7]:

- Single-pulse transcranial magnetic stimulation (sTMS) for acute treatment
- Electrical trigeminal nerve stimulation (eTNS) for acute and preventive treatment
- Non-invasive vagus nerve stimulation (nVNS) for acute treatment
- Remote electrical neuromodulation for acute treatment

Bio-behavioral therapies such as cognitive behavioral therapy (CBT), biofeedback and relaxation therapies techniques have shown to be useful in treatment of acute and preventive migraine. This can also help with patients who are deficient in stress-coping skills.

Another non-pharmacological treatment such as acupuncture has been shown to reduce the frequency of headache though the evidence is moderate[14].

4. TENSION - TYPE HEADACHE

Diagnosis and Classification

Tension-type headache (TTH) is very common, with a lifetime prevalence ranging from 30% to 78%[4]. It has a high socio-economic impact.

Tension-type headache (TTH)	Subtypes
Infrequent episodic TTH	● Associated with pericranial tenderness ● Not associated with pericranial tenderness
Frequent episodic TTH	● Associated with pericranial tenderness ● Not associated with pericranial tenderness
Chronic TTH	● Associated with pericranial tenderness ● Not associated with pericranial tenderness
Probable TTH	● Infrequent ● Frequent ● Chronic

Table 7: Types of Tension-type headache and its subtype

Infrequent episodic tension-type headache

Diagnostic criteria:

A. At least 10 episodes of headache occurring on < 1 day in a month on average

B. Lasting from 30 minutes to 7 days

Frequent episodic tension-type headache

Diagnostic criteria:

A. At least 10 episodes of headache occurring on 1 – 14 days in a month on average for > 3 months

B. Lasting from 30 minutes to 7 days

Chronic tension-type headache

Diagnostic criteria:

A. Headache occurring on ≥ 15 days in a month on average for > 3 months

B. Lasting hours to days, or unremitting

Pericranial tenderness can be detected and recorded by manual palpation. Local tenderness score may be determined by using small rotating movement with the second and third fingers over the frontal, temporal, masseter, pterygoid, sternocleidomastoid, splenius and trapezius muscles.

Treatment of Tension-type Headache (TTH)

Patient often can self-manage TTH with simple analgesics or non-steroidal anti-inflammatory

drugs (NSAIDs). Episodic TTH is self-limiting but most people consult doctors when it becomes frequent and no longer responds to painkillers. The treatment strategy can be divided into treatment of the acute episode and prophylaxis.

Table 8: Drug therapy for acute attack of tension-type headache

Medication	Daily dose	Comments
Paracetamol	• 500 – 4000 mg PO	
NSAIDs	• Diclofenac sodium 50 – 225 mg PO • Ibuprofen 400 mg PO • Naproxen sodium 275 – 550 mg PO	- Avoid excessive and frequent use to reduce risk of developing medication-overuse headache. - There are no clinical trials supporting the use of COX-2 inhibitors at present.

Only very few of these drugs have been tested systematically using properly classified patients using a placebo-controlled, double blind design

Triptans, muscle relaxants have not demonstrated to be effective in patients with TTH and opioids are not recommended as it may increase the risk of developing medication-overuse headache[15].

Table 9: Drug therapy for prophylaxis treatment of tension-type headache

Medication	Daily dose	Comments
Triptans	• Amitriptyline 10 – 50 mg PO	- Maintain for up to 6 months until remission is achieved, then withdraw. Mechanism of action is independent of its antidepressant actions.

Muscle relaxants & migraine-specific drugs have limited effectiveness and cannot be recommended.

Box 1: Non-pharmacological prophylaxis treatment of tension-type headache.

Prophylaxis treatment (non-pharmacological)
Triggers for TTH including inadequate sleep, sinus disease, shift work, improvement of posture, irregular meals and dental pathology, should be eliminated whenever possible. Furthermore, stress management and an analysis of any psychological trigger or depressive disorder may be of value. TTH is more common in sedentary people and regular exercise may help. Physical therapy is the treatment of choice for musculoskeletal symptoms. Different modalities including hot and cold packs, ultrasound and electrical stimulation, the improvement of posture, relaxation and exercise programmes can be tried but the majority of these have not been properly evaluated. In stress-related illness, lifestyle changes to reduce stress, and relaxation or cognitive therapy to develop strategies for coping with stress, are the mainstays of treatment. Pain management clinics may be able to teach patients how to cope with chronic pain.

5. OTHER PRIMARY HEADACHES

Trigeminal autonomic cephalalgias (TACs) has five headache disorder subtypes which share the clinical features of unilateral headache and prominent cranial parasympathetic autonomic features, which are lateralized and ipsilateral to the headache. Distinction between TACs is important as they respond to different therapies[4].

Other primary headache disorders	Subtypes

Trigeminal autonomic cephalalgias (TACs)	● Cluster Headache (episodic & chronic)
	● Paroxysmal hemicrania
	● Short-lasting unilateral neuralgiform headache attacks
	  ● SUNCT (episodic & chronic)
	  ● SUNA (episodic & chronic)
	● Hemicrania continua

Table 10: Other type of primary headache disorders and its subtypes

1. Cluster headache

Description:

Attacks of severe, strictly unilateral pain lasting from 15 minutes to 3 hours, which is orbital, supraorbital, temporal or in any combination of these sites and may spread to other regions.

The term cluster denotes the fact that the attacks tend to appear in bouts lasting weeks or months separated by periods of remission lasting months to years. There is usually a striking circadian, usually nocturnal and occasionally, a seasonal periodicity. Cluster headache may be episodic or chronic.

Diagnostic criteria:

A. At least 5 attacks fulfilling criteria B – D

B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15 to 180 minutes (when untreated)

C. Either or both of the following:

1. at least one of the following symptoms or signs, ipsilateral to the headache:
    - conjunctival injection and/or lacrimation
    - nasal congestion and/or rhinorrhea
    - eyelid oedema
    - forehead and facial sweating
    - miosis and/or ptosis
2. a sense of restlessness or agitation

D. occurring with a frequency between one every other day to 8 per day

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

1.1 Episodic cluster headache

Episodic cluster headache is when there is at least 2 cluster episodes lasting from 7 days to 1 year and separated by pain-free periods of remission of ≥ 3 months. Normally, clusters last from 2 weeks to 3 months.

1.2 Chronic cluster headache

Chronic cluster headache is when attacks occur for > 1 year or longer without remission or the remission period is < 3 months. Chronic cluster headache may be primary (i.e. chronic from onset) or develop from episodic cluster headache. Some may switch from chronic to episodic cluster headache.

Headache may be triggered by alcohol, and other vasodilator substances such as histamine or nitroglycerin. During attacks, the pain can be excruciating. The pain usually recurs on the same side of the head during a single cluster period. The patients are unable to lie down and characteristically pace the floor.

Treatment for Cluster Headache

Acute attack treatment[16]		
Medication	**Daily dose**	**Comments**
Sumatriptan	● Subcutaneous: 6 mg ● Intranasal spray: 20 mg ● Oral: 50 –100 mg, do not exceed 100 mg/dose	- Only the oral preparation is available in Malaysia. Randomized controlled trials have only been carried out with subcutaneous and intranasal preparations.
Zolmitriptan	● Intranasal: 5 mg ● Oral: 10 mg	- Shown to be effective for episodic cluster headache but not chronic cluster headache. - Not available in Malaysia.
High flow (100%) oxygen	● 12 L/min through a non-rebreathing mask (for 15 minutes)	- Higher flow (up to 15 L/min) may be tried if no response initially. - Beware of risk of respiratory suppression in patients with chronic obstructive airways disease.
Prophylaxis treatment		
Medication	**Daily dose**	**Comments**
Verapamil	● Oral: 240 – 480 mg daily (higher doses may be required)	- Useful for long term prophylaxis, as first line therapy if no contraindications present - Constipation and leg swelling possible side-effects. Baseline and

		serial ECGs for monitoring.
Corticosteroids	● Prednisolone ● e.g. 60 mg daily for 5 days, then reduced by 10 mg every 2 days until discontinued	- Shown to be effective for short term prophylaxis when multiple daily attacks are occurring.
Lithium	● Oral: 900 – 1200 mg daily PO	- Maintain serum level < 1.2 mEq/L. Check serum levels weekly for a month, then monthly thereafter.

Table 11: Drug therapy for cluster headache

2. Paroxysmal hemicrania

Paroxysmal hemicrania has features similar to cluster headache with shorter duration; lasting 2 – 30 minutes, occurring many times a day. It responds absolutely to indomethacin.

Diagnostic criteria:

A. At least 20 attacks fulfilling criteria B – E

B. Severe unilateral orbital, supraorbital and/or temporal pain lasting 2 - 30 minutes

C. Either or both of the following:

1. at least one of the following symptoms or signs, ipsilateral to the headache:
    - conjunctival injection and/or lacrimation
    - nasal congestion and/or rhinorrhea
    - eyelid oedema
    - forehead and facial sweating
    - miosis and/or ptosis
2. a sense of restlessness or agitation

D. occurring with a frequency between of > 5 times per day

E. Prevented absolutely by therapeutic doses of indomethacin.

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

3. Short-lasting unilateral neuralgiform headache attacks are attacks of moderate or severe, strictly unilateral head pain lasting for 1 – 600 seconds as a single stabs/series of stabs, occurring at least once a day and usually associated with prominent lacrimation and redness of the ipsilateral eye.

3.1 SUNCT (Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing) are brief attacks of pain around the eye associated with conjunctival injection and lacrimation.

3.2 SUNA (Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms) are brief attacks of pain around the eye associated with only one or neither of conjunctival injection and lacrimation.

4. Hemicrania continua is a persistent, strictly unilateral headache present for > 3 months of moderate or severe intensity. The headache is responsive to indomethacin.

6. MANAGEMENT OF HEADACHE IN EMERGENCY SETTING

In the emergency department, a precise history is the priority so that the doctor can prescribe effective treatment.

The following important diagnoses to consider are:

1. Identification of secondary causes of headache with red flag symptoms, using SNOOP as a useful guide.
2. Always ask about analgesic intake; prescription and over the counter (OTC) medications to consider medication-overuse headache (MOH) as a cause of frequent severe headaches and treatment advise to stop all rescue medications, and detoxification with or without steroids.
3. Be familiar with the established criteria (ICHD 3) to diagnose primary headaches; tension-type headache, migraine, cluster headache, probable cluster headache.
4. For rapid effect and relief, intravenous or intramuscular route is preferred, and usually one dose is necessary. Always consider presence of allergies and co-morbid illnesses.
5. The use of opioids is not recommended due to its addictive potential, safety concerns and side effects profile (such as nausea and vomiting). Its use can be considered in the presence of allergy to NSAID and other special situations.
6. Make sure recent analgesic intake is known prior to deciding on treatment to avoid repeating medications that are ineffective orally.
7. Ensure patient is well hydrated, commence intravenous fluids if indicated.

Migraine		
Medication	**Dose**	**Comments**
Triptans	● Sumatriptan 6 mg SC	- Best studies and effective but currently not available in Malaysia.
Antiemetics	● Prochlorperazine 12.5 mg IM/IV [17] ● Metoclopramide 10 – 20 mg IV/IM [17]	- Can be considered first line therapy. Highly likely to be effective. Adverse events including akathisia and drowsiness uncommon. Useful for relief of nausea, and doses may be repeated. - Hydration with IV fluids is important especially with repeated vomiting.
Paracetamol	● 1000 mg IV	- Useful, safe with minimal sode effects
NSAIDs	● Ketorolac 30 – 60 mg IM/IV ● Diclofenac 75 mg IM ● Parecoxib 40 mg IM/IV [18]	- Ketorolac – effective but availability may be limited in Malaysia. - Diclofenac – Contraindicated if hypertensive, gastritis,

	• Dexketoprofen 50 mg IV	coronary artery and renal disease. - Parecoxib - useful and effective but aproved for relief of pain (off-label use).
Combinations may be useful although evidence for this is lacking. No indication for **(avoid)** tramadol or other opioids unless allergy is present; caution with inducing severe nausea and sedation[19].		
Corticosteroids	• Dexamethasone 8 – 12 mg IV	- Effective for PREVENTION of RECURRENCE or if migraine continue for > 24 hours. - Safe for acute use only.
Anaesthetic Block	• Greater Occipital Nerve block (Dexamethasone 4 – 8 mg combined with Lignocaine 2% or Bupivacaine 0.5%)	- Performed by Neurologist. - Useful to end severe migraine.

Table 12: Drug therapy for migraine in emergency setting.

Tension-type headache		
Medication	**Dose**	**Comments**
Paracetamol	• 1000 mg IV	- Availability may be limited.
NSAIDs	• Diclofenac sodium 75 mg IM • Ketorolac 30 – 60 mg IM/IV	- Diclofenac – Contraindicated if hypertensive, gastritis, coronary artery and renal disease. - Ketorolac – effective but availability may be limited.
The above treatment can be combined with:		
Medication and Dose		**Comments**
Metoclopramide 10 – 20 mg IV		- Akathisia, oculogyric crisis
Chlorpromazine 10 – 12.5 mg IV (max 37.5 mg) [20]		- Postural hypotension, rarely used.

Table 13: drug therapy for tentison-type headache in emergency setting

Treatment of headache in an emergency setting		
Cluster Headache		
Medication	**Dose**	**Comments**
Acute		
Sumatriptan[1,2]	• Sumatriptan 6 mg SC [21,22] • Sumatriptan 20 mcg intranasal [23]	- Highly effective, not more than twice daily. - Currently not available in Malaysia.
Oxygen[1]	• 100% (10 - 15 L/min) for 10	- Delivered through non-

	- 15 mins [21]	rebreathing face mask and regulator required.
Tramadol	● 50 – 100 mg IV/IM	- Can be useful, with anti-emetic for nausea. Caution with repeated use.
Methylprednisolone	● 500 – 1000 mg (one dose) IV/IM	- Case reports of use effective in severe attacks or resistant cases.
Anaesthetic Block	● Greater Occipital Nerve block (Dexamethasone 4 – 8 mg combined with Lignocaine 2% or Bupivacaine 0.5%)	- Performed by Neurologist. - Useful to end severe migraine.

Table 14: Treatment for cluster headache in emergency setting

Commence preventive treatment to reduce frequency and severity of attacks. Frequent follow-up for patient with active cluster headache is required to ensure that optimum treatment is maintained and to monitor for treatment toxicity.

7. SECONDARY HEADACHES

Identification of secondary headache requires an appraisal of patient specific risk factors; age, comorbidities, associated symptoms, presentation of the headache in relation to the context in which it occurred[24]. Detailed account of onset and progression of the headache is helpful. A potentially serious cause is more likely with a new severe headache compared to a recurrent headache over the course of several years.

Certain pointers in the history and/or examination, may indicate a secondary cause for the headache, and warrants investigations. The mnemonic “SNOOP” helps to detect secondary headache with significant morbidity and mortality (red flags).

While ‘SNOOP’ plays a role in detecting the red flags in patient, other features that do not fit into a primary headache should also be evaluated. Investigations of secondary headaches must be used judiciously based on the history and clinical examination.

Headache features that suggest a secondary underlying cause include[25]:

- Recent onset of headaches
- Headaches of uncertain pattern
- Presence of progressive neurological signs or systemic disturbance (including papilloedema, alteration of conscious level, etc)
- Presence of fever
- Presence of associated epileptic seizures
- A change in an existing headache pattern
- Unusual age of onset for a particular diagnosis

Findings	Rule out
Vital signs	
• Elevated temperature	• Infectious causes, Giant cell arteritis (GCA)
• Elevated blood pressure	• PRES, CVD
• Tachycardia	• Orthostatic hypotension, POTS
• Bradycardia	• Hypothyroidism
• Body mass index > 25	• Idiopathic intracranial hypertension
General	
• Wasted appearance	• HIV, malignancy, GCA
• Joint hypermobility • Skin laxity	• Intracranial hypotension • Intracranial hypertension • Cervical artery dissection
• Hair loss, Dry skin, Edema, Hoarse voice	• Hypothyroidism
• Diaphoresis, Rhinorrhea, Mydriasis, Restlessness, Yawning, Tremor	• Opioid withdrawal
Cardiac	
• Temporal artery tenderness / induration • Diminished / asymmetric pulse • Aortic regurgitation	• GCA
Neurologic	
• Papilledema	• Intracranial hypertension
• Horner's sign	• Carotid artery dissection
• Trigeminal sensation loss	• Trigeminal neuropathy
• Abducens paresis	• Intracranial hypertension • Other focal lesion
• Oculomotor paresis and/or mydriasis	• Intracranial aneurysm, ION • Other focal lesion
Head and Neck	
• Trochlear tenderness aggravated by vertical duction	• Trochlear headache
• Tympanic vesicles	• Herpes zoster
• Hard papule near frenulum or adjacent to 2nd upper molar	• Sialolithiasis
• Restricted neck rotation	• C2/3 facet arthropathy
• Pericranial and/or occipital nerve tenderness	• Trigeminal branch or occipital neuralgia
• Limited TMJ range of motion	• TMJ syndrome

Table 15: List of findings and issues to rule out in diagnosing secondary headache

Onset /duration	Differential diagnoses
Acute severe headache Thunderclap headache – severe in character and reaching maximum severity within seconds or minutes of onset	With neck rigidity • Subarachnoid haemorrhage • Meningitis Without neck rigidity • Pressor responses (pheochromocytoma, reaction while on MAO inhibitors) • Acute obstructive hydrocephalus • Expanding intracranial aneurysm • Intracerebral haemorrhage • Carotid or vertebral artery dissection • Reversible cerebral vasoconstriction (RCVS) • Posterior reversible encephalopathy syndrome (PRES) • Intracranial hypotension • Pituitary apoplexy
Subacute headache	• Expanding intracranial lesion (haematoma, tumour, abscess) • Progressive hydrocephalus • Temporal arteritis • Benign intracranial hypertension
Recurrent discrete episodes of headache or facial pain	• Trigeminal neuralgia • Intermittent obstructive hydrocephalus • Paroxysmal hypertension (pheochromocytoma) • Tolosa-Hunt syndrome • Benign cough, exertional and sex headaches • Cold-stimulus headache (ice-cream headache) • Ice-pick pains • Sinusitis
Chronic headache or facial pain	• Post-traumatic headache • Persistent idiopathic facial pain (PIFP) (atypical facial pain) • Post-herpetic neuralgia

Table 16: Differential diagnosis of headache based on onset and duration

Investigation of headache

Investigations, including neuroimaging and blood tests, do not contribute to the diagnosis of any of the common headache syndromes. They are indicated only when history or examination suggest headache may be secondary to some other condition.

1. Full blood count, ESR and other blood/urine tests

These blood tests are mandatory in patients with fever, or suspicion of infection, and in patients above the age of 55 years whom the possibility of temporal arteritis must be ruled out. The full blood count may also reveal unsuspected polycythemia or leukaemia, both of which may cause headache.

2. Plain radiographs

Skull radiographs are useful in the following conditions:

- Skull fracture
- Temporomandibular joint (TMJ) disease

In addition, raised intracranial pressure may be suspected from the separation of skull sutures in young children and the "beaten-copper" appearance of the cranial vault.

3. Computed axial tomography (CT) of the brain

In patients with recent onset headaches, a brain CT should be requested if the history and/or physical examination suggest the following diagnoses:

- Subarachnoid haemorrhage
- Haemorrhagic stroke
- Intracranial space-occupying lesion

4. Magnetic resonance imaging (MRI) of the brain

Certain lesions can only be visualised or are better seen with MRI (with or without contrast), with MR Angiography or MR Venography as needed for:

- Posterior fossa lesions
- Vasculitis
- Cerebral venous thrombosis
- Arterial dissection
- Arteriovenous malformations (AVMs)
- Reversible cerebral vasocontriction syndrome (RCVS)

5. Lumbar puncture

A lumbar puncture (LP) is indicated in the following situations:

- High clinical suspicion of subarachnoid haemorrhage but brain CT normal
- Diagnosis of meningitis or encephalitis
- Measurement of CSF pressure in idiopathic intracranial hypertension

Where possible, a brain CT should always be performed before the LP[26]. The usual contraindications to a LP should always be observed whether the brain CT is available.

Empirical treatment for meningitis should never be delayed and can usually be started prior to receiving the cerebrospinal fluid (CSF) results.

6. Electroencephalography (EEG)

EEG is not routinely indicated in the evaluation of headache.

8. SPECIAL ISSUES IN HEADACHE

I. Chronic Daily Headache (CDH)

Chronic daily headache (CDH) encompasses headache occurring at least 15 days per month[4] CDH affects 1-4% of the general population[27]. CDH can be divided into primary and secondary CDH. Improper diagnosis of subtypes of headache and patients' self-medication can lead to the transformation of an episodic headache to CDH[28].

One of the ways to manage CDH is to prevent the development of CDH from episodic headache[28,29]. This is achieved by decreasing the number of modifiable trigger factors and identification of patients' comorbid illnesses[28]. In addition, choosing the right medications which are less likely to cause side effects and to start prophylactic treatment to reduce the frequency and the severity of the headache episodes, can help prevent formation of CDH[28].

The management of CDH involves exclusion of secondary headaches, and this is followed by classifying the primary headache disorder[30]. The patient's current acute therapy as well as previous prophylactic therapies should be properly evaluated and assessed[30]. Headache patients are encouraged to maintain a headache diary. A good headache action plan addressing acute treatment, prophylactic therapy and lifestyle factors can be designed for the individuals.

Importance of partnership with patients which may make it possible to convert CDH back to episodic headache responsive to acute and prophylactic therapies, needs to be emphasized[30]. A multidisciplinary approach of headache practices will assist in the management of the patients with CDH[31].

II. Medication-overuse Headache (MOH)

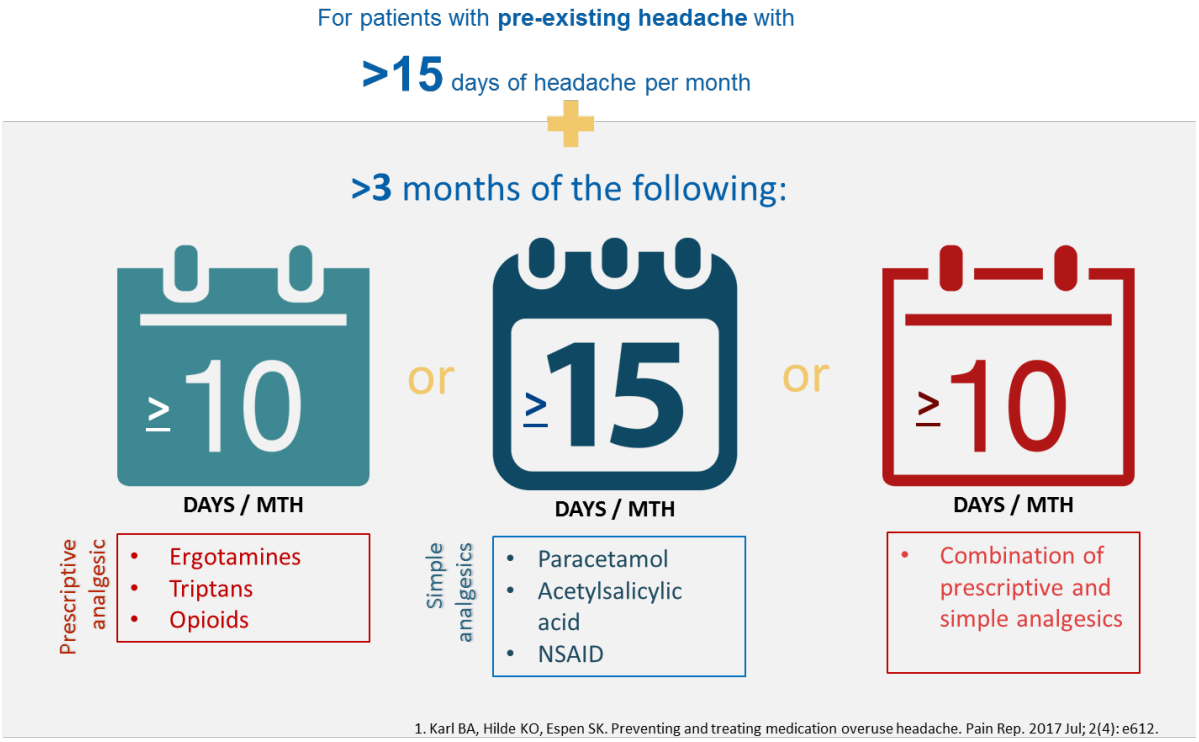


Figure 2: Dignostic criteria for medication-overuse headache

The prevalence of MOH is approximately 1% in the general population[32]. MOH is more common in the patients with chronic migraine[29,32]. The characteristics of the headache in MOH depends on the initial primary headache and the type of overused acute medication. An important risk factor for the development of MOH is predisposition for migraine or tension-type headache (TTH) as an underlying biological trait[29].

The first step in management of MOH involves educating the headache patients about the relationship between frequent ingestion of acute headache medication and MOH[29,32]. Patients who fail the first step will be started on prophylactic medication[32,33]. Lastly, these patients may undergo detoxification on an outpatient basis, daycare or inpatient setting, depending on the severity and comorbidities[32,33].

Treatment of comorbidities is important. The headache patients need to be screened for anxiety and depression. Programs on lifestyle factors, such as reduction of obesity, smoking and inactivity can be implemented to improve the outcome of MOH[29].

The success rate of treatment is approximately 50-70%[32]. The patients with opioid-overuse headache have higher relapse rates. Patient education and follow-up management are crucial.

III. Women and Migraine

Migraine affects women more than men at the rate of 3:1[34]. Hormonal factors underlie the main pathophysiology of migraine attacks in women[35]. The main challenge in management of women with migraine is the limited choices of effective and practical pharmacological migraine treatment due to the teratogenicity potential of the medications during their childbearing years. Therefore, this guideline focuses on several main strategies in women with migraine from womb to tomb including all the latest available treatment.

A. Menstrual migraine

Menstrual migraine (MM) occurs around the onset of menarche and peaks around the age of 40[36]. MM has caused more burden to women than non-menstrual migraine[37]. The attacks are usually prolonged, severe and likely to relapse within 24 hours. MM is caused by the oestrogen withdrawal trigger and release of uterine prostaglandins during menses causing neuronal excitability and neurogenic inflammation[38].

Menstrual migraine (MM) is described as attacks of migraine with or without aura occurring on day 1 ± 2 days of menstruation in at least two out of three menstrual cycles. It is further classified into either pure menstrual migraine (PMM) if the attacks occur exclusively during perimenstrual period or menstrual-related migraine (MRM) if the attacks occur at other times as well[4]. MRM is more common than PMM in women; with two thirds suffer from MRM and one third from PMM.

Management of MM consist of acute therapy, short term perimenstrual prevention and long-term prevention therapy. The acute treatment follows the general management for acute migraine headache[39]. New evidences favour frovatriptan for MM due to its longer half-life than other triptans, thus reducing the severity and recurrence[40,41] of migraine attack. Combination therapy with naproxen sodium and sumatriptan is also recommended[42].

Short term perimenstrual prevention or also known as 'mini-prophylaxis', is a unique approach in management of MM, either NSAIDs[43] (if no contraindication; naproxen sodium 550 mg bd with gastroduodenal protection) or triptans[44] (sumatriptan 25 mg tds or frovatriptan 2.5 mg daily) or combinations[42] can be given perimenstrually especially for women with regular cycle starting 2 days prior or at onset of MM and for a total duration of 5 days. The diagram below illustrates temporal use of perimenstrual prevention in a regular 28 days menstrual cycle.

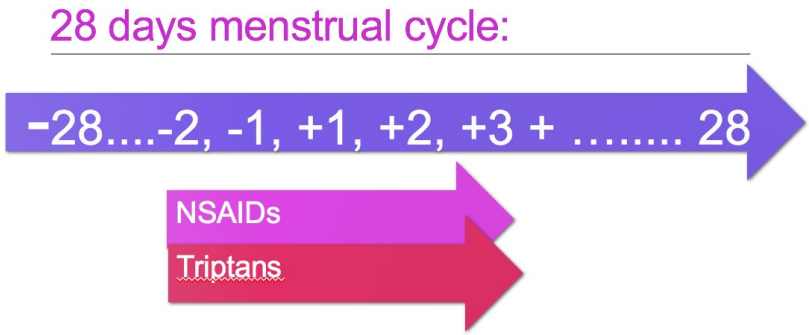


Figure 3: Use of drug therapy in perimenstrual prevention of menstrual migraine

Although NSAIDs appear to protect against chronification of migraine[45], women with MRM who are using NSAIDs or triptans at other times of the month should be advised that additional perimenstrual prophylaxis increases the risk of developing medication overuse headache

(MOH). For women who are already on long term prophylaxis treatment, transiently increasing the dose prior to the onset of the MM can be beneficial[46].

The use of hormonal strategies for MM either perimenstrually[47,48] (e.g oestrogen patch/ gel) or long term daily (e.g. combined oral contraception (COC) or Progestogen-only pill (POP)) is controversial as the available data is inconclusive and the benefits are offset by the increase of migraine attacks reported post use[40,49,50]. It should only be used in women with no contraindication and as a last resort to a refractory MM with consult of a gynaecologist. There is also limited evidence to suggest complementary approaches such asthe use of Vitamin E 400 units daily for 5 days starting 2 days prior to menstruation which may reduce migraine severity and disability as well as dysmenorrhea due to the anti-prostaglandin effect[51,52]. Magnesium use such as magnesium oxide 400mg daily also has been shown to reduce the pain of MM and premenstrual symptoms[53]. Acupuncture may be used additionally for adjunctive treatment and prevention of migraine[54].

B. Migraine, stroke and hormonal contraceptives

The stroke risk of migraine in men appears to be less established. On the contrary, migraine with aura and migraine without aura in presence with two vascular risk factors are associated with stroke in younger women of less than 55 years of age[55,56,57]. The mechanism linking migraine with stroke and the association with patent foramen ovale remains controversial. Furthermore, current evidences revealed an increased risk of ischemic stroke associated with the use of hormonal contraceptives in women with migraine[58,59,60,61,62].

COC should be used cautiously in clinical practice for women of reproductive age with high migraine prevalence. The diagram below illustrates the guidelines for the use of COC in women with migraine. COCs use (particularly high dose oestrogen content) should be avoided in migraine with aura in young women[61].

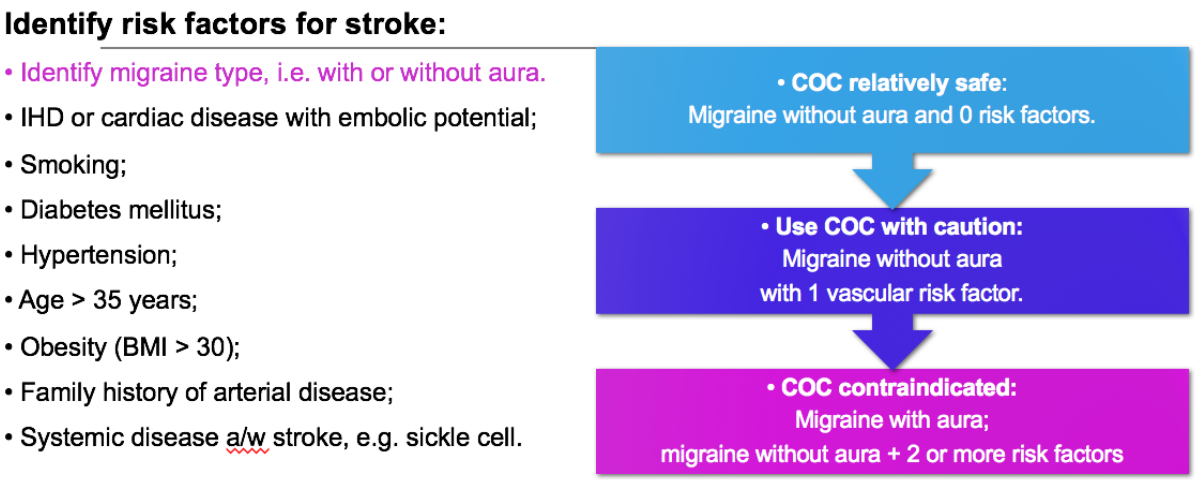


Figure 4: Guidelines for the use of combined oral contraceptives in woman with migraine.

If a young woman who is already taking the COC pill develops a new persisting headache, a new-onset migraine aura or a dramatic increase in headache frequency and intensity or a development of unusual and especially prolonged auras, the COC should be stopped, in view of the increased risk of possible ischaemic stroke in young women[62]. However, a small number of patients (6%), will experience an improvement of their headaches with commencement of COC[64].

At present, there is no evidence for aspirin or other treatments in young women with migraine for primary stroke prevention[65,66]. Furthermore, the significance of deep white matter lesions and other infarct-like lesions seen on MRI in patients with migraine remain unclear[66,68,69].

Treatments to reduce migraine frequency might be reasonable to reduce the risk of stroke but there is no evidence from randomized trials indicating that migraine prophylaxis decreases the risk of stroke. Smoking cessation and alternatives to COC should be recommended in women with migraine headaches with aura[70].

C. Migraine and childbearing women

In childbearing women, 50% of pregnancies are usually unplanned, therefore limiting choices of effective pharmacological treatment due to the teratogenicity potential.

Valproate sodium, topiramate and anti CGRP therapy should be avoided in women who are not on contraception[63]. Propranolol and amitriptyline are probably the safest option but the decision on the choice of prophylaxis should be discussed with the patient and the risk benefit ratio should be documented[64].

D. Migraine and Pregnancy

Several studies have shown a tendency for migraine headaches to cease in the second and third trimesters in two-thirds of pregnant women, especially those who experience migraine onset at menarche and those with menstrual migraine[71]. However, approximately 25% of women experience no changes in their migraine[39]. About 8% reported worsening of headaches and it is important to exclude secondary headache especially if the women developed the first presentation of migraine with aura during pregnancy or if there is a change in the usual migraine symptoms. Important differentials to be ruled out are cerebral venous thrombosis; arteriovenous malformation and pre-eclampsia[64].

Avoiding migraine triggers is important and non-pharmacological treatment should be the first step and the mainstay of migraine management in pregnant woman. Drug exposure should be minimized especially during first trimester and stop prophylactic drugs if possible[63]. Paracetamol 1000 mg is the initial choice, other alternative drugs such as IV prochlorperazine 10 mg or metoclopramide 10 mg can be used for treatment of acute migraine attacks[72]. Use of ibuprofen should be limited to the second trimester[73]. Triptan should be generally avoided throughout pregnancy as there is a risk of vasocontriction[74,75].

Non-pharmacological treatment such as acupuncture, biofeedback, and the neuromodulation such as transcranial magnetic stimulation[76] and transcutaneous nerve stimulator device are considered safe preventive therapies during pregnancy[63].

Prophylactic pharmacological treatment should generally be avoided in pregnancy if possible. If drug treatment is necessary, a treatment with the lowest risk of adverse effects to the fetus should be selected[77]. Beta-blockers such as propranolol may be one of the safer options used at the lowest safest dose[73]. However, the use should be avoided in the 3rd trimester due to the risk of intrauterine growth retardation (IUGR)[78]. In some small case series and individual cases, successful use of onabotulinumtoxin A in chronic migraine[79] and repeated nerve blocks of the greater occipital nerves with lignocaine[80] have been demonstrated. The table below summarises the migraine pharmacological treatment in pregnant women.

	Childbearing	Pregnant	Breastfeeding
Acute treatment	General migraine treatment	● Paracetamol when absolutely necessary ● Ibuprofen (NSAIDs) only short-term use and avoid during the 3rd trimester ● Triptans not recommended due to risk of vasoconstriction, only use in severe refractory case ● Anti-emetics ○ IV metoclopramide ○ IV prochlorperazine	- Safe to use: - Paracetamol, Ibuprofen, metoclopramide, sumatriptan
Prophylaxis treatment	Avoid sodium valproates, anti CGRP and topiramates without proper contraception.	● Avoid unless absolutely necessary ● B-adrenergic receptor antagonist (B-blocker) ○ Propranolol can be safely used in 1st and 2nd trimester. Avoid in 3rd trimester (IUGR).	- Pump and dump approach; discuss with paediatrician.

Table 17: Drug therapy for migraine in pregnancy and breastfeeding

E. Migraine, postpartum and breastfeeding

Migraine symptoms often emerge in the postpartum period as estrogen level falls rapidly. However, breastfeeding may delay the return of migraines by keeping estrogen level elevated. Paracetamol, ibuprofen, metoclopramide and sumatriptan are generally regarded as minimal risk. IV prochlorperazine 10 mg is safe and effective[78]. It is recommended that patient discusses the use of other migraine medications with the paediatrician to find the safest approach for both mother and infant. Some physicians recommend the 'pump and dump' method several hours after treating[81].

F. Migraine, Menopause and hormone replacement therapy (HRT)

At menopause, migraine improves in 65%, worsens in 10%, and is unchanged in 25%. Migraine worsens in most who undergo a surgical menopause. The indications and contraindications to the use of HRT are similar to women without migraine. The use of HRT for menopausal symptoms should be based on appropriate evaluation of risk and benefits, primarily focusing on stroke risk factors[82]. There is no strong evidence that risk of stroke is elevated or reduced with the use of HRT in women with migraine[83].

However, it would be advisable to seek consultation with a gynaecologist and a neurologist in

circumstances where migraine worsens while taking HRT. Changes in formulations and dosage may be all that is necessary[82].

IV. Neuropsychiatric Comorbities n Migraine and Tension-type headache

Migraine is common and very often, a severe incapacitating disorder. Neuropsychiatric signs and symptoms may feature prominently in the course of the attacks[84]. Psychological factors in migraine and tension-type headache are important, and these factors influence the diagnosis and treatment of these headaches.

Screening for psychiatric comorbidity and referral pathway

Due to the high prevalence of depression and anxiety in people with migraine, it is crucial to screen for psychiatric comorbidity, especially depression and anxiety during the evaluation of a new patient with migraine or tension-type headache. It is also advisable to annually screen for mood disorder in these patients. Among the screening tools that can be used are the Patient Health Questionnaire (PHQ-9 or PHQ-15)[85] and Generalized Anxiety Disorder 7-item (GAD-7) scale. [82] In PHQ-9 has nine items, each of which is scored 0-3, and providing a 0-27 severity score. The scores of 5, 10, 15 and 20 in PHQ-9 represent cut-off points for mild, moderately severe and severe depression, respectively. In the case of mild depression, it is recommended to repeat PHQ-9 during subsequent follow-up; therefore, no psychiatric or psychological referral may be needed unless clinically indicated otherwise. However, if the PHQ-9 scores indicate moderate severity, it is essential to refer the patient for mental health evaluation and treatment. PHQ-9 is available and validated in Malay[86] and Chinese[87] languages.

In the case of GAD-7, there are seven items, each of which is scored 0-3, providing a 0-21 severity score. The scores of 5, 10, and 15 represent cut-off points for mild, moderate and severe anxiety. If the patient has a score of 10 or more, it is recommended a referral be made for mental health evaluation and treatment. GAD-7 is also available and validated in Malay[88] and Chinese[89] languages.

Depression and Anxiety

Patients with migraine have higher risk of anxiety and depression. It is shown that the risk of a person with migraine headache, also suffering from depression or anxiety is at least 2- to 3-fold that of those without headache. In a combined USA/UK study of more than 300 adults with migraine sufferers, 47% of migraineurs have depression compared to only 17% without migraine[90]. Anxiety is another important comorbidity in migraine, and some studies showed that the risk of anxiety might even be higher than depression. Those with more frequent headache, regardless of the type of headache, are more likely to be depressed. It is also found that those migraine sufferers with aura may have higher rates of anxiety and depression. Since the risk of depression and anxiety in migraine may not be very different from those with other pain disorders such as arthritis and back pain, it has been suggested that the pain of headache that results in depression and anxiety[91]. The risk of suicide attempts is also increased in people with migraine and not all this additional risk may be explained by depression[92].

Personality and Stress

Most of the accounts on the personality and migraine sufferers are based on anecdotal observations. It is also related to selection bias in those studies as well. The evidence that a particular personality type predisposes a person to migraine is weak. Concerning stress, it is

common to find a period of stress, or even the anticipation of it are common, but by no means universally associated with migraine attacks. It has been demonstrated that sustained emotional tension and not acute emotional stress that may be more importantly associated with migraine[93].

Psychiatric Features Associated with Migraine Attacks

Neuropsychiatric manifestations are part of the migraine attacks almost universally. Anxiety and irritability commonly occur at the initial phase of the migraine episode and are followed by drowsiness, lethargy, cognitive impairment, and even psychosis as the headache continues. Florid psychosis is however rare.

Cognitive Impairment

Cognitive impairment has been reported during migraine attacks. The domains that are involved include information processing speed, attention, executive function, memory and verbal skills. Longitudinal studies do not support progressive cognitive decline over time in migraine patients. If such a decrease ~~is~~ was to be observed, it is imperative~~ly~~ to rule out co-existing mood disorders[94].

Psychiatric Treatment

Pharmacological treatment should only be part of the holistic treatment of migraine sufferers with psychiatric comorbidity. Attention is needed to look into the factors specific to the individuals such as lifestyle, sleep pattern, stress, and provocative substances in the diet. Psychosocial factors will usually warrant close consideration as well, if the attacks have become more frequent. It is imperative to detect mood disorders that may aggravate the headache. When treating psychiatric comorbidity in migraine sufferers, it is recommended to follow the treatment algorithm as other primary psychiatric disorders. Nevertheless, the selection of a psychotropic agent is crucial, as some of the antidepressants report headache as part of the common side effects seen.

V. Psychological Management of Chronic Headaches

Headaches are not only contributed by biological factors but may be maintained by psychosocial factors including one's mental health status, environment factors, coping skills, and other related matters. Therefore, a psychologist usually manage headaches by assessing the factors perpetuating the condition.

Psychological assessment of headache

When assessing a headache, the following questions are generally asked:

1. What are some of the symptoms of headaches?

The headache phenomenon is examined in detail with evaluation of sensory prodromata, nausea, vomiting, vertigo, tinnitus, photophobia, phonophobia, and even the possibility of anorexia.

2. What are the precipitating factors of headaches?

    - Emotional stimuli (i.e., anxiety, depression, anger)
    - Perceptual stimuli (i.e., flicker, glare, eyestrain, and noise)

- Lifestyle (i.e., diet patterns, sleep patterns, activity levels)
- Seasonal and meteorological factors (i.e. weather, room temperature, menstrual cycle)
- Head or neck trauma

3. How might people react to your headaches?
    - Empathize and support to different life aspects
    - Overrespond (e.g. overconcern, sympathy) that may lead to negative reactions (e.g. task avoidant, stress, pain behaviours)
    - Choosing to ignore; and that may lead to argument, stress, and neglect.
    - Long-term consequences including interpersonal conflict, dysfunctional behaviours, and emotional distress.
4. How may you react to your headaches?
    - Perceive headaches as unpredictable, unpreventable, and uncontrollable
    - Emotionally overwhelming (e.g. anxiety, depression, anger)
    - Overabundant focus with headaches and consequently, develop negative reactions (e.g. catastrophizing, task avoidant, ignorant, disruptive lifestyle)
    - Dysfunctional social life (e.g. social withdrawal, dysfunctional relationship, work absenteeism)

Instruments

Suggestion of psychological evaluation for headache:

1. Questionnaires on:
    - Headache and health questionnaire
    - Mood screening such as DASS-21
    - Disability levels and pain behaviour
    - Coping skills
2. Behavioural interviewing and observation
3. Self-Report
    - Time Sampling, Event Sampling, Daily Cards, Change & Control Cards (a record of behaviour / activity changes)

Psychological Management of Headaches

Psychological management plays a role in coping with headache which include managing overwhelming emotion, disruptive lifestyles and perceived disability that may aggravate pain. Psychosocial factors (e.g. irritability, overwork, insomnia, depressed mood) are found to be significantly associated with migraine and tension-type headache (TTH). Prevention efforts in managing this sphere may reduce the prevalence of primary headache disorders[95].

A meta-analysis of 27 randomized clinical trials showed that psychological management including relaxation and biofeedback, cognitive behavioral treatment and mindfulness-based treatment reduced headache frequency and headache index[13]. An integrated psychological approach focuseing on aspects of feelings, thoughts, and behaviours creates better outcomes in managing headaches, than a single approach. Active participation from the patient is also important.

1. Relaxation and Behavioral Therapies

Relaxation and behavioral therapies have been shown to have a positive effect in pain coping and emotion management. There are a wide variety of relaxation techniques that range from active muscular tension reduction methods to clinical hypnosis. The majority of methods or techniques would require special training and an understanding of cognitive processes and the limitations. However, anyone may potentially learn this with proper guidance and apply to self-management.

1.1 Breathing Techniques

Pain reactions generate physiological changes including increased heartbeat and rapid breathing that are likely lead to muscle tension and aggravate pain. Breathing techniques (e.g. diaphragmatic breathing) may help reduce muscle tension and hence lessen the pain. It focuses on expansion of the abdomen rather than chest, to optimize breathing in a shallow manner and exhale progressively. This activates the parasympathetic nervous system (e.g relax effect) and to fight against pain responses. Use of imagery-guided and attention-diversion approach may direct pain experience to a more tolerating mode. Mindfulness-based interventions (e.g. mindful breathing) serves to teach patient to approach the pain rather than avoiding the pain sensations; such as shifting the focus from pain experience to present life moments.

1.2 Progressive Muscle Relaxation (PMR)

Progressive muscle relaxation gives attention to area of pain and observes the changes in muscle groups from tensing to gradually relieving. This provides a calm and relaxed sense that may lessen pain.

An example of a progressive muscular relaxation sequence is given below:

- *Hands and Arms:* Settle back in the seat and be comfortable. Extend arms and make a fist as tight as you can. Feel the tightness and gradually relief by dropping the arms at your side to rest. Feel the relief of tenseness and be relaxed.
- *Arms and Shoulders:* Raise arms up and stretch them as like touching the ceiling. Hold and feel the tenseness. Drop the arms at your side and relax. Feel the relief of tenseness.
- *Shoulders and Neck:* Push shoulders up to the ears. Hold and feel the tenseness at neck and shoulders. Drop and return the shoulders to normal position. Feel the relief of tenseness and be relaxed.
- *Jaw:* Squeeze the jaws tightly together and tense your neck. Hold and feel the tenseness. Now relax and enjoy the relief of tenseness.
- *Face:* Wrinkle forehead and squint eyes tightly. Squeeze and feel the tenseness. Relax

the face and feel the relief of tenseness.

- *Stomach:* Push your stomach in and squeeze it hard. Hold and feel the tenseness. Relax the stomach. Feel the relief of tenseness and be relaxed.
- *Legs and feet:* Push the toes deep down the ground. Push strong and hold the tenseness. Relax the toes and feel the relief of tenseness.

2. Cognitive Therapy

Cognitive therapy focuses on altering unhelpful thoughts (that may create stress and worsen headache) to more constructive thoughts to cope with pain. This include modifying maladaptive thoughts and beliefs about the trigger factors of headaches. Some examples of the negative thoughts are as follows:

- "I can't get anything done because of the headache!"
- "Nothing I can do to stop the headache"; "no one can help me"

Self-efficacy and locus of control are important concepts in managing pain. This focuses mainly on the competence in engaging a task and believing on the positive outcome. Problem-solving and goal-setting skills also help to control over the triggering event of headache.

Psychoeducation on Pain Management

Diet Constituent

Some studies suggest that diet may be associate with pain. Poor diet quality may lead to altered acute nociceptive sensitivity, systemic inflammation thus causing persistent pain[96]. Therefore, lower inflammation and oxidative stress diet constituents may relate to lesser pain experienced[97]. Individualised elimination diet programmes involve restricted diet that is unlikely to precipitate headaches. Different food is then reintroduce one at a time to ensure the effects is solely due to the food in question. A food diary will be helpful to record the food consumed and noting its effects during the period. Fasting may cause headaches due to a drop in blood sugar levels. Thus, patient may need to have snacks on stand-by, if this is the case.

Perceptual Stimuli

Individuals with headache may be hypersensitive to some perceived stimuli (e.g. bright sunlight, fluorescent light, electronic device screens). Potential useful suggestions include wearing a hat, sunglasses, changing the illumination in a room, using tinted or polarised lenses, reducing eyestrain activities or rescheduling activities.

Sleep Hygiene

Sleep hygiene refers to good sleep habits include regular sleep cycle, restful sleep environment, control food intake before sleep (e.g. caffeine drinks). Sleep patterns such as interrupted sleep or oversleeping may lead to headaches. Therefore, practicing good sleep hygiene is helpful in managing headache. Research has shown that psychological sleep intervention improves headache frequency however, but conflicting evidence exists in relation to the impact on headache intensity[98].

Stress management

Stress is commonly associated with headaches. Example of the causes and intervention are as follow:

- family relationships – parenting skills, family therapy, marital therapy
- careers, finance, housing – coping skills, problem-solving
- dysfunctional socialisation – social skills, coping skill

9. RESOURCES ON HEADACHE

International Headache Society (HIS)
ihs-headache.org

The Australian and New Zealand Headache Society (ANZHS)

anzheadachesociety.org.

National Institute for Health and Care Excellence (NICE)

www.nice.org.uk

American Headache Society

americanheadachesociety.org

Migraine Trust UK

www.migrainetrust.org

American Migraine Foundation

americanmigrainefoundation.org

European Headache Federation

ehf-org.org

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