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National Guidelines for The Treatment Of Common Headaches Disorders in Pakistan

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NATIONAL GUIDELINES FOR THE TREATMENT OF COMMON HEADACHES DISORDERS IN PAKISTAN

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INTRODUCTION

The prevalence of headache disorders in Pakistan is expected to be as high as other parts of the world. Headaches are often overlooked and underdiagnosed due to several reasons including lack of physician knowledge, poor public awareness, and funding for healthcare.[1] Herekar et al. reported prevalence of migraine as 22.9% and tension type headaches as 44.7%.[2] It is higher than respective estimates of 14.7% migraine and 20.7% tension type headache (TTH) from the Global Burden of Disease Survey 2010.[3] Most prevalent headaches are tension-type and migraine headaches, which primarily affect young to middle-aged married women from low socioeconomic backgrounds.[4] According to another study diagnosis of primary headache was present in 76% and secondary headache was present in 24%.3 Migraine has high prevalence, affecting 15% of the general population.[4.5] In Pakistan alone prevalence of migraine has recently been estimated to 22.5%.[6-7] A nationwide study reported age and gender adjusted one-year prevalence of migraine as 22.5% [21.2–23.8%], tension-type headache as 44.6% [43.1–46.1%] and medication-overuse headache as 0.7% [0.5–1.0%]. All headaches peaked in age group 40-49 years with migraine more prevalent in females and TTH more common in males.[7]

No national guidelines for headache diagnosis and management exists in Pakistan. There is a need to develop guidelines with strategies to provide primary headache management at a primary care level and to standardize headache care at national level. The recommendations regarding most common headache disorders are largely in agreement with other international published guidelines. These guidelines may be useful for practicing general practitioners, primary care physicians, neurologists, and other health-care professionals.

METHODS

The following published headache guidelines were reviewed:

1. Diagnosis and treatment of headache disorders and facial pain. Danish Headache Society.[8]
2. European principles of management of common headache disorders in primary care. European Headache Federation.[9]
3. National Headache Management System for Adults 2019, British Association for the Study of Headache.[10]
4. Guideline on the use of on Botulinum toxin A in chronic migraine: a consensus statement from the European Headache Federation.[11]
5. Guideline on the use of monoclonal antibodies acting on the calcitonin gene related peptide or its receptor for migraine prevention, European Headache Federation.[12]
6. Position Statement on Integrating New Migraine Treatments into Clinical Practice by the American Headache Society.[13]

CLASSIFICATION OF HEADACHE DISORDERS

Headaches are classified as primary or secondary headaches (International Headache Society /IHS) (https://ichd-3.org/). Enclosure 1

Part 1: The primary headaches	**Part 2: The secondary headaches**
1. Migraine 2. Tension-type headache 3. Trigeminal autonomic cephalalgias 4. Other primary headache disorders	5. Headache attributed to trauma or injury to the head and/or neck 6. Headache attributed to cranial or cervical vascular disorder 7. Headache attributed to non-vascular intracranial disorder 8. Headache attributed to a substance or its withdrawal 9. Headache attributed to infection 10. Headache attributed to disorder of homoeostasis 11. Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure 12. Headache attributed to psychiatric disorder
Part 3: Painful cranial neuropathies, other facial pains and other headaches	
13. Painful cranial neuropathies and other facial pains 14. Other headache disorders	

ICHD-3 Beta . Cephalalgia 2013; 33: 629-808

EVALUATION OF HEADACHE DISORDERS

Based on thorough history & clinical evaluation it is necessary to differentiate primary from secondary headaches. The key is the history & relevant neurological examination to diagnose as well differentiate primary and secondary headaches.[14-16]

A complete history is vital to the diagnostics in all primary headache conditions. Differentiating features of primary headaches and useful questions are provided in Table 1 & 2.

Table 1: Differentiating among Common Headache Disorders (ICHD-3 Beta)

Migraine	Tension Type Headache	Cluster Headache
Episodic		
Unilateral (Although often bilateral)	Bilateral	Unilateral (Never Bilateral)
Pulsating	Pressing, tightening, non-pulsating	excruciating unilateral headache
Moderate or Severe	Mild- Moderate but not disabling	Very severe
Aggravated by, or causing avoidance of, routine physical activity	No aggravation by, or avoidance of, routine physical activity	Restlessness No aggravation by physical activity
Nausea and/or vomiting Photophobia Phonophobia	No nausea, vomiting, photophobia, or phonophobia	Ipsilateral to pain, there may be: Conjunctival injection Lacrimation Nasal congestion Rhinorrhoea Eyelid swelling/drooping
Attacks last hours to days (usually 4-72 hours)	Attacks last hours to days	Attacks last from 15 minutes to 3 hours
Frequency 1-2 attacks per month		Frequency 1-3 attacks per day (up to 8) and usually occur daily for 2-3 months at a time
Chronic		
Chronic migraine or chronic tension-type headache: At least 15 headache days per month for >3 months with the above clinical description, in the absence of medication overuse		Chronic cluster headache: Attacks occurring for more than 1 year without remission, or remission periods lasting <3 months
Medication-overuse headache		
Ergotamine, triptans, or opioids taken on 10 or more days per month, or 15 days for simple analgesics, for >3 months.		No medication overuse headache Medication-overuse headache only reported in patients with a predisposition to migraine and/or tension-type headache; clinical syndrome of the headache exacerbated by the acute-relief medication overuse is of the migraine and/or tension-type headache

Table 2: Useful Questions[8]

Increase over time	Why have you chosen to see a doctor now? When your pain started? How frequently do you have headache? For how long does each attack last?
Character	Quality and type of pain? Intensity of the pain? Location of pain and its spread? Associated symptoms? Nature of headache/facial pain?
Reasons	Trigger and/or predisposing factors? Aggravating and alleviating factors?
Reaction Pattern	How is your activity level during pain? What do you do during an attack? What medication u take for pain relief?
General state of health between attacks	Any symptoms between attacks? Anxiety or fear of new attacks and their causes?

Examination

Physical examination includes the following:

1. General neurological examination
2. Examination of cervical spine and neck muscles
3. Eye examination for papilledema and glaucoma
4. Examination for temporomandibular joints, teeth, external auditory canal

General Aspects of Headache Management

- Recurrent headache may be disabling.
- Headache disorders can be effectively treated.
- Reassurance is important to alleviate underlying fear.
- Genetic and environmental factors underlying headache disorders are poorly understood.

Follow-up: Patients may require regular follow ups if pain is not effectively controlled.

Patients who fail to respond to abortive and preventive therapy should be referred to headache specialist.

Diaries and calendars (Figures 1 & 2)

Diaries and calendars may be helpful in patients for diagnosis, medication use and overuse and identifying associations with the menstrual cycle and other triggers.

DIAGNOSTIC HEADACHE DIARY

تشخیص سر درد ڈائری

اس کو ہر اس شام مکمل کریں کہ جن دنوں میں سر درد ہوا کرتا ہے۔
ہدایات کے مطابق چیک باکس میں علامات کے ہر سوال کا مناسب حد تک حقیقت پر مبنی جواب دیں۔

نام: _____ عمر/تاریخ پیدائش: _____

آغاز رجسٹریشن تاریخ: _____ اختتام: _____

۱۔ سال _____ تاریخ _____
Year Date

		پیر Monday	منگل Tuesday	بدھ Wednesday	جمعرات Thursday	جمعہ Friday	ہفتہ Saturday	اتوار Sunday
۲۔ کیا آپ کو آج سر درد ہوا ہے؟ Did you hava a headache today	نہیں ہاں yes, no							
کتنے بجے سر درد کا آغاز ہوا؟ When did the headache begin?	ممکنہ کے یار میں وقت hour							
۳۔ کتنے بجے سر درد کا اختتام / ختم ہو گیا؟ When did the headache dissappear?	وقت بجے hour							
۴۔ کیا سر درد کے ہونے سے پہلے ان علامات میں سے کچھ ظاہر ہوا؟ Just before the headache began, was there any	بصری پریشانی حسی بولنے میں دشواری visual disturbance sensory disturbance, difficulty speaking							
۵۔ کیا آپ کا سر درد ماتھے کے دونوں جانب Was the headache	دائیں جانب / بائیں جانب on both sides, right sides, left sides							
۶۔ کیا آپ کا سر درد تھا؟ Was the headache	دباؤ / سخت / پڑھکتا / دھڑکتا pressing tightening, pulsating throbbing							
۷۔ اوسط سطح پر رکھتے ہوئے آپ کا سر درد کتنا تھا؟ Was the headache -on average (see *below)	ہلکا / درمیانہ / شدید mild, moderate, serve							
۸۔ کیا سر درد جسم کو حرکت دینے سے بڑھ جاتا ہے؟ مثلاً سیڑیوں چڑھنے / اترنے وغیرہ Was the headache aggravated by physical activity, e.g. walking on stairs?	نہیں ہاں yes, no							
۹۔ کیا سر درد کے نتیجے میں مٹلاہٹ محسوس ہوتی ہے؟ Did you suffer from nausea	نہیں / ہلکی / درمیانہ / شدید no, mild, moderate, serve							
۱۰۔ کیا روشنی درد کا باعث بنتی ہے؟ Were you bothered by light?	نہیں ہاں yes, no							
۱۱۔ کیا تیز آواز زحمت کا باعث بنتی ہے؟ Were you bothered by sounds?	نہیں ہاں yes, no							
۱۲۔ کیا کسی خاص خوشبو / بدبو / وجہ کے باعث سر درد کو بڑھاوا ملتا ہے؟ Did anything trigger this headache attack?	اگر ہاں تو وہ کیا؟ If yes, please specify							

۱۳۔ کیا آپ سر درد یا کسی درد کیلئے کوئی دوا استعمال کرتے ہیں؟ Did you take any medicine for headache or for any other pain? (for each, please write name, amount and the time you took it)		نام name	تعداد amount,	وقت time

Figure 1- Headache Diary

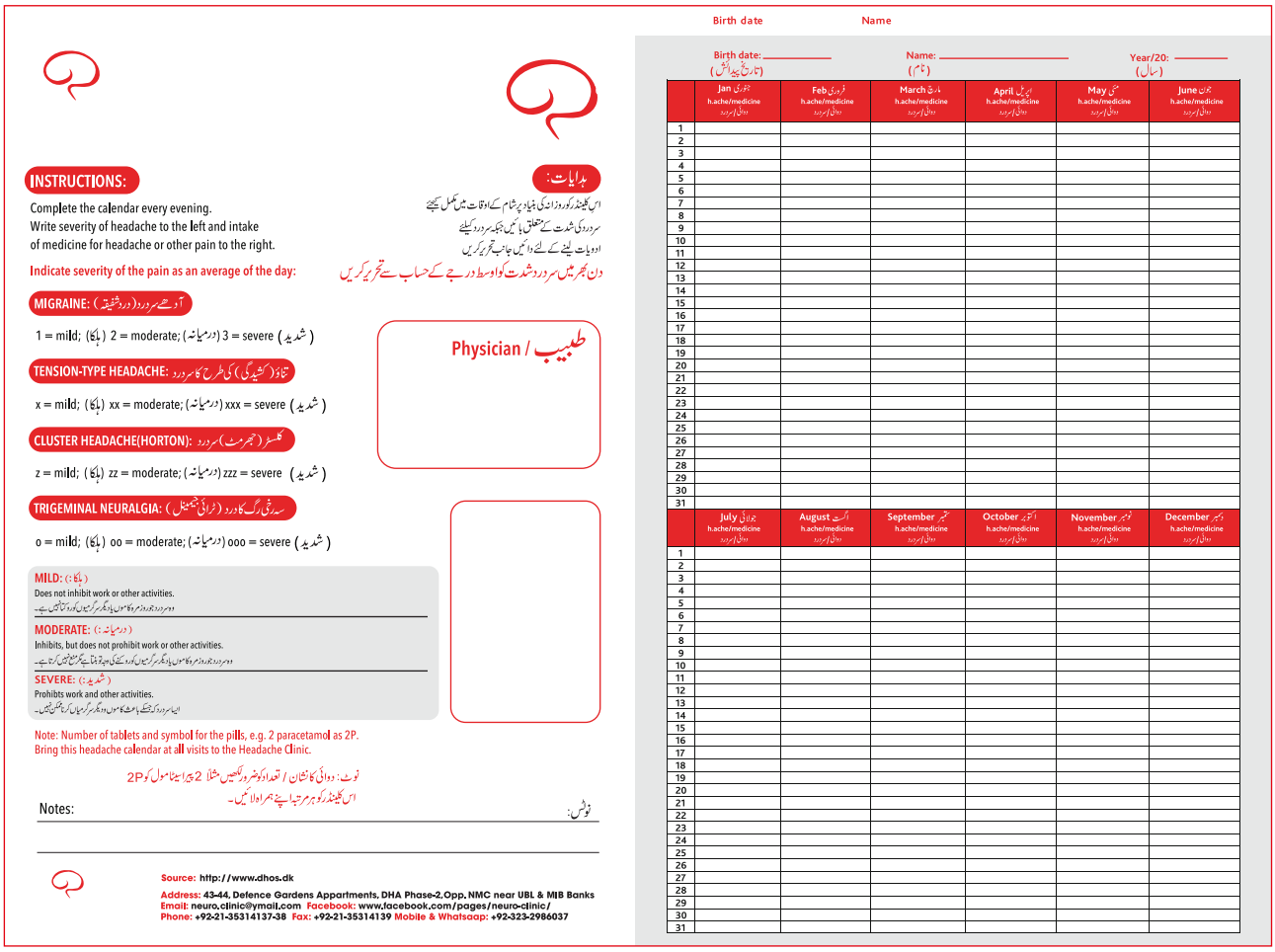

Figure 2- Headache Calendar

HEADACHE TREATMENT FACILITIES IN PAKISTAN

In the developed world the diagnosis and treatment are generally performed at multiple levels of care i.e., GP, Neurology Dept. & multidisciplinary headache Centre. In Pakistan there are only two levels of care i.e., GP & Neurology Departments (Figure 3). Only in major cities of the country we have a second level facility, where diagnosis and treatment are performed by practicing specialists of neurology.

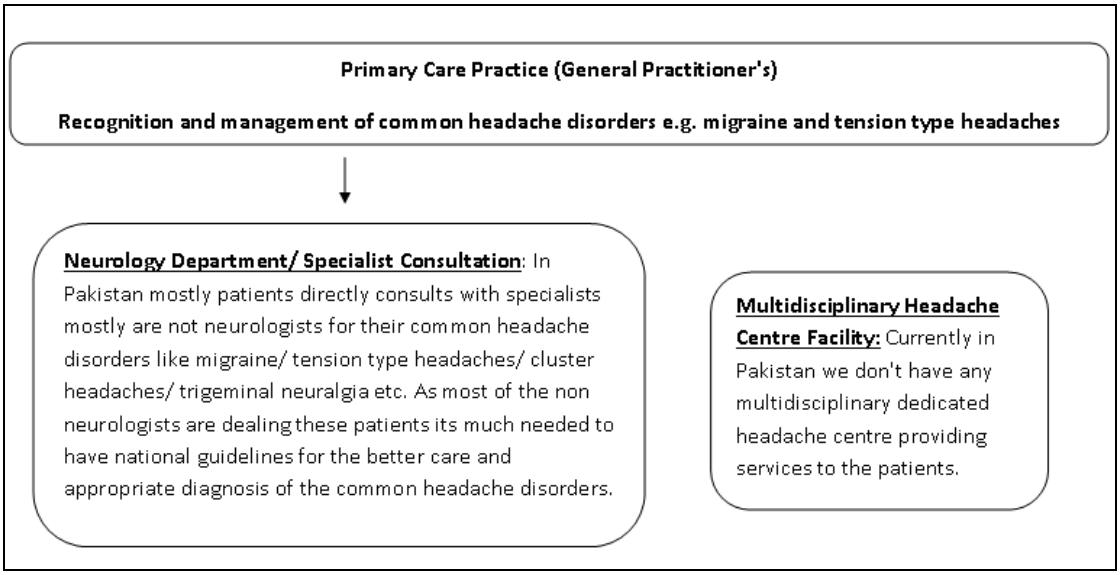

Figure 3- Organization of the Headache Disorders Care in Pakistan

PRIMARY HEADACHE DISORDERS

MIGRAINE

The complete diagnostic criteria for migraine with and without aura, as well as chronic, hemiplegic, and menstrual migraine is provided in Table 3. [17]

Table 3: Diagnostic Criteria of Migraine According to ICHD-3[17, 18]

Migraine without aura	
A.	At least 5 attacks fulfilling criteria B – D
B.	Headache attacks lasting 4 – 72 hours (untreated or unsuccessfully treated)
C.	Headache has at least two of the following characteristics: 1. Unilateral location 2. Pulsating quality 3. Moderate or severe pain intensity 4. Aggravation by routine physical activity (e.g. walking or climbing stairs)
D.	Headache is associated with at least one of the following: 1. Nausea and/or vomiting 2. Photophobia and vomiting
E.	Not better accounted for by another ICHD-3 diagnosis
Migraine with aura	
A.	At least 2 attacks fulfilling criteria B and C
B.	One or more of the following fully reversible aura symptoms: 1. Visual disturbances 2. Sensory symptoms 3. Speech and/or language 4. Motor symptoms
	5. Brainstem symptoms 6. Retinal symptoms
C.	At least 3 of the following aura characteristics: 1. At least one aura symptom spread gradually over at least5 minutes 2. Two or more aura symptoms occur in succession 3. Each individual aura symptom lasts 5 – 60 minutes 4. At least one aura symptom is unilateral 5. At least one aura symptom is positive 6. The aura is accompanied by, or followed within 60 minutes, by headache
D.	Not better accounted for by another ICHD-3 diagnosis
Chronic migraine	
A.	Headache (migraine-like or tension-type like) on at least 15 days per month, for more than 3 months, and fulfilling criteria B and C
B.	Occurring in a patient who suffers from migraine with or without aura
C.	On at least 8 days per month, the headache fulfills any of the following: 1. Criteria C and D for migraine without aura 2. Criteria B and C for migraine with aura 3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative
D.	Not better accounted for by another ICHD-3 diagnosis

Hemiplegic migraine	
A.	Attacks fulfilling criteria for *migraine with aura* and criterion B below
B.	Aura consisting of both of the following: 1. Fully reversible motor weakness 2. Fully reversible visual, sensory, and/or speech/language symptoms
Pure menstrual migraine without aura	
A.	Attacks, in a menstruating woman, fulfilling criteria for *migraine without aura* and criterion B
B.	Attacks occurring exclusively on day 1± 2 of menstruation in at least two out of three menstrual cycles and at no other time of the cycle
Menstrual-related migraine without aura	
A.	Attacks, in a menstruating woman, fulfilling criteria for *migraine without aura* and criterion B
B.	Attacks occurring exclusively on day 1 ± 2 of menstruation in at least two out of three menstrual cycles and additionally at other times of the cycle
Pure menstrual migraine with aura	
A.	Attacks, in a menstruating woman, fulfilling criteria for migraine with aura and criterion B
B.	Attacks occurring exclusively on day 1 ± 2 of menstruation in at least two out of three menstrual cycles and at no other time of the cycle
Menstrual-related migraine without aura	
A.	Attacks, in a menstruating woman, fulfilling criteria for *migraine with aura* and criterion B
B.	Attacks occurring exclusively on day 1 ± 2 of menstruation in at least two out of three menstrual cycles and additionally at other times of the cycle

Non-Pharmacological Treatment

In migraine therapy, a non-pharmacological approach can play an important role as an add-on to medical treatment.[18] Important non-pharmacological interventions may include:

- Education regarding causes of migraine and use of abortive and preventive treatment.[18]
- Identifying comorbid conditions including stress, depression or anxiety.[18]
- Identifying and eliminating any triggering factors, such as poor sleep pattern or consumption of certain foods (wine, cheeses, chocolates etc.).[18]
- Physiotherapy to learn about proper body posture and instruction in exercises that can be performed at home.[19]
- Behavioral and cognitive therapy, e.g., stress and pain management plans.[20]
- Acupuncture in conjunction with acute medication.[21]

Pharmacological Treatment

Acute treatment: Simple analgesics are the first choice for the acute treatment of migraine.[22] Triptans should be taken in early phase of headache.[23] Triptans are not effective in aura phase in migraine with aura patients. [24.25] A patient shall try three different triptans, in three separate migraine attacks each.[26] Approximately 25% of patients will experience relapse of their migraine attack within 24 hours and may be successfully treated with an additional dose of triptan.[27] To avoid medication overuse headache

triptan use should be limited to less than nine days per month.[27] Of the seven available triptans, only sumatriptan and zolmitriptan are currently available in Pakistan. Recommended doses of simple analgesics and triptans are provided in Table 4 & 5.

Table 4: Recommended Dosage of Simple Analgesics and Antiemetics in the Acute Treatment of Migraine[22]

Analgesics	Initial dose	Antiemetic	Initial dose
Acetylsalicylic acid	1000 mg	Metoclopramide	10-20 mg
Ibuprofen	200-800 mg	Domperidone	20-30 mg
Naproxen	500–1000 mg		
Diclofenac	50–100 mg		
Paracetamol	1000 mg		

Table 5: Recommended Dosage of Triptans in the Acute Treatment of Migraine[22]

Triptan	Formulation	Single dose
Sumatriptan	Tablet Nasal spray* S.C.	50 - 100 mg 10 - 20 mg 6 mg
Zolmitriptan	Pill Nasal spray	2.5 - 5mg 2.5 - 5mg
Naratriptan*	Pill	2.5 mg
Rizatriptan*	Pill	10 mg
Almotriptan*	Pill	12.5 mg
Eletriptan*	Pill	20 - 40 mg
Frovatriptan*	Pill	2.5 mg

*Currently not available in Pakistan

Preventive treatment: Preventive treatment should be considered when the patient experiences four or more disabling migraine attacks in one month, quality of life is significantly diminished, or the patient experiences frequent, prolonged, or uncomfortable auras.[18, 22, 28] Preventive medications for migraine are listed in Tables 6 & 7.

Table 6: Preventive Treatment of Episodic Migraine Listed in Order of Choice[18]

Medication	Daily dose
Metoprolol	50-200 mg
Propranolol	40-240 mg
Topiramate	25-100 (200) mg
Amitriptyline	10-100 mg
Flunarizine	5-10 mg
Valproate	500-2000 mg

Table 7: Preventive Treatment of Chronic Migraine Listed in Order of Choice[18]

Medication	Daily dose
Metoprolol	50-200 mg
Propranolol	40-240 mg
Candesartan	16 (24-32) mg
Topiramate	25-100 (200) mg
Botulinum type A toxin	155-195 units intramuscular every 3 months
CGRP antibodies*	
Erenumab	70-140 mg sub cutaneous every month
Galcanezumab	120 mg sub cutaneous every month

*currently not available in Pakistan

TENSION TYPE HEADACHE

TTH is the most prevalent primary headache disorder with a mean overall lifetime prevalence of 42% (Range 19-83%).[37]

Clinical Features

Four main types and their diagnostic criteria for TTH are as follows.

Infrequent episodic tension-type headache: Infrequent episodes of headache, typically bilateral, pressing or tightening in quality and of mild to moderate intensity, lasting minutes to days. The pain does not worsen with routine physical activity and is not associated with nausea, although photophobia or phonophobia may be present.	**Frequent episodic tension-type headache:** Frequent episodes of headache, typically bilateral, pressing or tightening in quality and of mild to moderate intensity, lasting minutes to days. The pain does not worsen with routine physical activity and is not associated with nausea, although photophobia or phonophobia may be present.
Chronic tension-type headache: A disorder evolving from frequent episodic TTH, with daily or very frequent episodes of headache. The pain does not worsen with routine physical activity, may be associated with mild nausea, photo or phonophobia.	**Probable tension-type headache:** Tension-type-like headache missing one of the features required to fulfill all criteria for a type or subtype of tension-type headache coded above, and not fulfilling criteria for another headache disorder.

(https://ichd-3.org/2-tension-type-headache/)

General Approach for Assessment

Patients with TTH should maintain a headache diary.

All patients should undergo physical examination of scalp muscles, sinuses, temporomandibular joints.

Psychiatric comorbidity especially underlying depression should be identified and treated.[8]

Non-pharmacological Treatment

Expert recommendations for non-pharmacological treatment of TTH are listed in table 8

Table 8: Non-Pharmacological Treatment of Tension-Type Headache[8]

Recommendations are based on ‘‘expert opinion’’ [29]

- Educate and reassure patient
- Rule out depression and other underlying causes
- Evaluate excessive use of pain medications
- Minimize stress
- Physiotherapy (daily exercise and posture correction)
- Cognitive behavioral therapy (CBT)

Pharmacological Treatment for TTH is outlined in Table 9 & 10

Table 9: Acute Treatments in Tension-Type Headache

Treatment	Single Dose	Maximum Daily Dose
Paracetamol[30, 31]	1000 mg	3000 mg
Ibuprofen[32, 36]	400 mg	2000 mg
Diclofenac[33]	25-75 mg	150 mg
Ketoprofen[34]	50 mg	250 mg
Naproxen[35]	250-500 mg	1000 mg
Aspirin[36]	500-1000 mg	3000 mg

Table 10: Preventive Treatments in Tension-Type Headache

Drug	Starting Dose	Titration	Max. Daily Dose
Amitriptyline[8]	10 mg	10-25 mg	150 mg
Mirtazapine[8]	15 mg	15-30 mg	30 mg
Venlafaxine[8]	37.5 mg	37.5-75mg	150 mg

1. ***Amitriptyline tablets, 10–75 mg.***

Effect: 30% reduction of the headache versus placebo.

• ECG should be checked before treatment initiation.

• 10 mg ×1, increased by 10 mg/week until an effect is achieved or until side effects occur.

• The entire dose should be given 1 h before bedtime to improve sleep and minimize tiredness the following day.

• Typical side effects include, among others, dry mouth, fatigue, dizziness and weight gain.

2. Mirtazapine tablets, 15–30 mg.

Effect: 30% reduction of the headache versus placebo.

• 15 mg ×1, increased to 30 mg × 1 after a week.

• Administered approximately 1 h before bedtime.

• Typical side effects include, among others, fatigue, weight gain and dizziness.

CLUSTER HEADACHE

Cluster headache is uncommon with prevalence 0.1%.[38] The peak age of onset is between the 3rd and 4th decades.[40,42] The disorder is four times more common in men.[38] Cluster headache sufferers are often smokers.[40] Even after 10-15 years, 80% of patients still have attacks.[41]

Clinical Features and imaging

Diagnostic criteria of cluster headache including episodic and chronic headache along with differentiating features from Migraine are outlined in Table 11.

Table 11: Diagnostic Criteria of Cluster Headache According to ICHD-3[17, 18]

Cluster Headache Diagnostic Criteria

A. Severe/very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes (untreated)
B. Either or both of the following:
1. At least one of the following symptoms or signs, ipsilateral to the headache:
a. Conjunctival injection and/or lacrimation
b. Nasal congestion and/or rhinorrhea
c. Eyelid oedema
d. Forehead and facial sweating
e. Forehead and facial flushing
f. Sensation of fullness in the ear
g. Miosis and/or ptosis
2. A sense of restlessness or agitation
C. Frequency between one every other day up to 8/day for > half the time the disorder is active

Episodic Cluster Headache

A. Attacks fulfilling criteria for Cluster headache and occurring in bouts (cluster periods)
B. At least two cluster periods lasting from 7 days to one year (when untreated) and separated by pain-free remission periods of three months

Chronic Cluster Headache

Attacks fulfilling criteria for Cluster headache and occurring without a remission period, or with remissions lasting < 3 months, for at least 1 year

Clinically features to distinguish between migraine and cluster headache include:

- Cluster sufferers can have nausea and vomiting, photophobia and phonophobia[40, 42]
- Aura can be experienced in up to 23% of cluster headache sufferers[42-44](though in practice is rare)
- The duration of untreated migraine attacks in adults is invariably longer than four hours[42]
- A key feature in cluster headache is restlessness and lack of motion sensitivity, while migraine sufferers prefer to be still[40, 42]

Non-pharmacological Treatment

In general, there is no outcome of non-pharmacological management on cluster headache.[45]

Pharmacological treatment

Treatment recommendations for acute cluster attack and prevention of attacks is provided in table 12 and 13.

Table 12: Recommended Acute Cluster attack treatments

Treatment	Formulation	Strength	Maximum Daily Dose
Oxygen[45]	Inhalation through non-re breathable mask	10-15 L/min	No limit
Sumatriptan[8]	Subcutaneous injection	6 mg	12 mg
Sumatriptan[45]	Nasal spray	20 mg	40 mg
Zolmitriptan[45]	Nasal spray	5 mg	15 mg

Table 13: preventive treatments for cluster headaches

Name	Start dose	Increment	Daily Dose	Comments
Greater occipital nerve block[46]	Depot steroid + local anesthetic	Not applicable	Not applicable	Different formulations of steroid & anesthetic used*
Lithium[8]	200 mg/day	200 mg/week	According to serum lithium levels. Note preparations vary widely in bioavailability	Monitor levels
Prednisolone/prednisone[8]	75mg for 5 days	Taper thereafter	Short term interim use only	
Melatonin[45]	10mg		10mg	
Verapamil[47]	80 mg TDS	Increase 80 mg every 2 weeks	960 mg	ECG monitoring shall be done
Non-Invasive Vagal Nerve Stimulation[45]	As per specialist recommendation			

*There does not seem to be a difference between different local anesthetics

TRIGEMINAL AUTONOMIC CEPHALALGIAS (TAC) AND TRIGEMINAL NEURALGIA (TGN)

Differential diagnosis and treatment for these headaches is provided in Table 14

Table 14: Differential diagnosis of The Trigeminal Autonomic Cephalalgias (TAC) and Trigeminal Neuralgia (TGN)

TAC	Hemicrania Continua	Cluster Headache	Paroxysmal Hemicrania	SUNA	Trigeminal neuralgia
Predominant gender	Female	Male	Female	Male	Female
Attack duration	Constant	15 minutes – 3 hours	5 – 30 minutes	1-600 seconds	Few sec. - 2 min.
Attack freq.	N/A	Up to 8 / day	Up to 5 / hr.	Up to 30 / hr.	1-50 / day
Restlessness	±	++	±	±	-
Inter paroxysmal pain*	NA	Yes	Yes	Yes	Yes
Other differentiating features	Typically more migrainous features than other TACs Can be potentiated by acute-relief medication overuse	Strongest association with restlessness	Spontaneous, shorter and more frequent attacks than cluster.	Attacks of pain can be spontaneous and triggered e.g. eating, brushing teeth, cold wind, neck movements. All attacks can be spontaneous. Pain is always primarily in the distribution of the ophthalmic division of the trigeminal nerve with radiation to affect	Attacks of pain can be spontaneous and always triggered e.g. eating, brushing teeth, cold wind, neck movements. Pain is always primarily in the distribution of the 2nd and 3rd division of the trigeminal nerve - should rarely affect V1 and should not affect C2 (back of head and neck) No autonomic features
Episodic or chronic tendency	Chronic	Episodic	Chronic	Chronic	Currently undefined
Acute attack treatment	None – prone to development of medication-overuse	Sumatriptan 6mg Subcutaneous	High flow oxygen	None	None – too short
Preventive treatment	Indomethacin	Verapamil	Indomethacin	Indomethacin	Carbamezapine

* The paroxysmal trigeminal autonomic cephalalgias can have pain between acute attacks. In most cases the inter-paroxysmal pain is part of the same disorder. In some cases, hemicrania continua may be co-exist. Therefore, a trial of Indomethacin should be considered[48].

MEDICATION OVERUSE HEADACHE

Diagnostic criteria of medication overuse headache are provided in table 15.

Table 15: Diagnosis of Medication-Overuse Headache

- Consider a diagnosis of medication overuse headache in patients with headache on ≥ 15 d/mo and assess patients for possible medication-overuse (use of triptans, ergots, combination analgesics, or opioid-containing medications on ≥ 10 d/mo, or use of acetaminophen or NSAIDs on ≥ 15 d/mo)
- When medication-overuse headache is suspected, the patient should also be evaluated for the presence of the following:

1. Psychiatric co-morbidities i.e. depression and anxiety; need to be considered in planning an overall treatment approach
2. Psychological and physical drug dependence
3. Use of inappropriate handling strategies. Rather than relying on medication as a main management factor, patients with suspected medication-overuse might benefit from training in and development of more adaptive self-management strategies (eg, identification and management of controllable headache triggers, relaxation exercises, effective stress management skills, and activity pacing)

- It is necessary to have record of acute medication intake for the prevention and treatment of medication-overuse headache

((https://ichd-3.org/8-headache-attributed-to-a-substance-or-its-withdrawal/8-2-medication-overuse-headache-moh/

Non-pharmacological Treatment

Important aspects of treatment are outlined in Table 16.

Table 16: Non-Pharmacological Treatment of Medication Overuse Headache[8]

The primary treatment elements:

- Abrupt discontinuation of all analgesics and acute migraine medicine or a reduction of the intake of attack medication to a maximum of 2 days/week during a 2-months period.
- Training and information to patients as well as relatives and medical staff.
- Psychological support, information and treatment of any withdrawal symptoms such as severe headache, nausea, vomiting, sleep disturbances, increased sweating, agitation, anxiety, nervousness, hypotension and tachycardia for 2–10 days depending on the type and amount of medicine taken.
- Admission to a neurology department in cases with considerable medication overuse and/or significant co-morbidity
- Initiation of prophylactic medications
- A sick leave up to three weeks is recommended.
- Follow-up for 6–12 months.
- Spontaneous and marked reduction of headache over weeks to months. Many patients also experience a considerable general improvement of their general condition as they are no longer affected by a daily medicine intake

Pharmacological Treatment

Pharmacological management of MOH is detailed in table 17.

Table 17: Pharmacological treatment of medication overuse headache[8]

Support medicine may be needed during the first week and the following may then be used:

- Promethazine 25 mg x as needed maximally three times per day for a week followed by rapid tapering off (1–2 weeks)
- Metoclopramide suppositories 20 mg in case of severe nausea and vomiting
- Phenobarbital 100–200 mg x 2–3 for the first 4–5 days in case of severe withdrawal symptoms after discontinuation of opioids/ combination medicines.

After 2 months

- Prophylactic medication can be initiated at time of withdrawal or after two months in accordance with standard guidelines depending on the type of headache
- Thorough information to the patient on the correct use of acute and prophylactic medical treatment
- Previously used medication, which during the medication overuse period had no effect, may now have effect
- Close follow-up to avoid relapse into medication overuse
- Limited re-initiation of attack medication
- Bridge therapy is used to provide symptomatic relief for patients with MOH during withdrawal of the overused medications to create a bridge from the acute medications to prophylaxis, however, two double-blind controlled randomized studies showed that the steroid prednisolone was no more effective than placebo [50]

SECONDARY HEADACHES

Diagnostic features of secondary headache are provided in table 18.[17]

Table 18: General diagnostic criteria of secondary headaches according to ICHD-3[17].

Criteria	
A	Any headache fulfilling criteria C
B	Diagnoses of another disorder scientifically documented to be able to cause headache and evidence of causation demonstrated by at least two of the following: 1. Headache developed in temporal relation to the presumed causative disorder 2. At least one of the following: i. worsening of headache in parallel with worsening of the presumed causative disorder ii. improvement of headache in parallel with improvement of the presumed causative disorder 3. Headache has characteristics which are typical for the causative disorder[1] 4. Other evidence exist of causation[2]
C	Not better accounted for by another ICHD-3 diagnosis

[1]e.g. thunderclap (very sudden) onset of acute headache attributed to non-traumatic subarachnoid hemorrhage.

[2]e.g, changes in neuroimaging or other laboratory measures.

Red Flags

A secondary cause of headache is identified in less than 3% of patients with red flags.[49] Overview of red flags identified from the clinical assessment is presented in Table 19.[50]

Table 19: Red flags identified from the clinical assessment[51]

1. New onset of headache or changed pattern of pre-existing headache
2. Thunderclap headache (sudden onset of severe headache)
3. Headache with atypical aura (la sting >1 h or includes motor outcomes)
4. Headache with aura developed during the use of contraceptive pills
5. Headache accompanied by focal neurological signs (except transient due to migraine aura)
6. Sudden headache occurring during strenuous physical, sneezing, coughing or sexual activity
7. New onset of headache in a patient with cancer or HIV infection
8. Headache accompanied by fever
9. Progressive headache over weeks
10. New onset headache in patients <10 or>40 years of age
11. Headache that is dependent on position

Adapted from: Schytz et al., 2020. Reference programme: diagnosis and treatment of headache disorders and facial pain. Danish Headache Society, 3rd edition, 2020[51]

Most Common Secondary Headaches

The two most common forms of secondary headaches are medication overuse headache (MOH) and post-traumatic headache. Sinusitis is another common cause of secondary headache.

Post-Traumatic Headache

Diagnostic criteria of post traumatic headache are provided in table 20.

Table 20: Diagnostic Criteria of Persistent Posttraumatic Headache According to ICHD-3[17].

Criteria	
A	Any headache fulfilling criteria C and D
B	Traumatic injury to the head
C	Headache developed within 7 days after one of the following: 1. Injury to the head 2. Recovering consciousness following the injury to the head 3. Discontinuation of medication(s) hindering ability to sense or report pain 4. Other evidence exist of causation
D	Headache > 3 months after its onset
E	Not better accounted for by another ICHD-3 diagnosis

Non-Pharmacological Treatment

There is currently no evidence-based non-pharmacological treatment.

Pharmacological Treatment

Currently, there is no specific evidence-based treatment for post-traumatic headache. Use of acute therapies should not exceed 14 days per month in total due to risk of medication overuse headache. Patients with post-traumatic headache and medication overuse should follow the detoxification therapy (See section "MOH"). This therapy may improve headache in about half of the patients.[52]

Most Serious Secondary Headaches

It is important to assess the time course of the headache. Acute onset of headache within seconds with maximum pain intensity (e.g., thunderclap, popping sensation) should always lead to investigation of subarachnoid hemorrhage. Sub-acute, progressive headache onset after head trauma should lead to suspicion of epidural hematoma or raised intracranial pressure. Sub-acute headache with fever, malaise, or seizures, should raise suspicion of a neuro-infection (e.g., meningoencephalitis, cerebral abscess) or cerebral venous sinus thrombosis.[50-51] Progression of headache over weeks or months and occurrence of epileptic seizures, affected speech, hemiparesis, and/or change of personality, may indicate a space-occupying brain tumor or a chronic subdural hematoma. The most serious secondary headaches are briefly presented below:[51]

Subarachnoid Hemorrhage

Acute onset of headache (e.g., thunderclap headache), which may present as seizures or altered level of consciousness.

Giant Cell Arteritis (Arteritis Temporalis)

Typical onset after 50 years of age. Common symptoms and signs are headache with fatigue, fever, and weight loss, feeling of claudication on chewing, chewing claudication, Amaurosis fugax, tenderness of temporal artery, and Increased Levels of CRP Or Erythrocyte Sedimentation Rate (Of Note: May Be Normal in Rare Cases)

Primary Glaucoma

Narrow-angle glaucoma may cause headache and occurs rarely before 50 years of age. It may debut as acute ocular hypertension. The glaucoma is characterized by painful red eye, pupillary dilatation with poor light reflex, blurred vision, and colored halos around objects. It is an ophthalmological emergency.

Cerebral Venous Thrombosis (CVT)

Onset is sub-acute with gradually increasing headache and fluctuating neurological symptoms, such as altered level of consciousness, seizures, papilledema, cranial nerve palsies. [51] In 17% of cases in women, the cerebral venous thrombosis occurred during pregnancy or puerperium.[50]

Idiopathic intracranial hypertension (IIH)

It is more common in women with obesity. Papilledema is present. Brain MRI and MR Venogram must be done. Lumbar puncture with raised CSF pressure is diagnostic. Delay in treatment may lead to blindness.

Non-Pharmacological Treatment

There is currently no evidence-based non-pharmacological treatment.

Pharmacological Treatment

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Non-pharmacological treatment is weight-loss (5%– 20%). Pharmacological treatment is Acetazolamide (daily dose 1000–4000 mg) as first choice or Topiramate (25–150/200 mg) as second choice (monotherapy or add-on). In refractory cases optic nerve fenestration and ventriculoperitoneal shunt is needed to prevent blindness.

Arterial dissection

The headache may be accompanied by neck pain and Horner's syndrome. Typical onset of headache in relations to twist or trauma to the neck.

Neurological infections

Headache usually presents with fever and neck stiffness, cognitive impairment, petechiae, and seizures.

Brain Tumour

Headache is present in 60% patients with brain tumor, and it may be only symptom in 2% cases. Other associated features may include worsening of headache in the morning, nausea, seizures, cognitive change and slurring of speech and/or hemiparesis.

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