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Review Article

# A REVIEW ON CLASSIFICATION, PATHOPHYSIOLOGY, DIAGNOSIS, AND PHARMACOTHERAPY OF HEADACHE

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#### ABSTRACT

Headache disorders, characterized by recurrent headache, are among the most common disorders of the nervous system. Headache disorder is classified mainly into two major types, primary headache and secondary headache by the International Classification of Headache Disorders. Most types of headache are diagnosed by the clinical history and from headache classification committee of the International Headache Society (IHS). A number of intrinsic or extrinsic factors can trigger headache attack which release neurotransmitters and activate trigeminal vascular system. The grading of headache intensity is done by headache severity scale of IHS. Headache management includes pharmacological and non-pharmacological treatment.

Keywords: Clinical history, International classification of headache disorders, International Headache Society, Primary headache, Secondary headache.

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#### INTRODUCTION

Headache disorders, characterized by recurrent headache, are the most common disorders of the nervous system. Headache itself is a painful and disabling feature of a small number of primary headache disorders, namely, migraine, tension-type headache (TTH), cluster headache (CH), and chronic daily headache (CDH) syndromes cause substantial levels of disability [1]. Headache is an extremely common and universal symptom with a complex and heterogeneous set of causes. Nearly half of the world's adult population has an active headache disorder. The World Health Organization reports that almost half of all adults worldwide will experience a headache in any given year and it has a major impact on public health [2]. In 1962, the Ad Hoc Committee on Classification of Headache, on the basis of general consensus, delineated 15 categories of headaches [3]. In the second edition of the International Classification of Headache Disorders (ICHD-2), headache is divided into primary disorders, without an underlying cause and the secondary disorders, attributable to a specific etiology [4]. The generally accepted diagnostic criteria for primary headaches are those published by the International Headache Society (IHS), such as the ICHDs [5]. Headache affects people of all ages, races, and socioeconomic status and is more common in women.

Primary CDH is subdivided into transformed migraine, chronic TTH, hemicrania continua (HC), and new daily persistent headache (NDPH), they constitute nearly 98% of all headaches [6]. However, secondary headaches are important to recognize as these are serious and may be life threatening. Headaches are often treatable with medications and/or lifestyle changes. Headaches somewhat more broadly cover both painful and non-painful discomforts of the entire head [7]. They are one of the most common medical complaints; most people experience them at some point in their life. Headaches occur typically with regular circadian timings and circannual (mainly in the autumn and spring) [8]. In general population, headache is very common that it is difficult to identify individuals who have never had a headache. Migraine is the second most common cause of headache disorder [9]. For many individuals, the consumption of an analgesic or taking a short rest period is a sufficient remedy. However, there are also many other individuals who are severely in capacitated by headache and for whom no known effective treatment exists [3]. In the past, most headache classifications have been based on hypothetical pathogenetic mechanisms example, "vascular headache" and "muscle contraction headache." Due to poor understanding of the pathophysiology of most headaches, the current headache classification developed in the year 1988 by the IHS according to the expertise of groups of field specialists. Following the example of Diagnostic and Statistical Manual of Mental Disorders (which are similar to headaches as regards the lack, in both disorders, of laboratory or instrumental markers), operational diagnostic criteria for each headache type and subtype were established. Such an approach inevitably implies the need for subsequent revisions based on field testing and clinical experience to improve the adherence of the classification to clinical reality. Several studies have shown that the IHS classification is a suitable tool for describing headache in the general population.

#### CLASSIFICATION OF HEADACHE

Headache disorder is mainly classified into two major types; they are as follows:

- 1. Primary headache
- 2. Secondary headache.

The short-lasting primary headache syndromes may be such as conjunctival injection, lacrimation, nasal congestion, and conveniently divided into those exhibiting marked autonomic rhinorrhea, ptosis, or eyelid edema. Almost all reported activation and those without autonomic activation [10].

#### **Primary headaches**

- 1. Migraine
- 2. TTH
- Trigeminal autonomic cephalalgias
- 4. Other primary headache disorders.

## Migraine

Migraine is a neurovascular disease with a broad spectrum of symptoms and is a common disabling primary headache disorder. The migraine headache is ubiquitous, disabling, prevailing, and essentially treatable, but still under-estimated and under-treated [11]. Migraine headache is usually frontotemporal. Migraine, high prevalence and high socioeconomic, was

documented in the epidemiological studies. One in 10 people will surely have migraine [12]. Migraine is a common chronic headache disorder characterized by recurrent attacks lasting 4 h–72 h. It has been termed the seventh disabler due to its considerable impact on the quality of life of patient. It is the most frequent cause of headache in the children and adolescents. Unilateral pain is usually seen in late adolescence or in the early adult life [13]. The IHS criteria are very helpful in the diagnosis of migraine [12]. There are two major subtypes of migraine.

- A clinical syndrome which is characterized by headache with some specific features and also associated symptoms is migraine without aura
- Migraine with aura is characterized by transient focal neurological symptoms and they usually precede or sometimes accompany the headache. Migraine aura symptoms include temporary visual or sensory disturbances that usually strike before other migraine symptoms, they are like head pain, nausea, and sensitivity to light and sound which usually seen within an hour before head pain starts and last less than an hour after the attack [13].

#### Classification of migraine

The classification of migraine has been impeded by the lack of pathognomonic markers for migraine, cooccurrence of migraine, and its subtypes as well as TTH within the same individual, the lack of validity of inclusion criteria, and thresholds for distinguishing disorder from non-disorder and the boundaries between migraine and other headache subtypes and classification of migraine is given in Table 1.

#### Migraine without aura

It is the recurrent headache disorder manifesting in attacks lasting 4 h–72 h. Migraine headache as compared with adults, it is more often bilateral in children and adolescents (aged <18 years) and the unilateral pain usually seen in the early adult life [11]. In some cases, people with migraine have some specific warning symptoms or an aura before the onset of their headache. Some of those warning signs includes as from flashing lights/blind spot in one eye to numbness/weakness involving one side of the body. By some routine physical activity, the headache may be aggravated sometimes, occurs at unilateral location and it is in

# Table 1: Classification of migraine from the international classification of headache disorders, 3<sup>rd</sup> edition (beta version)

- 1.1 Migraine without aura
- 1.2 Migraine with aura
  - 1.2.1 Migraine with typical aura
  - 1.2.1.1 Typical aura with headache
  - 1.2.1.2 Typical aura without headache
- 1.2.2 Migraine with brainstem aura
- 1.2.3 Hemiplegic migraine
  - 1.2.3.1 Familial hemiplegic migraine
  - 1.2.3.1.1 Familial hemiplegic migraine type 1
  - 1.2.3.1.2 Familial hemiplegic migraine type 2
  - 1.2.3.1.3 Familial hemiplegic migraine type 3
  - 1.2.3.1.4 Familial hemiplegic migraine, other loci
  - 1.2.3.2 Sporadic hemiplegic migraine
- 1.2.4 Retinal migraine
- 1.3 Chronic migraine
- 1.4 Complications of migraine
  - 1.4.1 Status migrainosus
- 1.4.2 Persistent aura without infarction
- 1.4.3 Migrainous infarction
- 1.4.4 Migraine aura-triggered seizure
- 1.5 Probable migraine
  - 1.5.1 Probable migraine without aura
- 1.5.2 Probable migraine with aura
- 1.6 Episodic syndromes that may be associated with migraine
  - 1.6.1 Recurrent gastrointestinal disturbance
  - 1.6.1.1 Cyclical vomiting syndrome
  - 1.6.1.2 Abdominal migraine
  - 1.6.2 Benign paroxysmal vertigo
  - 1.6.3 Benign paroxysmal torticollis [13]

pulsating quality with mild, moderate, or severe intensity and associated with nausea or vomiting, phonophobia, and photophobia. Photophobia and phonophobia may be inferred from their behavior in young children. Migraine without aura often has a menstrual relationship [11,13]. Diagnostic criteria for migraine without aura are shown in Table 2.

#### Migraine with aura

It occurs as recurrent attacks which lasts within few minutes as unilateral fully reversible sensory, visual, or some other symptoms are seen which will usually develop slowly and some of the main migraine aura symptoms include temporary visual or sensory disturbances that usually strike before other migraine symptoms, they are such as head pain, nausea, and sensitivity to light and sound [14]. Aura is described as a complex of neurological symptoms that occur before the headache starts. Symptoms of aura can be visual or sensory and may include blind spots, zigzag lines, shimmering stars, changes or loss in vision, and flashes of light [2]. Migraine aura consists of a usually transient clinical disturbance and that may attributed to brain dysfunction. Five aura symptoms may last longer than 7 days in migraine sufferers and the second edition of the classification defines migraine [15]. Migraine has a variety of subtypes, some of which are associated with hemiplegia. Aura is highly variable and is thought to be generated from many areas of the cortex or brain stem. Aura symptoms include as visual, sensory, motor, brainstem, retinal, speech, and language.

#### Visual disturbances

The visual aura symptoms of migraine are subjective phenomenon and it is seen in 90% with migraine with aura patients and it is inaccessible to normal people that which a migraine person will experiences [13,16]. Most migraineurs have increased sensitivity to light and other visual stimuli during migraine attacks and can see visuals like Fig. 1 [17].

Positive symptoms, such as light flashes, spots, or zig-zag lines

- Negative symptoms, which are present when there is any loss of vision or blind spots as part of the aura phase
- Distorted vision symptoms
- Vertigo and dizziness
- · Light sensitivity and photophobia [16].

#### Sensory symptoms include

It most commonly begins with some unilateral tingling or the "Paresthesia" in the distal portion of one of the extremities, mainly the upper extremities then after it will slowly spread to the hands and forearms also [18]. Tingling and paresthesia are the first sensory symptom [19].

#### Motor symptoms include

The unilateral tearing, bilateral tearing, neck pain before headache, and neck pain during headache.

Types: Along with above-mentioned symptoms, migraine with aura is further classified into fallowing types, they are as follows:

# Table 2: Diagnostic criteria for migraine without aura, from headache classification committee of the International Headache Society. 2018

- A. At least five attacks fulfilling criteria B–D
- B. Headache attacks lasting 4 h-72 h (when untreated or unsuccessfully treated)
- C. Headache has at least two of the following four characteristics:
- 1. Unilateral location
- 2. Pulsating quality
- 3. Moderate or severe pain intensity
- 4. Aggravation by or causing avoidance of routine
- 5. Physical activity (e.g., walking or climbing stairs)
- D. During headache at least one of the following:

Nausea and/or vomiting

Photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis [13]

- a. Migraine with typical aura
- b. Migraine with brainstem aura
- c. Hemiplegic migraine
- d. Retinal migraine [13,16].

Table 3 shows diagnostic criteria for migraine with aura, from the headache classification committee of the IHS.

#### Chronic migraine

The IHS defines chronic migraine as more than 15 headache days per months over a period of 3 months and in the absence of medication over use, more than 8 are migrainous. Headache that occurs for 15 days or more days/months for more than 3 months, at least 8 days/months, has migraine headache features. It is a chronic daily/near-daily headache with migraine [20].

#### **Complications of Migraine**

- a. Status migrainosus
- b. Persistent aura without infarction
- c. Migrainous infarction
- d. Migraine aura-triggered seizure.

#### Probable migraine

Migraine-like attacks missing one of the features are required to fulfill all criteria for a type or subtype of the migraine which is coded above and not fulfilling criteria for another headache disorder. These are classified into:

- a. Probable migraine without aura
- b. Probable migraine with aura.

#### **Episodic migraine**

- a. Recurrent gastrointestinal disturbance
- b. Cyclic vomiting syndrome
- c. Abdominal migraine
- d. Benign paroxysmal vertigo
- Benign paroxysmal torticollis.

## TTH

TTH is a neurological disorder and most common, prevalent types of headache and important type of primary headaches. It represents a considerable health and socioeconomic problem. It is a disabling and associated with some psychiatric comorbidities [21-23]. Since many years, this headache has been called by various names such as tension headache, muscle contraction headache, psychomyogenic headache, psychogenic headache, ordinary headache, idiopathic headache, essential headache, and stress headache [24]. It is characterized

Table 3: Diagnostic criteria for migraine with aura, from headache classification committee of the International Headache Society, 2018

- A. At least two attacks fulfilling criteria B and C  $\,$
- B. One or more of the following fully reversible aura
  - a. Symptoms:
  - b. Visual
  - c. Sensory
  - d. Speech and/or language
  - e. Motor
  - f. Brainstem
- g. Retinal
- C. At least three of the following six characteristics
  - $1. \, At \, least \, one \, aura \, symptom \, spreads \, gradually \, over \, 5 \, min$
  - $2. \ Two \ or \ more \ aura \ symptoms \ occur \ in \ succession$
  - 3. Each individual aura symptom lasts 5 min–60 min
  - 4. At least one aura symptom is unilateral
  - 5. At least one aura symptom is positive
- 6. The aura is accompanied, or followed within 60 min, by headache
- E. Not better accounted for by another ICHD-3 diagnosis [13]

by a predisposition to attacks of mild-to-moderate headache with some associated symptoms [22]. Increased tenderness of pericranial myofascial tissues to manual palpation is the most prominent abnormal finding in patients with TTH. Painful impulses from these tissues may be related to the head and perceived as headache and myofascial mechanisms may, therefore, play a major role in the pathophysiology of TTH [21]. The diagnostic criteria for TTH are different and they are negation of those for migraine, for example, not bilateral, non-pulsating, and not aggravated by physical activity and so sometimes people experience both types, migraine and TTH [24]. The diagnosis ranges from non-life-threatening processes such as migraine to life-threatening conditions such as subarachnoid hemorrhage. Missing a life-threatening condition may result in adverse patient outcomes and may also pose the potential for medico legal liability. For these reasons, the American college of emergency physicians choose headache as a clinical policy topic [25]. The original headache clinical policy was published in June 1996. The pathogenetic mechanism underlying TTH is still unclear. The exact mechanism of TTH is unknown [13,25]. Diagnostic criteria for TTH are given in Table 4 and its classification is shown in Table 5.

In IHS classification (ICHD II), TTH have been divided into two forms, episodic (ETTH) and chronic (CTTH) and divided into three types based on the frequency of attack, they are shown in Table 6:

#### Trigeminal autonomic cephalalgias

The trigeminal autonomic cephalalgias (TACs) are a group of primary headache syndromes which are characterized by strictly unilateral head pain and they are rare, short-lasting, disabling primary headaches

# Table 4: Diagnostic criteria for tension-type headache, from headache classification committee of the International Headache Society, 2018

- A. At least 10 episodes fulfilling the criteria B-D
- B. Headache lasting from 30 min to 7 days
- C. Headache has at least two of the following characteristics
  - 1. Bilateral location
  - 2. Pressing/tightening (non-pulsating) quality
  - 3. Mild or moderate intensity
  - Not aggravated by routine physical activity such as walking or climbing stairs
- D. Both of the following
  - 1. No nausea or vomiting (anorexia may occur)
  - 2. No more than 1 episode of photophobia or phonophobia
- E. Not attributable to another disorder [13]

# Table 5: Classification of tension-type headache from the international classification of headache disorders, 3<sup>rd</sup> edition (beta version)

- 2.1. Infrequent episodic tension-type headache
- 2.1.1 Infrequent episodic tension-type headache associated with pericranial tenderness
- 2.1.2 Infrequent episodic tension-type headache not associated with pericranial tenderness
- 2.2. Frequent episodic tension-type headache
- $2.2.1\ Frequent\ episodic\ tension-type\ headache\ associated\ with$  pericranial tenderness
- 2.2.2 Frequent episodic tension-type headache not associated with pericranial tenderness
- 2.3. Chronic tension-type headache
  - 2.3.1 Chronic tension-type headache associated with pericranial tenderness
- 2.3.2 Chronic tension-type headache not associated with pericranial tenderness
- 2.4. Probable tension-type headache
  - 2.4.1 Probable infrequent episodic tension-type headache
- 2.4.2 Probable frequent episodic tension-type headache
- 2.4.3 Probable chronic tension-type headache [13]

and associated with ipsilateral cranial autonomic features such as conjunctival injection and tearing (SUNCT) [27,28]. The TACs primary headache disorders include CH, paroxysmal hemicrania (PH), and short-lasting unilateral neuralgiform headache attacks.

TACs are classified as five types depending on the severity, frequency, and location of headache and they are given in Table 7.

#### CH

It is a form of primary neurovascular headache with some features like severe unilateral, though the headache may alternate on sides, commonly retro-orbital lasting for about 15 min-180 min, pain accompanied by restlessness and cranial autonomic symptoms like conjunctival injection [13]. CH is a rare disorder mainly effects men, with a prevalence of <1%. A cluster bout or period refers to the duration of recurrent cluster attacks. CH is included with the shorter-lasting headaches to attempt a nosological analysis of these syndromes [10]. Some autonomic symptoms, during the headache attacks accompanying CH, include nasal congestion, unilateral ptosis, lacrimation, miosis, ear fullness, and conjunctival injection. Based on this symptoms, CH is classified as a prototype autonomic cephalalgia by the diagnostic criteria of the ICHD [10,13]. CH attacks vary individually and usually last between 15 min and 180 min, and during cluster periods, they occur up to 8 times/days with regular circannual and circadian timing [29]. Some older terms of CH are as ciliary neuralgia, migrainous neuralgia, and Horton's headache histaminic cephalalgia. Based on frequency of episodes and duration, CH is divided into

Table 6: Frequency characterization of tension-type headaches [26]

Feature	Infrequent ETTH	Frequent ETTH	Chronic TTH
Frequency	<12 days/year	More than 12 days and <180 days/year At least 10 episodes occurring more than 1 day and <15 days/ month for at least 3 months	days/year more than 15 days/months for at least 3

Table 7: Classification of trigeminal autonomic cephalalgias from the international classification of headache disorders, 3<sup>rd</sup> edition (beta version)

- 3.1 Cluster headache
- 3.1.1 Episodic cluster headache
- 3.1.2 Chronic cluster headache
- 3.2 Paroxysmal hemicrania
- 3.2.1 Episodic paroxysmal hemicranias
- 3.2.2 Chronic paroxysmal hemicranias
- 3.3 Short-lasting unilateral neuralgiform headache attacks
- 3.3.1 Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)
  - 3.3.1.1 Episodic SUNCT
- 3.3.1.2 Chronic SUNCT
- 3.3.2 Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA)
  - 3.3.2.1 Episodic SUNA
- 3.3.2.2 Chronic SUNA
- 3.4 Hemicrania continua
- 3.4.1 Hemicrania continua, remitting subtype
- 3.4.2 Hemicrania continua, unremitting subtype
- 3.5 Probable trigeminal autonomic cephalalgia
  - 3.5.1 Probable cluster headache
  - 3.5.2 Probable paroxysmal hemicranias
  - 3.5.3 Probable short-lasting unilateral neuralgiform headache attacks
  - 3.5.4 Probable hemicrania continua [13]

- Episodic CH, manifests bout periods lasting from 7 days to 1 year, accounts for 80–90% of CH cases, during which patients may experience daily attacks at a high frequency and asymptomatic outof-bout remission periods that last for months to years at a time and
- When patients experience a full year without remission or if the duration of remission is <30 days then, it is diagnosed as chronic CH (10-20% of cases) [13].

#### PH

In this type of headache, symptoms such as severe attacks, strictly unilateral pain which is supraorbital, orbital, temporal, or in any other combination of such type which lasts in about 2 min–30 min and occurs several/many times a day are seen. Pain attacks are associated with the ipsilateral conjunctival injection, lacrimation, rhinorrhea, sweating of facial and forehead, eyelid edema, and ptosis [13,30]; in 1974, Sjaastad and Dale first described the chronic PH is a primary headache disorder and included in the IHS classification of 1988 [30].

PH is classified into

- 1. Episodic CH
- 2. Chronic CH.

#### Short-lasting unilateral neuralgiform headaches attacks

This type of headache is seen with, severe-to-moderate attacks, which may be associated usually with prominent lacrimation and redness of ipsilateral eye and strictly unilateral head pain which is lasting from seconds to minutes which is seen at least once a day.

Without a refractory period, these subtypes usually be triggered [13].

Short-lasting unilateral neuralgiform headache attacks are recognized

- a. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)
  - 1. Episodic SUNCT
  - 2. Chronic SUNCT.
- Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA)
  - 1. Episodic SUNA
  - Chronic SUNA [13].

#### HC

HC is an indomethacin responsive headache disorder characterized by a continuous, strictly unilateral headache associated with nasal congestion, ipsilateral conjunctival injection, sweating of facial/forehead, eyelid edema, miosis, waning, and waxing which did not disappears completely [13,31]. It takes precedence over the diagnosis of other types of CDH. HC is included in Group 4 of ICHD ICHD-II [32].

- a. HC, remitting subtype: HC characterized by pain that is not continuous but is interrupted by remission periods of at least 24 h duration
- HC, unremitting subtype: HC characterized by continuous pain for at least 1 year, without remission periods of at least 24 h [13].

#### **Probable TAC**

Headache attacks are the type or subtype of TACs, in which one of the features required to fulfill all the criteria for any of the type and subtypes coded above are missing and do not fulfill all criteria for another headache disorder.

- a. Probable CH
- b. Probable PH
- $c. \quad \text{Probable short-lasting unilateral neuralgiform headache attacks}$
- d. Probable HC [13].

# Other primary headache disorders

# Primary cough headache

It is defined as headache precipitated by coughing, but not by prolonged physical exercise, in the absence of any intracranial disorder. Headache immediately reaches to its peak and subsides over several seconds to few minutes. Primary cough headache is usually bilateral and posterior

and patients who are older than 40 years of age are predominantly affected. Two-thirds of patients with primary cough headache have been reported some associated symptom such as vertigo, nausea, and abnormality in sleeping.

Based on diagnostic criteria, it is classified as follows:

a. Probable primary cough headache

The diagnostic criteria are shown in Table 8.

#### Primary exercise headache

Headache which is precipitated by any form of exercise in the absence of any intracranial disorder is defined as primary exercise headache. It occurs particularly in hot weather or at high altitude. Diagnostic criteria are given in Table 9, and based on diagnostic criteria, it is classified as follows:

a. Probable primary exercise headache.

#### Primary headache associated with sexual activity

Headache which is precipitated by sexual activity is defined as primary headache associated with sexual activity, usually starting as a dull bilateral ache as sexual excitement increases and suddenly becoming intense at orgasm, in the absence of any intracranial disorder.

Based on diagnostic criteria as shown in Table 10, it is classified as follows:

a. Probable primary headache associated with sexual activity.

#### Primary thunderclap headaches

High-intensity headache of sudden onset, mimicking ruptured cerebral aneurysm, in the absence of any intracranial pathology and is like clap of thunder. Thunderclap headache is frequently associated with serious vascular intracranial vascular disorders and its diagnostic criteria are shown in Table 11.

#### Cold-stimulus headache

Headache which is seen when any cold stimulus applied externally to the head or any cold product was ingested or inhaled. Based on diagnostic criteria as shown in Table 12, it is classified as follows:

# Table 8: Diagnostic criteria of primary cough headache

- A. At least two headache episodes fulfilling criteria B-D
- B. Brought on by and occurring only in association with coughing, straining, and/or other Valsalva maneuver
- C. Sudden onset
- D. Lasting between 1 s and 2 h
- E. Not better accounted for by another ICHD-3 diagnosis [13]

# Table 9: Diagnostic criteria of primary exercise headache

- A. At least two headache episodes fulfilling criteria B and C
- B. Brought on by and occurring only during or after strenuous physical exercise
- C. Lasting <48 h
- D. Not better accounted for by another ICHD-3 diagnosis [13]

# Table 10: Diagnostic criteria of primary headache associated with sexual activity

- A. At least two episodes of pain in the head and/or neck fulfilling criteria B-D
- B. Brought on by and occurring only during sexual activity
- C. Either or both of the following:
- 1. Increasing in intensity with increasing sexual excitement
- 2. Abrupt explosive intensity just before or with orgasm
- D. Lasting from 1 min to 24 h with severe intensity and/or up to 72 h with mild intensity
- E. Not better accounted for by another ICHD-3 diagnosis [13]

- Headache caused/associated or seen by an external application of a cold stimulus
- b. Headache caused due to ingestion or inhalation of a cold stimulus
- c. Probable cold-stimulus headache.
  - I. Headache probably seen due to external application of a cold stimulus
  - II. Headache probably seen due to ingestion or inhalation of a cold stimulus

## **External pressure headaches**

It is defined as headache which is resulting from a sustained compression or traction on pericranial soft tissues. It is classified as follows:

- a. External compression headache
- b. External traction headache
- c. Probable external pressure headache.
  - I. Probable external compression headache
  - II. Probable external traction headache.

#### Primary stabbing headache

Transient and localized stabs of pain in the head that occur spontaneously in the absence of organic disease of underlying structures or of the cranial nerves are seen in this type of headache. It involves extra-trigeminal regions in 70% of cases.

Based on diagnostic criteria given in Table 13, primary stabbing headache is classified as follows:

a. Probable primary stabbing headache.

#### Nummular headache

Pain of highly variable duration, but often chronic, in a small circumscribed area of the scalp and in the absence of any underlying structural lesion is seen in this type of headache.

Based on diagnostic criteria shown in Table 14, nummular headache is classified as follows:

a. Probable nummular headache.

## Hypnic headache

Frequently recurring headache attacks that are developing only during sleep and causing wakening and lasting for up to 4 h, without characteristic associated symptoms and not attributed to other

#### Table 11: Diagnostic criteria of primary thunderclap headache

- A. Severe head pain fulfilling criteria B and C
- B. Abrupt onset, reaching maximum intensity in <1 min
- C. Lasting for  $5\ min$
- D. Not better accounted for by another ICHD-3 diagnosis [13]

#### Table 12: Diagnostic criteria of cold-stimulus headache

- A. At least two acute headache episodes fulfilling criteria B and C
- B. Brought on by and occurring only during application of an external cold stimulus to the head
- C. Resolving within 30 min after removal of the cold stimulus
- D. Not better accounted for by another ICHD-3 diagnosis [13]

## Table 13: Diagnostic criteria of primary stabbing headache

- A. Head pain occurring spontaneously as a single stab or series of stabs and fulfilling criteria B and C
- B. Each stab lasts for up to a few seconds
- C. Stabs recur with irregular frequency, from one to many per day
- D. No cranial autonomic symptoms
- E. Not better accounted for by another ICHD-3 diagnosis [13]

pathology. Hypnic headache is a rare headache syndrome first described by Raskin in 1988 and has also been called clockwise headache or alarm clock headache and is regarded as an idiopathic headache disorder [33].

Diagnostic criteria is given in Table 15, and based on diagnostic criteria, it is classified as follows:

a. Probable hypnic headache.

#### New Daily Persistent Headache (NDPH)

Persistent headache which occurs on daily basis with past history of frequent headaches. Diagnostic criteria are given in Table 16, and based on diagnostic criteria, it is classified as follows:

a. Probable NDPH.

#### Differential diagnosis of headache

Most of the types of headache are diagnosed by the clinical history alone also. Sometimes neuroimaging and lumbar puncture may be necessary and Table 17 shows differential diagnosis of headache.

#### The secondary headaches

When the headache occurs in a patient due to a secondary or with any underlying cause, it is said to be secondary headache. A secondary headache is a symptom of a disease that can activate the pain-sensitive nerves of the head. The secondary headaches are "attributed to" another disorder since "the causal link between the underlying disorder and the headache is in most cases well-established." According to the ICHD-II, one of the main consequences of the rigorous separation is that the classification and diagnostic criteria differ in that they are etiological for secondary headaches and symptom based for primary headaches. The following constellations are possible:

- A new headache that occurs together along with another disorder is known to cause the headache. This type of headache independent of the clinical phenotype is said to be as a secondary headache
- During the time of occurrence of another disorder if a pre-existing headache is worsened, then that is known to cause headache and it has to be decided by seeing whether the patient is given the diagnosis of the pre-existing headache or the diagnosis of both the primary headache and the secondary headache. Factors in favor of a secondary headache are as follows:

#### Table 14: Diagnostic criteria of nummular headache

- A. Continuous or intermittent head pain fulfilling criterion B
- B. Felt exclusively in an area of the scalp, with all of the following four characteristics:
  - 1. Sharply contoured
  - 2. fixed in size and shape
- 3. Round or elliptical
- 4. 1-6 cm in diameter
- C. Not better accounted for by another ICHD-3 diagnosis [13]

#### Table 15: Diagnostic criteria of hypnic headache

- A. Recurrent headache attacks fulfilling criteria B-E
- B. Developing only during sleep and causing wakening
- C. Occurring on >10 days/month for >3 months D. Lasting from 15 min up to 4 h after waking
- E. No cranial autonomic symptoms or restlessness
- F. Not better accounted for by another ICHD-3 diagnosis [13]

# Table 16: Diagnostic criteria of new daily persistent headache

- A. Persistent headache fulfilling criteria B and C
- B. Distinct and clearly remembered onset, with pain becoming continuous and unremitting within 24 h
- C. Present for >3 months
- D. Not better accounted for by another ICHD-3 diagnosis [13]

- A close temporal relationship between the worsening of headache and the manifestation of the probable causative disorder
- ii. A significant worsening
- iii. Evidence which shows that the disorder can aggravate the primary headache and
- Improvement of the headache after relief of the causative disorder.

In other words, a secondary headache can either be diagnosed if the additional disorder can cause headache or if certain associations are present between the additional disorder and the headache. Otherwise, the primary disorder is diagnosed [35]. Any number of conditions varying greatly in severity may cause secondary headaches. Possible causes of secondary headaches include:

- Acute sinusitis (sinus infection)
- Arterial tears (carotid or vertebral dissections)
- Venous thrombosis within the brain
- Brain aneurysm (a bulge in an artery in your brain)
- Brain arteriovenous malformation: An abnormal formation of brain blood vessels
- Brain tumor and stroke
- Chiari malformation (structural problem at the base of your skull)
- Dehydration
- Dental problems and ear infections
- Encephalitis
- Giant cell arteritis (inflammation of the lining of the arteries)
- Glaucoma
- Hangovers
- High blood pressure (hypertension)
- Influenza and other febrile illnesses
- · Intracranial hematoma
- · Medications to treat other disorders
- Meningitis
- Monosodium glutamate
- Overuse of pain medication
- Panic attacks and panic disorder
- Post-concussion syndrome
- Pressure from tight headgear, such as a helmet or goggles
- Trigeminal neuralgia (as well as other neuralgias, all involving irritation of certain nerves connecting the face and brain).

Diagnostic criteria of secondary headache are given in Table 18 from the headache classification committee of the IHS.

Secondary headaches are classified as following types based on ICHD diagnostic criteria they are as follows:

- a. Headache attributed to trauma or injury to the head and/or neck
- b. Headache attributed to cranial and/or cervical vascular disorder
- c. Headache attributed to non-vascular intracranial disorder
- d. Headache attributed to a substance or its withdrawal
- e. Headache attributed to infection
- f. Headache attributed to disorder of homoeostasis
- g. Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cranial structure
- $h. \quad \mbox{Headache attributed to psychiatric disorder [13]}.$

Headache attributed to trauma or injury to the head and/or neck Headache of <3 months duration caused by traumatic injury to the head.

### Classification

- Acute headache attributed to traumatic injury to the head
- Persistent headache attributed to traumatic injury to the head
- Acute headache attributed to whiplash
- · Persistent headache attributed to whiplash
- Acute headache attributed to craniotomy
- Persistent headache attributed to craniotomy.

Table 17: Differential diagnosis of headache [34]

Headache feature	Tension-ty headache	•	Migraine (v	with or without aura)	Cluster headac	che	New daily persistent headache	Cervicogenic headache
Pain location	on Bilateral		Unilateral or bilateral		Unilateral (around the eye, above the eye, and along the side of the head/face)		Bilateral	Unilateral
Pain quality	ty Pressing/tightening (non-pulsating)		Pulsating (throbbing or banging in young people aged 12 years–17 years)		Variable (can be sharp, boring, burning, throbbing, or tightening)		Consistent pain	Non-throbbing, non- lancinating, pain usually starts in neck
Pain Mild or moderate intensity		Moderate or severe		Severe or very severe		Mild to moderate	Moderate or severe	
Effect on activities	Effect on Not aggravated by		Aggravated by, or causes avoidance Restlessness or agitation of, routine activities of daily living		-	-		
Other symptoms.	r None.		Unusual sensitivity to light and/or sound or nausea and/or vomiting Aura symptoms can occur with or without headache and:  a. Are fully reversible b. develop over at least 5 min c. Last 5 min-60 min.  Typical aura symptoms include visual symptoms such as flickering lights, spots or lines and/or partial loss of vision; sensory symptoms such as numbness and/or pins and needles; and/or speech disturbance		On the same side as the headache: 1. Red and/or watery eye 2. Nasal congestion and/or runny nose 3. Swollen eyelid 4. Forehead and facial sweating 5. Constricted pupil and/or drooping eyelid			None
Duration of 30 min-continuous headache		4 h–72 h in adults 1 h–72 h in young people aged 12 years–17 years		15 min-180 min		Duration of at least 4 h daily	1 h to weeks	
Frequency of headache	<15 days/ month	≥15 days/ month for more than 3 months	<15 days/ month	≥15 days/month for more than 3 months	1 every other day to 8 per day, with remission >1 month	1 every other day to 8 per day, with a continuous remission<1 month in a 12-month period	Occur in periods of 15 days a month for 3 months	Chronic, episodic
Final diagnosis	Episodic tension- type headache	Chronic tension- type headache	Episodic migraine (with or without aura)	Chronic migraine (with or without aura)	Episodic cluster headache	Chronic cluster headache	New daily persistent headache	Cervicogenic headache

# Headache attributed to cranial and/or cervical vascular disorder

An underlying cranial and/or cervical vascular condition is the onset, usually sudden, of a new headache, so far unknown to the patient. Whenever this occurs, vascular conditions should urgently be looked for.

# Classification

- Headache attributed to cerebral ischemic event
- Headache attributed to non-traumatic intracranial hemorrhage
- Headache attributed to unruptured vascular malformation
- Headache attributed to arteritis
- Headache attributed to cervical carotid or vertebral artery disorder
- Headache attributed to cranial venous disorder
- Headache attributed to other acute intracranial arterial disorder
- Headache and/or migraine-like aura attributed to chronic intracranial vasculopathy
- Headache attributed to pituitary apoplexy.

# Headache attributed to non-vascular intracranial disorder

After successful treatment if headache persisting for more than 1 month or spontaneous resolution of the intracranial disorder usually has other

mechanisms. Usually headache persists for more than 3months after treatment or remission of intracranial disorders.

# ${\it Classification}$

- Headache attributed to increased cerebrospinal fluid (CSF) pressure
- Headache attributed to low CSF pressure
- Headache attributed to non-infectious inflammatory intracranial disease
- Headache attributed to intracranial neoplasia
- Headache attributed to intrathecal injection
- Headache attributed to epileptic seizure
- Headache attributed to Chiari Malformation Type I
- Headache attributed to other non-vascular intracranial disorder.

# Headache attributed to a substance or its withdrawal

Associations between headache and substances are often anecdotal, many based on reports of adverse drug reactions. Headache can occur by chance and may be a symptom of a systemic disease and drugs given to treat such a condition will be associated with the headache.

Some disorders may predispose to drug-related headache alone, neither the drug nor the condition would produce headache.

#### Classification

- Headache attributed to use of or exposure to a substance
- Medication overuse headache
- Headache attributed to substance withdrawal.

#### Headache attributed to infection

Headache is a common accompaniment for some of the systemic viral infections such as influenza and also with sepsis and more rarely, it may accompany other systemic infections. In the intracranial infections, headache is most frequently encountered symptom and usually the first.

Occurrence of a new type of headache that is diffuse and associated with focal neurological signs and/or altered mental state and a general feeling of illness and sometimes fever should be an attention toward an intracranial infection even in the absence of neck stiffness.

#### Classification

- Headache attributed to intracranial infection
- Headache attributed to systemic infection.

#### Headache attributed to disorder of homoeostasis

The headache disorders within this category were previously referred to as headache associated with metabolic or systemic disease.

However, headache attributed to disorder of homoeostasis was felt to more fully encompass disorders of homeostatic mechanisms affecting a variety of organ systems, including altered arterial blood gases, systemic arterial pressure, volume disturbances that occur as a result of dialysis, and disorders of endocrine function.

#### Classification

- · Headache attributed to hypoxia and/or hypercapnia
- · Dialysis headache
- Headache attributed to arterial hypertension
- · Headache attributed to hypothyroidism
- · Headache attributed to fasting
- · Cardiac cephalalgia
- Headache attributed to other disorder of homoeostasis.

# Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial/cranial structure

Disorders of the cervical spine and of other structures of the neck and head have been regarded as common causes of headache, since many headaches seem to originate from the cervical, nuchal, or occipital regions or are localized there. Degenerative changes in the cervical spine can be found in virtually all people over 40 years of age.

Spondylosis or osteochondrosis is, therefore, not conclusively the explanation of associated headache.

#### Classification

- Headache attributed to disorder of cranial bone
- Headache attributed to disorder of the neck
- Headache attributed to disorder of the eyes
- Headache attributed to disorder of the ears
- · Headache attributed to disorder of the nose or paranasal sinuses
- · Headache attributed to disorder of the teeth
- Headache attributed to temporomandibular disorder
- Head or facial pain attributed to inflammation of the stylohyoid ligament
- Headache or facial pain attributed to other disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cervical structure.

# Table 18: Diagnostic criteria for secondary headaches from headache classification committee of the International Headache Society, 2018

- A. Any headache fulfilling criterion C
- B. Another disorder scientifically documented to be able to cause headache has been diagnosed
- C. Evidence of causation demonstrated by at least two of the following:
- Headache has developed in temporal relation to the onset of the presumed causative disorder
- 2. Either or both of the following:
- a. Headache has significantly worsened in parallel with worsening of the presumed causative disorder
- b. Headache has significantly improved in parallel with improvement of the presumed causative disorder
- 3. Headache has characteristics typical for the causative disorder
- 4. Other evidence exists of causation
- D. Not better accounted for by another ICHD-3 diagnosis [13]

#### Headache attributed to psychiatric disorder

Headache disorders that occur coincidentally some psychiatric disorders such as depressive disorders, acute stress disorder, anxiety disorders, trauma, and stress-related disorders (reactive attachment disorder, post-traumatic stress disorder, and adjustment disorders).

In such conditions, when there is no evidence of a causal relationship, headache diagnosis and also a separate psychiatric diagnosis both should be made.

#### Classification

- 1. Headache attributed to somatization disorder
- 2. Headache attributed to psychotic disorder [13].

# Clinical features of headache

Headache symptoms depend on the type of headache. The frequency of headaches and the intensity of the symptoms may vary as well. Symptoms that may suggest a more serious headache include any of the following:

- Headaches that start early in the morning
- Pain that is worsened by strain, such as a cough or a sneeze
- Vomiting without nausea
- Sudden onset of pain and the "worst headache" ever
- Headache that is becoming more severe or continuous
- · Personality changes
- · Changes in vision
- Weakness in the arms or legs
- Seizures and

Some common symptoms are such as dull, aching head pain, sensation of tightness or pressure across your forehead or on the sides and back of your head, tenderness on your scalp, neck, and shoulder muscles, nausea and vomiting, giddiness, phonophobia, and photophobia (pain in the eyes when looking into bright lights), tightness sensation in the head, hyperactivity or hypo activity, food cravings, and depression.

#### **Pathophysiology**

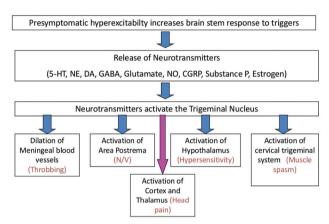
The brain itself is not sensitive to pain because it lacks pain receptors. Some areas of head and neck do have pain receptors and can sense pain. These include extracranial arteries, large veins, middle meningeal artery the meninges, falx cerebri, parts of the brainstem, venous sinuses, cranial and spinal nerves, head–and-neck muscles, eyes, ears, teeth, and lining of the mouth. Pial arteries, rather than Pial veins are responsible for pain production and process of headache pathophysiology is shown in Fig. 2.

- 1. Stimulation of primary nociceptors
- 2. Lesions in pain producing pathways of PNS and CNS.

#### Pain producing pathways

- Scalp
- Middle meningeal artery
- Dural sinuses
- Falx cerebri and
- · Proximal segments of the large pial arteries.

The ventricular ependyma, choroid plexus, pial veins, and much of the brain parenchyma are not pain producing.



Marcus, DA. Headache Simplified 2008.

#### Diagnosis process of headache

Diagnosis of a headache is made with a careful history, physical examination, and by some diagnostic tests and also based on type, location of headache, severity, and frequency, type of headache was finally diagnosed.

#### Severity scale

The IHS Grading of Headache Intensity contains 4 steps, including the "zero", "mild", "moderate" and "severe" diagrammatically shown in Fig. 3 [36].

- 0: No pain
- 1: Faint pain The patient's mobility and daily activities are not impacted and administration of medications is also not necessary
- 2: Mild pain Headache pain should be noticed but headache can be ignored very easily
- 3: Moderate pain Uncomfortable but the pain can be tolerable level and is easily noticeable, ignored and the subject can do their daily activities also
- 4: Uncomfortable pain This level of throbbing head pain that is
  constantly on your mind and the ability to do their daily activities
  will be difficult and the headache is untreated. The pain starts from
  head and slowly moves to the neck also for overtime
- 5: Distracting pain Piercing migraine pain that makes it difficult
  to manage the activities of daily living. The subject becomes more
  anxious and psychologically impacted by their pain symptoms and
  also experiences the weakness, blurred vision, and radiating pain in
  the neck-and-head region
- 6: Distressing pain Intense migraine pain that controls subjects mind set and psychological outlook on their body's ability to recover.
   In this stage, the subject concerns clinical expertise for a diagnosis and treatment regime
- 7: Unmanageable pain In this pain score, the pain level dominating subjects mindset and outlook on recovery. Subjects reached to a stage that the pain level disturbs the subjects the ability to do their daily functions and cognitive thinking, so more medical management and medical advice are necessary
- 8: Intense pain Here, the pain is so intense and both the head and neck are experiencing shooting pain which results in tingling, numbness, and extreme discomfort is seen, which disturbs the ability to do daily activities
- 9: Severe pain In these levels, the pain is so intense that the subject cannot tolerate the pain and look for more stronger medications and

- medical advice for psychological intervention for the management of pain is needed  $% \left( 1\right) =\left( 1\right) \left( 1\right$
- 10: Debilitating pain This unimaginable level is so intense and the subject may go unconscious. During a severe accident, this type of pain is likely incurred (e.g., head injury). Emergency treatment is needed and the body is unable to recover on its own [36].

#### **Treatment**

The ultimate goal of treatment is to stop headaches from occurring and the adequate headache management depends on the identification of the type of headache and may include the following:

- Avoiding known triggers, such as certain foods and beverages, lack of sleep and fasting, journey, stress, environmental triggers, and head hath
- · Changing eating habits
- Exercise
- Resting in a quiet, dark environment
- · Medications, as recommended by your doctor
- Stress management.

#### Pharmacological treatment

Headache may require some pharmacological treatment and that can be acute (abortive) or preventive and some requires both approaches in case of frequent severe headaches.

#### Acute treatment

Acute attacks are treated with ERGOT ALKALOIDS, nonsteroidal antiinflammatory drugs (NSAIDs), and triptans and the adjunctive therapy includes antiemetic drugs. These drugs control severity of headaches at particular level; however, no complete recovery from headache is present to treat recurrent attacks [37].

#### **NSAIDs**

Some NSAIDs and its doses are shown in Table 19.

#### Mechanism of action

NSAIDs are a heterogeneous group of compounds. These heterogeneous agents have a similar therapeutic action for the treatment of pain, fever, and inflammation. The major mechanism of NSAIDs is the inhibition of cyclooxygenase, enzyme catalyzing the synthesis of prostaglandins. Appropriate and effective treatment for migraine depends on an accurate diagnosis.

Ibuprofen is used to relieve pain of headache. Migraine treatment includes simple analgesics and NSAIDs [38].

## Adverse effects

The most common side effects are vomiting, nausea, constipation, diarrhea, reduced appetite, dizziness, and drowsiness. The most serious side effects are ulcers, bleeding, kidney failure, and rarely liver failure.

NSAIDs also may cause swelling of the arms and legs due to the retention of fluid from their renal effects.

# Triptans

The 5-HT1B/1D receptor agonists, collectively known as triptans, are a major advance in the treatment of headache and considered as breakthrough in the management of headache [39]. The beneficial effects of the triptans in patients with headache are related to their multiple mechanisms of action at sites implicated in the pathophysiology of headache.

Triptans are thought to work in three main ways:

- Peripheral inhibition of release of CGRP and substance P from trigeminal nociceptive afferents
- Modulation of second-order neurons centrally in the trigeminocervical pathway, including trigeminal nucleus caudalis, periaqueductal gray, and the thalamus and finally
- 3. Vasoconstriction [40,41].

Triptans are classified as given in Table 20.

Administration of sumatriptan that belongs to the highly effective anti-migraine drugs called triptans or 5-HT1B/1D agonists results in alleviation or less the severity of the headache [42].

These mechanisms are mediated by 5-HT1B/1D receptors. The high affinity of the triptans for 5-HT1B/1D receptors and their favorable pharmacologic properties contribute to the beneficial effects of these drugs, including rapid onset of action, effective relief of headache and associated symptoms, and low incidence of adverse effects [43].

#### Adverse effects

There are only few ADRs with triptans if they are used in proper dose and frequency.

There is a risk of coronary spasm in patients with established cardiac events and heart disease after taking triptans may occur rarely.

### Ergot alkaloids

Ergot alkaloids were the first antimigraine drugs available to treat. These are a large group of compounds. Ergot alkaloids are potent  $\alpha$ -blockers that cause direct smooth muscle contraction. They are products of the fungus *Claviceps purpurea*. Only products of lysergic acid are of clinical importance.

Table 19: Nonsteroidal anti-inflammatory drugs

Aspirin 600–900 mg Ibuprofen 600–800 mg Naproxen 500–1000 mg Diclofenac 50–75 mg Tolfenamic acid 200 mg

Table 20: Triptans classification

Triptans	Starting dose	Target dose
Sumatriptan	50 mg-100 mg tablet	300 mg
_	10 mg-20 mg nasal spray	40 mg
	25 mg suppository	-
	6 mg subcutaneous injection	12 mg
Zolmitriptan	2.5 mg-5 mg tablet	10 mg
	5 mg nasal spray	10 mg
Eletriptan	40 mg tablet	80 mg
Frovatriptan	2.5 mg tablet	5 mg
Rizatriptan	10 mg tablet	20 mg
Naratriptan	2.5 mg tablet	5 mg
Almotriptan	12.5 mg	25 mg

Mechanism of action: The ergot alkaloids are nonspecific 5-HT agonists and vasoconstrictors. They constrict the arteries and veins by direct stimulation of cerebral vascular smooth muscle.

- a. Ergotamine and
- b. Dihydroergotamine: It is an  $\alpha$ 1-adrenoceptor antagonist [43].
  - · Adverse effects: Nausea and vomiting
  - Antiemetic: An adjunctive antiemetic is useful drug that is effective against vomiting and nausea that accompany headache and medication used to treat acute attacks.
  - · Mechanism of action

Antiemetic drugs help to block specific neurotransmitters in the body and these neurotransmitters trigger impulses such as nausea and vomiting so blocking such impulses will shut down them.

#### Types are as follows:

- Dopamine antagonists: Prochlorperazine, metoclopramide, chlorpromazine, and domperidone
  - Adverse effects: Fatigue, constipation, restlessness, and muscle spasms
- Antihistamine: Promethazine
  - Adverse effects: Sleepiness, dry mouth, and dry nasal passages
- Serotonin (5-hydroxytryptamine 3) antagonist: Ondansetron
  - Adverse effects: Fatigue, dry mouth, and constipation

#### Prophylactic/preventive treatment

Preventive treatment might preclude the progression of headache and also results in reductions in cost of health care.



Fig. 1: Appearance of a common form of typical migraine visual aura [18]

Table 21: Prophylactic/preventive treatment

Drug class	Medication	Starting dose	Target dose
Beta-blockers	Propranolol	10 mg three times daily	40-80 mg 3 times daily
	Metoprolol	25 mg twice daily	100 mg twice daily
	Atenolol	25 mg once daily	100 mg once daily
Serotonin antagonist	Pizotifen	0.5 mg OD, increase by 0.5	3 mg daily
		mg every 1-2 weeks	
Antidepressant	Tricyclic: Amitriptyline (alternatively nortriptyline)	10 mg	50-75 mg daily
	Dosulepin	25 mg	7 5–100 mg
	SNRI: Duloxetine (alternatively venlafaxine)	30 mg	60-90 mg
Antiepileptic	Topiramate	100 mg	25 mg
	Sodium valproate	1000 mg	200 mg
Angiotensin based	Candesartan	4 mg OD	12-16 mg OD
	Lisinopril	10 mg OD	20-40 mg OD
Calcium channel blocker	Flunarizine	5 mg OD	5 mg for a month, then 10 mg
Nutraceutical	Riboflavin (Vitamin B2)	400 mg daily	-
	Magnesium	600 mg DAILY	-
	CoQ10	100 mg TID	-
	Alpha-lipoic acid	600 mg DAILY	-
Neuromuscular blocker	Onabotulinum toxin A (Botox)	200 U	-

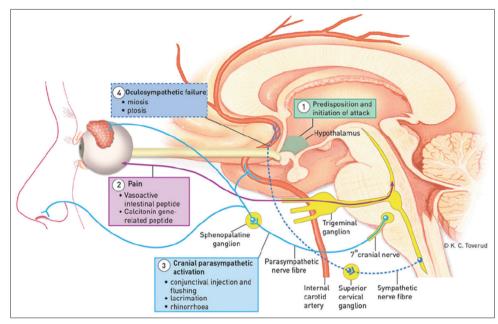


Fig. 2: Uploaded by Karl Bjørnar Alstadhaug, (PDF) Cluster headache. Available from: https://www.researchgate.net/publication/281484295\_Cluster\_headache [accessed Oct 01 2018]

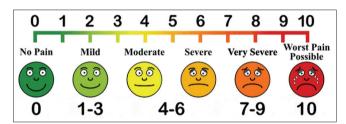


Fig. 3: Headache severity scale: The International Headache Society grading of headache intensity

Thus, headache preventive treatment has to be considered in patients with:

- Two or more attacks per months that significantly interfere with the patient's daily routine activity and produce disability for 4 or more days/months
- An unsatisfactory or scarce response to acute therapy
- Contraindication to acute treatments and adverse effects related to them
- The use of abortive medications more than twice per week
- Uncommon migraine conditions, including hemiplegic migraine, migraine with prolonged aura, or migrainous infarction.

Some drug classification and their doses are given in Table 21.

The current NICE guideline suggests first trying either topiramate or a beta-blocker. If both are ineffective or contraindicated, then consider the acupuncture, gabapentin, botulinum toxin, or riboflavin.

# Non-pharmacological treatment

The non-pharmacological therapy is also used in the preventive headache treatment. In addition to pharmacological therapy, lifestyle changes help in treating headaches [44]. Many non-drug techniques are available that can reduce or prevent head pain, such as massage, applying cold or heat packs, and avoiding the triggers of headache. Hundreds of scientific studies have shown that the behavioral therapies for headache yield a substantial headache improvement.

Recently concluded four different behavioral treatments, they are scientifically sound options for headache prevention.

- Relaxation training
- Temperature biofeedback (for hand warming) combined with relaxation training
- Electromyographic biofeedback (for muscle tension reduction)
- Cognitive behavior therapy (stress management training) [45]
- · Complementary treatments and some lifestyle modifications
- Sleep and exercise and reducing the stress and increase posture [45,46].

# CONCLUSION

Headache itself is a painful and disabling feature of a small number of primary headache disorders, namely, migraine, TTH, CH, and CDH syndromes cause substantial levels of disability and headache occurs due to a secondary or with any underlying cause it is said to be secondary headaches. Based on diagnostic criteria and intensity of headache, classification of headache is done. The ultimate goal of treatment is to stop headaches from occurring and the adequate headache management depends on the identification of the type of headache and may include avoiding known triggers, non-pharmacological, and pharmacological treatment. Pharmacological treatment includes NSAIDs, triptans, and ergot alkaloids, and preventive treatment is used to reduce the frequency, duration, or severity of attacks.

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