World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Primary Headache

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World Journal of Advanced Research and Reviews, 2025, 27(03), 707–713

Publication history: Received on 20 July 2025; revised on 28 August 2025; accepted on 03 September 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.27.3.3114

Abstract

Primary headache is a type of headache characterized by the absence of underlying structural or metabolic damage. About 90% of headaches are primary headaches. The incidence rate of primary headaches is high, reaching up to 86.9%. Primary headaches can disrupt daily activities and result in the loss of productivity. Additionally, primary headaches also cause financial losses. There are many factors that can trigger primary headaches. Gender, age, stress, fatigue, and lack of sleep are some of the triggers. A literature review on primary headaches is important, and we will discuss various aspects ranging from the pathophysiology to the treatment of primary headaches.

Keywords: Migraine; Tension type headache; Cluster headache; Primary Headache

1. Introduction

Primary headache is a type of headache where there is no underlying structural or metabolic damage. Primary headache is one of the most commonly reported complaints. Approximately 90% of headaches are primary headaches. Primary headaches can be divided into migraine, tension-type headache (TTH), cluster headache, and other trigeminal autonomic cephalalgias, as well as other types of primary headaches (1).

Based on research conducted by Al-Hashel (2019) in Kuwait, the one-year prevalence of primary headache is 61% (2). A similar study by Al-Jumah et al. (2020) in Saudi Arabia found a one-year prevalence of primary headache to be 65.8% (3). Another study by Abukanna et al. (2021) reported a one-year prevalence of primary headache as 86.9% (4). These studies indicate that primary headaches have a relatively high incidence.

Primary headaches have an impact on the quality of life (5). Some of the resulting effects include loss of workdays, disruption of daily activities, and loss of productivity (4). Additionally, primary headaches also impose an economic burden. In a study by Oliveira et al. (2020) in Brazil, the economic burden due to headaches, partially attributed to migraine, can reach 33.5 billion per year (6). In Indonesia, not many people report primary headaches because it is considered common, and individuals often prefer self-treatment (7).

There are many factors that can trigger primary headaches (8). Some reported factors include age, stress, dietary patterns, poor sleep quality, fatigue, menstruation, and weather changes (9)(10)(11). Gender, educational status, and socio-economic status also play a role (12). In migraine and TTH, it is known that the incidence is higher in females, while cluster headaches are more common in males. Some studies mention the influence of gender on the duration, intensity, and frequency of headaches (13).

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The high incidence and the numerous losses caused by primary headaches make it important to study them. By studying primary headaches, the public can understand the causes, risk factors, and even the treatment for primary headaches. People can also prevent primary headaches by avoiding triggers. In addition to the general public, studying primary headaches is also important for medical professionals to assist in diagnosis and contribute to the development of prevention and treatment strategies. In this study, we will focus on migraine, tension-type headache, and cluster headache.

2. Primary Headache

2.1. Migraine

2.1.1. Pathophysiology

The pathophysiology of migraine is still not fully understood. Numerous studies suggest that the activation of the trigeminovascular pathway is related to its pathophysiology. Migraine sufferers typically experience a prodromal phase with symptoms related to the hypothalamus (fatigue, irritability, and yawning), brainstem (neck stiffness and muscle stiffness), cortex (hypersensitivity to light, sound, and aroma), and limbic system (depression and anhedonia). Nevertheless, there is no definitive evidence explaining how the prodromal phase precisely initiates the headache phase or what events trigger the activation of meningeal nociceptors (14).

There are several theories explaining the relationship between these two aspects. The first theory is that hypothalamic neurons, which respond to changes in physiological and emotional homeostasis, alter the balance between the parasympathetic and sympathetic nervous systems within the meninges, shifting towards parasympathetic dominance. It can activate meningeal nociceptors. Another theory suggests that neurons in the hypothalamus and brainstem, which control reactions to shifts in physiological and emotional balance, may reduce the threshold for transmitting trigeminovascular nociceptive signals from the thalamus to the cortex. (14).

2.1.2. Prevalence

Migraine is one of the common types of headaches. The prevalence of migraine ranges from 10% to 18% (15). Migraine occur two to three times more frequently in women than in men. The highest incidence of migraine is observed between the ages of 25 and 55. About 90% of migraine sufferers experience migraine attacks before the age of 40 (16). According to a study by Bamalan et al. (2021) conducted in Jeddah, Saudi Arabia, the prevalence of migraine was found to be 37.2%. The study also revealed that the majority of migraine sufferers were women, accounting for 81.1%, while men constituted only 18.9% (17). The higher incidence of migraine in women is believed to be associated with estrogen hormones, which can trigger migraine (15).

2.1.3. Risk factors

There are several risk factors associated with the occurrence of migraine, including genetics, gender, and age. If one parent has a history of migraine, the probability of experiencing migraine is 40%. If both parents have a history of migraine, the probability increases to 75%. Migraine occurrence is reported to be higher in women compared to men. Other factors that can increase the risk of migraine include obesity, stress, caffeine, food additives, artificial sweeteners, and irregular or inadequate eating (18). Additionally, low education, socioeconomic conditions, head trauma, lack of sleep, fatigue, loud noises, specific odors, and sunlight are also reported as triggers for migraine (16).

2.1.4. Characteristics

Migraine can last for 4 to 72 hours and typically occur on one side of the head or unilaterally. The headache is often described as throbbing and ranges from moderate to severe intensity. Physical activities like walking or ascending stairs can worsen migraine. Nausea and/or vomiting, as well as photophobia and phonophobia, may accompany migraine. In migraine with aura, aura symptoms such as visual, sensory, and motor disturbances may occur (19).

2.1.5. Diagnosis

The diagnosis of migraine is established through a medical history, clinical symptoms, and general as well as neurological examinations. However, typically, a medical history and physical examination are sufficient for making the diagnosis. Additional examinations, such as a computed tomography (CT) scan or magnetic resonance imaging (MRI), may be conducted if there is a concern about a central nervous system origin. During the medical history, information is gathered about the characteristics of the headache, the pattern of the headache, symptoms preceding or accompanying the headache, and the family history of migraine (20).

2.1.6. Treatment

Paracetamol or ibuprofen 600-800 mg are the first-line treatment for migraine. Aspirin 900 mg, either alone or in conjunction with an anti-emetic such as domperidone at 10-20 mg, can also be used. In patients who frequently experience migraine, preventive treatment may also be considered. Beta-blockers such as propranolol, tricyclic antidepressants like amitriptyline, and anticonvulsants such as topiramate are the first-line preventive treatments that is commonly used (21).

2.2. Tension Type Headache

2.2.1. Pathophysiology

The pathophysiology of tension-type teadache (TTH) remains unclear and not fully understood. This complicates the management of TTH. The pathophysiology of TTH is believed to involve multiple factors, with connections to central dysfunction in pain processing pathways and peripheral myofascial elements. In TTH patients, myofascial pericranial tension is often present, indicating a disturbance in pain modulation pathways characterized by central and peripheral nerve hyperexcitability (22).

It is theorized that autonomic dysfunction may be involved in the pathophysiology of TTH due to sleep disturbances. Sleep disturbances lead to fatigue, resulting in increased sympathetic activity and subsequently causing headaches. Another hypothesis concerns myofascial trigger points, which, when subjected to pressure, can cause pain. Excessive contraction of pericranial muscles may result in ischemia and the release of detrimental substances like substance P, subsequently causing TTH (23).

2.2.2. Prevalence

The lifetime prevalence of TTH is estimated to be between 46% and 78%. It is typically begin between the ages of 25 and 30. The prevalence is highest between 30 and 39 years of age, decreasing as individuals get older. Women experience a slightly higher incidence than men, with a ratio of 5:4 (22). Based on a study by Karaaslan et al. (2023) conducted in children and adolescents in Istanbul, the occurrence of TTH was higher in females at 27.5% and in males at 24.6%. This aligns with the theory above that females tend to experience TTH more frequently (24).

2.2.3. Risk factors

Menstruation and alcohol are sometimes reported as triggers. Other factors commonly worsening migraine are also reported to exacerbate TTH (22). Educational level is also known to be associated with episodic TTH but not with chronic TTH. Additionally, fatigue, young age, female gender, lack of rest, and insufficient sleep are reported to be correlated with the occurrence of TTH (25).

2.2.4. Characteristics

Tension-type headache (TTH) typically lasts for 30 minutes to 7 days. TTH occurs on both sides of the head or bilaterally and is usually described as a sensation of pressure or tightness on the head with mild to moderate intensity. Physical activity does not worsen TTH, and there are no associated symptoms of nausea or vomiting, but may include photophobia or phonophobia (19).

2.2.5. Diagnosis

The diagnosis of tension-type headache (TTH) is typically determined according to a detailed medical history and examinations to rule out secondary causes (22). The medical history includes information about the onset, duration, frequency, triggers, and characteristics of TTH (26). TTH is typically described as a dull ache, a pressing sensation, and a feeling of fullness or tightness in the head. Unlike migraine, TTH is not worsened by physical activity, a crucial point to differentiate between TTH and migraine. Another indicator of TTH is its bilateral location (22).

2.2.6. Treatment

Treatment for tension-type headache (TTH) is divided into pharmacological and non-pharmacological approaches. For patients with episodic TTH, acute treatment is usually provided with basic analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs). Commonly used simple analgesics include aspirin and paracetamol (acetaminophen). Caffeine, codeine, and sedatives are often combined with NSAIDs for enhanced effectiveness. However, this combination should be avoided due to the risk of misuse and dependency. Some episodic TTH patients also experience migraine and need education to distinguish between TTH and migraine for appropriate treatment. For patients with chronic TTH,

pharmacological treatment may include ibuprofen, acetylsalicylic acid (ASA), naproxen sodium, and acetaminophen. However, acute treatment alone may not be very helpful. Comorbid conditions like depression and anxiety need to be evaluated and addressed appropriately. For optimal treatment, a combination of pharmacological, physical therapy, and behavioral modalities is needed. For prevention, the most effective medication is amitriptyline. The administration of amitriptyline should start at a low dose, typically 10 mg - 25 mg per day. Its effects are usually observed within 3-4 weeks. If there is no improvement within 4 weeks, an evaluation is necessary. After stopping therapy, some patients remain pain-free, while others may experience pain again and require long-term treatment. Non-pharmacological therapy may include physical and psychological treatments. Physical therapy encompasses enhancements in posture, relaxation, exercise routines, the application of hot and cold packs, ultrasound, and electrical stimulation. Psychological therapy might involve teaching relaxation techniques, utilizing EMG biofeedback, and employing cognitive-behavioral therapy. In addition to physical and psychological therapy, there are other treatments such as oromandibular care and acupuncture (22).

2.3. Cluster Headache

2.3.1. Pathophysiology

The pathophysiology of cluster headaches is complex and not fully understood. Cluster headaches are neurovascular disorders where the activation of the hypothalamus and the trigemino-autonomic reflex plays a crucial role in understanding their manifestations. Hypothalamic activation is involved in the circadian and circannual periodicity of cluster headache attacks and their accompanying autonomic symptoms. Additionally, trigemino-autonomic reflex and neuropeptide release also contribute to its pathophysiology. Neurogenic inflammation is hypothesized as another mechanism underlying cluster headache pain, although supporting evidence is limited (27).

Hypothalamic Activation

Hypothalamic activation is involved in the circadian and circannual periodicity of cluster headache attacks. The biological clock located in the suprachiasmatic nucleus of the hypothalamus determines the periodicity of many biological functions. The autonomic nervous system is controlled by hypothalamus, and hypothalamic dysfunction can explain the periodicity of cluster headache attacks and their autonomic symptoms. In patients with cluster headaches, the anterior hypothalamus is known to enlarge, and the hypothalamic gray matter is activated during attacks (27).

Trigemino-Autonomic Reflex

The trigeminovascular system, along with the parasympathetic and sympathetic systems, controls the vascular tone of blood vessels in the head. The trigemino-autonomic reflex involves neurons from the trigeminal nerve gathering in the trigeminal ganglion. Sensory information is relayed to the brain from the trigeminocervical complex, Initiating the activation of efferent reflexes through stimulation of the superior salivatory nucleus. Activation of the sphenopalatine ganglion (SPG) results in vasodilation and cranial outflow associated with cluster headaches (27).

Neuropeptide Release

In individuals with cluster headaches, there is an increase in neuropeptide levels such as CGRP, VIP, and PACAP during attacks. These neuropeptides are vasoactive and contribute to the neurovascular component of cluster headache pain. CGRP and PACAP appear in the trigeminocervical complex, while VIP appears in the SPG. Changes in stimulus thresholds by CGRP can activate the caudal trigeminal nucleus, leading to pain associated with cluster headaches (27).

Neurogenic Inflammation

Neurogenic inflammation is hypothesized as a mechanism in cluster headache pain. Electrical stimulation of the trigeminal ganglion in mice results in the release of CGRP, mast cell degranulation, and changes in venule endothelial cells, consistent with neurogenic inflammation. Positive interactions between glia, trigeminal ganglion, and neurogenic inflammation might play a role in the development of cluster headaches' pathophysiology (27).

2.3.2. Prevalence

Cluster headaches are rare, its prevalence approximately 0.1% in the general population. While cluster headaches can occur at any age, they mostly occur in people in their 30s and decrease with age. The condition affects more men than women, with a ratio of 3:1. However, in recent years, there has been a decline in this ratio, with more women experiencing cluster headaches. The reasons for this decline are not yet detailed, but it is speculated to be due to improved diagnostic accuracy in women (27).

2.3.3. Risk factors

Several risk factors influence the occurrence of cluster headaches, including male gender, age over 30, drinking alcohol, and a record of trauma or brain surgery (28). Males are known to be more prone to cluster headaches, likely associated with sex hormone regulation and environmental factors (29).

2.3.4. Characteristics

Cluster headaches typically last between 15 and 180 minutes and are located unilaterally around the orbital, supraorbital, and/or temporal regions. The pain is described as sharp, with an intensity ranging from severe to extremely severe. This pain is accompanied by autonomic symptoms on the same side, such as conjunctival injection, tearing, nasal congestion, runny nose, sweating on the forehead and face, constriction of the pupil, drooping of the eyelid, and/or swelling of the eyelid. Symptoms of restlessness may also occur (19)(30).

2.3.5. Diagnosis

The diagnosis of cluster headaches relies on its clinical criteria. Anamnesis and neurological physical examinations are performed to rule out secondary causes. If the anamnesis indicates characteristics of cluster headache and no abnormalities are found in the neurological physical examination, additional tests such as MRI are not mandatory. During a physical examination conducted during a cluster headache attack, one may observe constricted or dilated pupils. However, these symptoms do not always appear (31). Sometimes, cluster headache pain may be perceived as originating from the sinuses or teeth, leading patients to seek ENT specialists or dentists. Cluster headaches are often underdiagnosed and suboptimally treated, with patients frequently receiving a delayed diagnosis (29).

2.3.6. Treatment

Therapy for cluster headaches includes acute and preventive treatments. Acute therapy aims to stop individual attacks. Medications that show good response include triptans. The recommended routes for administering triptans for cluster headaches are subcutaneous or intranasal, with oral administration not recommended due to delayed effects compared to subcutaneous and intranasal routes. Inhalation therapy with oxygen can also be given. Triptans and inhalation oxygen therapy are the first line of treatment for cluster headaches. Inhalation therapy with oxygen is effective in approximately two-thirds of patients. If triptans and oxygen therapy are not effective, intranasal lidocaine administration can be considered. For preventive therapy, high-dose verapamil (360 to 960 mg), lithium, steroids, greater occipital nerve block, and melatonin can be used (27).

3. Conclusion

Primary headaches should not be overlooked, as the burden they cause can significantly affect various aspects such as the economy and quality of life. Their risk factors include a wide range of elements such as sex, age, hormones, dietary habits, and others. While the pathophysiology is now better understood, the exact mechanisms remain unclear. A deeper understanding of these risk factors and precise mechanisms may contribute to the development of more accurate prevention and treatment strategies.

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