Comprehensive Clinical Approach to Chronic Headaches Diagnosis, Differential Diagnosis, and Evidence-Based Management

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Abstract

Background: Chronic headache disorders are among the most prevalent neurological conditions worldwide and represent a major cause of disability, reduced quality of life, and increased healthcare utilization. They comprise a heterogeneous group of primary and secondary headache disorders with distinct etiologies, pathophysiological mechanisms, clinical manifestations, and therapeutic approaches.

Aim: This review aimed to provide a comprehensive overview of chronic headache disorders, emphasizing their epidemiology, etiology, pathophysiology, clinical evaluation, diagnostic approaches, and evidence-based management strategies.

Methods: A narrative review was conducted using current evidence derived from the International Classification of Headache Disorders (ICHD-3), clinical guidelines, and published literature addressing the diagnosis and management of chronic headache disorders. Relevant information regarding disease classification, risk factors, clinical assessment, laboratory and imaging investigations, and pharmacological and non-pharmacological treatment modalities was synthesized.

Results: Chronic headaches affect approximately 1–4% of the general population and occur more frequently in women. Chronic migraine and chronic tension-type headache constitute the majority of cases, while medication overuse headache represents a common secondary cause. Central sensitization, trigeminovascular activation, serotonin dysregulation, and calcitonin gene-related peptide (CGRP) signaling play fundamental roles in disease pathogenesis. Accurate diagnosis relies on comprehensive clinical evaluation, recognition of secondary headache red flags, and appropriate use of neuroimaging when indicated. Contemporary management integrates lifestyle modification, preventive pharmacotherapy, behavioral interventions, patient education, and emerging targeted biological therapies.

Conclusion: Chronic headache disorders require individualized, multidisciplinary management supported by accurate diagnosis and evidence-based therapeutic strategies. Early recognition, appropriate preventive treatment, and modification of reversible risk factors can substantially reduce headache burden, improve functional outcomes, and enhance patients' quality of life.

Keywords: Chronic Headache, Chronic Migraine, Chronic Tension-Type Headache, Medication Overuse Headache, Trigeminovascular System, Calcitonin Gene-Related Peptide, Diagnosis, Management.

Introduction

Chronic headache represents a broad clinical syndrome rather than a distinct disease entity, encompassing a heterogeneous group of headache disorders characterized by persistent or recurrent symptoms that substantially impair quality of life and functional capacity. It is among the most common neurological complaints encountered in clinical practice and constitutes a major public health concern because of its considerable impact on physical health, psychological well-being, occupational productivity, and healthcare utilization. According to the International Headache Society (IHS), chronic daily headache (CDH) is defined as the occurrence of headache on 15 or more days per month for a minimum duration of three consecutive months [1]. Although this definition provides a practical clinical framework for identifying patients with persistent headache disorders, chronic daily headache is regarded as a descriptive clinical term rather than a formal diagnostic category within the International Classification of Headache Disorders (ICHD) [2]. Consequently, the diagnosis of chronic headache requires careful characterization of the underlying headache phenotype and exclusion of secondary etiologies before an appropriate management strategy can be established. The descriptive classification of chronic daily headache encompasses several primary and secondary headache disorders recognized in the third edition of the International Classification of Headache Disorders (ICHD-3). These include chronic migraine, chronic tension-type headache, medication overuse headache (MOH), hemicrania continua, and new daily persistent headache. Each of these disorders possesses unique clinical characteristics,

underlying pathophysiological mechanisms, diagnostic criteria, and therapeutic considerations despite sharing the common feature of frequent or continuous headache episodes. Accurate differentiation among these headache syndromes is essential because their prognosis, response to treatment, and long-term clinical outcomes vary considerably, necessitating individualized diagnostic and therapeutic approaches.

From an etiological perspective, chronic headaches are broadly classified into primary and secondary headache disorders. Primary chronic headaches occur independently without an identifiable structural, metabolic, infectious, or systemic pathological cause and are believed to arise from intrinsic neurobiological mechanisms involving altered pain modulation, neuronal excitability, and central sensitization. Within this category, headaches are frequently classified according to attack duration. Headache episodes lasting fewer than four hours are generally categorized as short-duration headaches, whereas those persisting for more than four hours are classified as long-duration headaches. The latter category predominantly includes chronic migraine and chronic tension-type headache, both of which account for the majority of primary chronic headache presentations encountered in neurological practice [1]. This temporal classification provides additional clinical value by facilitating differential diagnosis and guiding subsequent therapeutic decision-making. In contrast, secondary chronic headaches develop as manifestations of identifiable underlying pathological conditions that require prompt recognition and targeted intervention. Numerous disorders may contribute to secondary headache syndromes, including medication overuse, intracranial neoplasms, central nervous system (CNS) infections, elevated intracranial pressure, metabolic disturbances, post-traumatic complications, cerebrovascular diseases, and various structural abnormalities affecting the brain and surrounding tissues [3]. Failure to identify these underlying causes may delay appropriate treatment and increase the risk of serious neurological complications. Consequently, comprehensive clinical evaluation, detailed history taking, thorough neurological examination, and appropriate diagnostic investigations are fundamental components of the assessment of patients presenting with chronic headache. It is increasingly recognized that chronic headache disorders frequently arise from the interaction of multiple biological, psychological, behavioral, and environmental factors rather than from a single isolated mechanism. Many patients demonstrate overlapping headache phenotypes, while primary headache disorders may coexist with medication overuse, psychiatric comorbidities, sleep disturbances, or other contributing conditions that influence headache frequency, severity, and treatment response. Accordingly, chronic headaches should be regarded as existing along a dynamic clinical continuum rather than as rigid diagnostic entities, emphasizing the importance of individualized patient assessment and multidisciplinary management strategies that address both the primary headache disorder and its contributing risk factors [3].

Etiology

The etiology of chronic headache is highly complex and encompasses a wide spectrum of primary neurological disorders as well as secondary conditions arising from identifiable systemic or intracranial pathology. Chronic headache should therefore be regarded as a clinical manifestation rather than a single pathological entity, with diverse mechanisms contributing to its development and persistence. The International Classification of Headache Disorders (ICHD) recognizes more than 200 distinct headache disorders, which are broadly categorized into three principal groups including primary headache disorders, secondary headache disorders, and painful cranial neuropathies together with other facial pain syndromes [4]. This comprehensive classification system is hierarchical in structure, allowing progressive diagnostic refinement through multiple levels of subclassification based on clinical characteristics, underlying mechanisms, temporal patterns, and associated neurological features. Such a structured approach facilitates accurate diagnosis, supports evidence-based therapeutic decision-making, and promotes consistency in clinical practice and research. Despite their considerable heterogeneity, all chronic headache disorders share a common temporal criterion characterized by headache occurring on at least 15 days per month for a minimum of three consecutive months. Nevertheless, this shared frequency criterion should not obscure the substantial differences that exist among headache disorders with respect to their pathophysiology, clinical manifestations, precipitating factors, disease progression, and treatment response. Consequently, differentiating between primary and secondary headache disorders remains one of the most important objectives during the diagnostic evaluation, as management strategies and prognostic implications differ substantially according to the underlying etiology.

Primary chronic headache disorders arise independently of structural, infectious, metabolic, or vascular abnormalities and are generally attributed to intrinsic disturbances in central nervous system pain processing, altered neuronal excitability, neurovascular dysfunction, and central sensitization. Among these disorders, headaches lasting longer than four hours include chronic migraine, chronic tension-type headache, new daily persistent headache, and hemicrania continua. These disorders account for the majority of chronic headache presentations encountered in neurological and primary care settings and represent a substantial burden on healthcare systems worldwide because of their chronicity, high prevalence, and impact on functional capacity. Chronic migraine represents one of the most prevalent and disabling forms of primary headache. It is typically characterized by unilateral pain of moderate to severe intensity with a pulsating or throbbing quality and may occur either with or without aura [4]. The transition from episodic migraine to chronic migraine is recognized as a dynamic process influenced by multiple biological and environmental factors including genetic susceptibility, medication overuse, obesity, sleep disturbances, psychological

stress, depression, anxiety, and ineffective management of acute migraine attacks. Central sensitization, increased cortical excitability, dysfunction of trigeminovascular pathways, and abnormal modulation of nociceptive signaling have all been implicated in the pathogenesis of chronic migraine. In pediatric populations, chronic migraine often presents differently from the classical adult phenotype. Children and adolescents frequently experience bilateral rather than unilateral headache, while associated symptoms such as photophobia and phonophobia may be inferred from behavioral responses instead of explicit verbal descriptions because younger patients may have difficulty articulating these symptoms [5].

Chronic tension-type headache represents another major category of primary chronic headache disorders and differs clinically from chronic migraine in several important respects. Patients generally experience bilateral headache with a pressing or tightening quality rather than a pulsating sensation, and the pain is usually mild to moderate in intensity without the prominent nausea, vomiting, photophobia, or phonophobia commonly associated with migraine attacks [4]. Physical examination frequently reveals tenderness of the pericranial muscles, suggesting an important contribution of sustained muscle tension and peripheral nociceptive input. However, increasing evidence indicates that central pain sensitization and impaired endogenous pain inhibitory mechanisms also play important roles in maintaining chronic tension-type headache, particularly in patients with longstanding symptoms. Psychological stress, emotional distress, poor posture, prolonged muscle contraction, sleep disturbances, and occupational factors frequently contribute to symptom persistence and progression. New daily persistent headache (NDPH) constitutes a relatively uncommon but clinically challenging primary headache disorder. It is distinguished by its abrupt onset, with patients often recalling the precise day and circumstances under which the headache began. The headache rapidly becomes continuous within 24 hours of onset and persists without remission thereafter [6]. Unlike chronic migraine or chronic tension-type headache, individuals with NDPH generally have little or no previous history of recurrent headaches before symptom onset. Although the precise pathophysiological mechanisms remain poorly understood, proposed etiological factors include preceding viral infections, immune-mediated responses, inflammatory processes, stressful life events, and dysregulation of central pain processing pathways. NDPH is widely recognized as one of the most treatment-resistant chronic headache syndromes, with many patients experiencing persistent symptoms despite multiple pharmacological and non-pharmacological therapeutic interventions.

Hemicrania continua is another distinctive primary headache disorder characterized by persistent unilateral headache accompanied by intermittent exacerbations of severe pain and ipsilateral cranial autonomic symptoms such as lacrimation, conjunctival injection, nasal congestion, rhinorrhea, or ptosis. One of its most important diagnostic characteristics is its dramatic and often complete response to indomethacin therapy, a feature considered virtually pathognomonic and invaluable for differentiating hemicrania continua from other unilateral chronic headache disorders. Failure to respond to indomethacin should prompt reconsideration of the diagnosis and investigation for alternative etiologies. Primary headache disorders with attacks lasting fewer than four hours comprise chronic cluster headache, short-lasting unilateral neuralgiform headache attacks, and primary stabbing headache. Chronic cluster headache differs from episodic cluster headache primarily by the absence of sustained remission periods, with attacks occurring continuously for at least one year. The pain is characteristically unilateral, localized within the trigeminal nerve distribution, and accompanied by ipsilateral cranial autonomic manifestations including conjunctival injection, lacrimation, nasal congestion, rhinorrhea, eyelid edema, facial sweating, or miosis [4]. Patients frequently exhibit marked psychomotor agitation during attacks, contrasting with the tendency of migraine sufferers to remain still during painful episodes. Short-lasting unilateral neuralgiform headache attacks include short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA). Both disorders are characterized by recurrent episodes of extremely severe unilateral pain associated with ipsilateral autonomic manifestations. SUNCT is specifically defined by the simultaneous presence of conjunctival injection and excessive lacrimation, whereas SUNA may present with either conjunctival injection or lacrimation but not necessarily both simultaneously. Additional autonomic manifestations such as rhinorrhea and nasal congestion may also accompany SUNA episodes, contributing to diagnostic differentiation between these closely related disorders.

Primary stabbing headache is characterized by transient episodes of sudden, sharp, stabbing pain that occur spontaneously and typically involve the temporal, frontal, or peri-orbital regions. Individual attacks usually last only a few seconds but may recur multiple times throughout the day. Although generally benign, primary stabbing headache may coexist with migraine or other primary headache disorders and occasionally necessitates exclusion of secondary causes when clinical presentation is atypical. Secondary chronic headache disorders result from identifiable underlying pathological conditions requiring targeted investigation and management. These include medication overuse headache, central nervous system infections, intracranial hematomas, intracranial neoplasms, elevated intracranial pressure, spontaneous intracranial hypotension, cerebral vasculitis, intracranial aneurysms, and cerebrospinal fluid (CSF) leakage [2]. Unlike primary headache disorders, secondary headaches frequently represent manifestations of potentially serious neurological disease, emphasizing the importance of comprehensive clinical assessment, neuroimaging when indicated, and prompt identification of red flag symptoms suggestive of secondary pathology. Among secondary headache disorders, medication overuse headache represents one of the most prevalent and

clinically significant causes of chronic daily headache. This condition commonly develops in patients with pre-existing migraine or tension-type headache who progressively increase their consumption of symptomatic medications in an attempt to achieve sustained pain relief. Rather than improving headache control, excessive use of analgesics paradoxically promotes increasing headache frequency, perpetuating a self-sustaining cycle of medication dependence and chronic pain. The International Classification of Headache Disorders further categorizes medication overuse headache according to the specific medication class involved, including nonsteroidal anti-inflammatory drugs (NSAIDs), triptans, ergotamine derivatives, non-opioid analgesics, and opioid-containing medications [7]. Withdrawal of the offending medication often results in temporary worsening of headache symptoms before gradual clinical improvement occurs, highlighting the importance of patient education, supervised withdrawal strategies, and preventive therapeutic interventions to interrupt this cycle. Although numerous additional secondary causes of chronic headache exist, including infectious, vascular, inflammatory, metabolic, traumatic, and structural disorders affecting the central nervous system, detailed discussion of these conditions extends beyond the scope of this chapter. Nevertheless, their recognition remains critically important because timely diagnosis and appropriate treatment of the underlying pathology may prevent irreversible neurological complications and significantly improve patient outcomes.

Epidemiology

Headache disorders constitute one of the leading causes of neurological disability worldwide and represent a substantial public health challenge because of their high prevalence, recurrent nature, and significant socioeconomic consequences. Both acute and chronic headache disorders affect individuals across all age groups; however, their highest prevalence is observed from adolescence through the fifth decade of life, corresponding to the most economically productive years of adulthood [8]. As a result, chronic headaches contribute considerably to reduced work productivity, increased absenteeism, impaired academic performance, diminished quality of life, and escalating healthcare expenditures. The chronic and often disabling nature of these disorders places a significant burden not only on affected individuals but also on families, employers, and healthcare systems worldwide. The estimated prevalence of chronic headache disorders in the general population ranges from approximately 1% to 4%, reflecting variations in diagnostic criteria, study methodologies, and population characteristics [9]. Globally, chronic headache affects nearly one billion individuals, while approximately 39 million people in the United States experience chronic headache disorders [4]. These figures emphasize the widespread nature of the condition and highlight its importance as a major neurological disorder requiring effective preventive and therapeutic strategies. In specialized headache clinics, chronic headache disorders account for nearly 40% of patient diagnoses, illustrating the substantial demand for expert neurological evaluation and multidisciplinary management among individuals with persistent headache symptoms [4].

Sex-related differences are consistently observed across epidemiological studies of chronic headache disorders. Women are affected approximately three to five times more frequently than men, particularly in disorders such as chronic migraine and chronic tension-type headache [4]. Hormonal influences, including fluctuations in estrogen levels throughout the menstrual cycle, pregnancy, and menopause, are believed to contribute significantly to this disparity. In addition to hormonal factors, genetic susceptibility, psychosocial influences, differences in pain perception, and healthcare-seeking behaviors may further explain the increased prevalence among women. Chronic migraine represents one of the most prevalent and disabling forms of chronic headache and is frequently associated with numerous medical and psychiatric comorbidities. Individuals with chronic migraine exhibit increased rates of obesity, obstructive sleep apnea, depression, chronic pain syndromes, and cardiovascular disease compared with the general population [10]. These comorbid conditions may influence headache frequency, disease progression, treatment responsiveness, and long-term prognosis, underscoring the importance of comprehensive patient assessment and integrated multidisciplinary care. Although chronic migraine is often considered an adult disorder, it also affects pediatric populations with considerable frequency. The reported prevalence among children and adolescents ranges from approximately 7% to 17% [5]. Before the age of 12 years, the prevalence is generally comparable between boys and girls; however, following the onset of puberty, females become increasingly affected, likely reflecting the influence of hormonal changes during adolescence [5]. Early recognition and appropriate management during childhood are essential to reduce disease progression, minimize educational disruption, and improve long-term quality of life.

Other primary chronic headache disorders demonstrate distinct epidemiological characteristics. Hemicrania continua is considerably less common than chronic migraine or chronic tension-type headache and exhibits a female predominance, with an approximate female-to-male ratio of 2:1. The condition is most frequently diagnosed during the third decade of life, although cases may occur across a broad age spectrum. Chronic cluster headache, in contrast, occurs more commonly in men; however, it also affects women, who may present with accompanying nausea and vomiting. These associated symptoms can resemble migraine, occasionally leading to delayed or incorrect diagnosis during the initial clinical evaluation [11]. Such epidemiological variations among chronic headache disorders emphasize the importance of considering age, sex, associated clinical features, and comorbid conditions when establishing an accurate diagnosis and developing individualized management strategies.

Pathophysiology

The pathophysiology of chronic headache disorders is complex and multifactorial, involving intricate interactions among genetic predisposition, neurovascular dysfunction, altered pain modulation, central and peripheral sensitization, inflammatory mediators, and environmental influences. Although the underlying biological mechanisms differ among the various chronic headache syndromes, several common pathophysiological processes have been identified across these disorders. These shared mechanisms include persistent sensitization of the trigeminovascular system, functional and structural alterations within pain-processing regions of the brain, neurochemical dysregulation, and the cumulative effects of environmental and lifestyle-related risk factors [12]. Most chronic headache disorders arise through the gradual transformation of an episodic headache condition into a chronic syndrome, reflecting progressive changes within central pain pathways rather than the emergence of an entirely new disease process. The transition from episodic to chronic headache is influenced by multiple modifiable and non-modifiable factors. Clinical evidence suggests that recurrent headache attacks induce progressive sensitization of nociceptive pathways, resulting in increased headache frequency and reduced pain thresholds over time. Several modifiable risk factors accelerate this transformation, including obesity, sleep disturbances, excessive caffeine intake, chronic psychological stress, anxiety, depression, and medication overuse. These factors contribute to persistent activation of central pain networks, ultimately promoting the development of chronic headache disorders. Consequently, early identification and modification of these risk factors have become important therapeutic objectives aimed at preventing headache chronification and reducing long-term neurological disability.

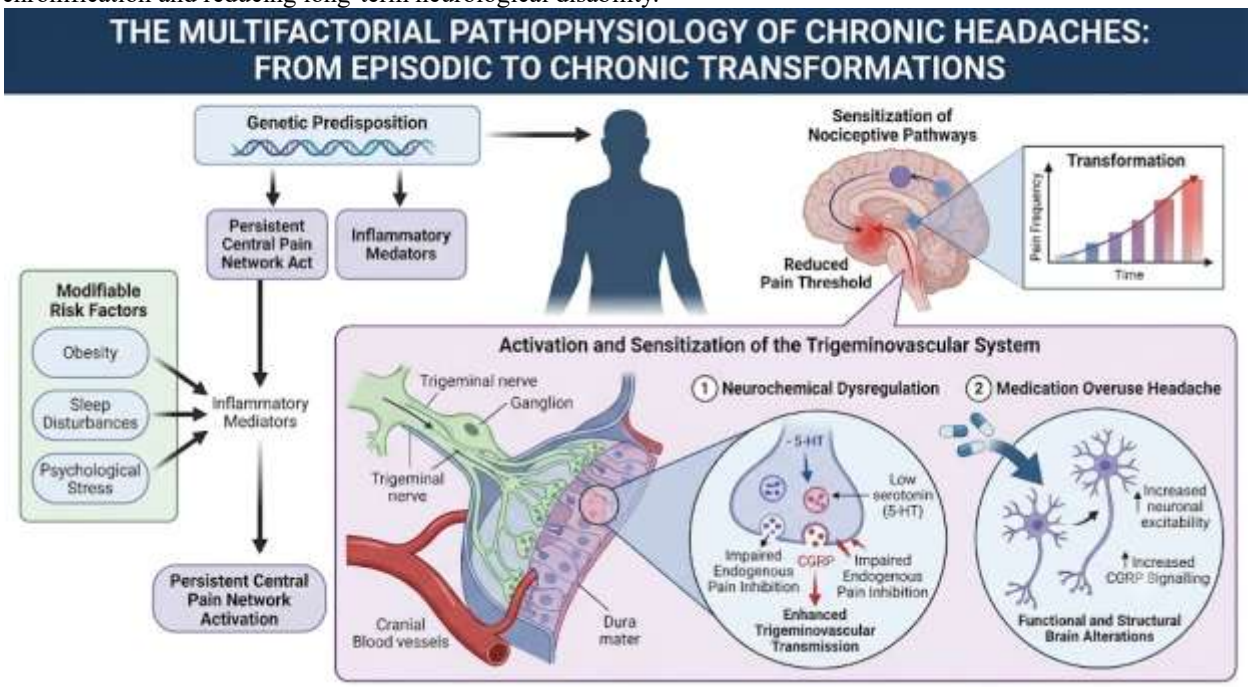

Fig. 1: Pathophysiology of Chronic Headache.

One of the fundamental mechanisms underlying chronic headache disorders is activation and sensitization of the trigeminovascular system. The trigeminal nerve provides sensory innervation to the intracranial blood vessels, dura mater, and meninges, serving as the principal pathway responsible for transmitting nociceptive signals from cranial structures to higher central nervous system centers. Repeated activation of trigeminal afferent fibers leads to both peripheral sensitization, characterized by increased responsiveness of primary nociceptors, and central sensitization, whereby neurons within the brainstem and higher cortical pain-processing regions become increasingly excitable. As central sensitization progresses, patients experience heightened pain perception, reduced thresholds for headache initiation, prolonged headache duration, and increased susceptibility to normally non-painful sensory stimuli, including light, sound, and mechanical stimulation. This phenomenon is considered one of the defining neurobiological characteristics of chronic headache disorders and contributes substantially to treatment resistance. Serotonin, also known as 5-hydroxytryptamine (5-HT), plays a pivotal role in the regulation of nociceptive transmission and cerebral vascular function. Owing to its vasoconstrictive and anti-inflammatory properties, serotonin has become an important therapeutic target in migraine management, particularly through the use of selective serotonin receptor agonists such as triptans. Serotonin is primarily released from the serotonergic nuclei within the brainstem and participates in multiple pathways involved in central pain modulation. Nevertheless, its precise role in

migraine pathogenesis remains incompletely understood and continues to be the subject of ongoing investigation. Current evidence suggests that serotonin concentrations decrease during the interictal period, resulting in impaired endogenous pain inhibition and increased susceptibility to activation of the trigeminovascular system. Serotonin may influence headache generation through several complementary mechanisms, including direct effects on cranial blood vessels, modulation of central pain control pathways, and regulation of cortical neuronal activity through projections originating from the brainstem serotonergic nuclei [13][14].

Another key mediator in the pathophysiology of chronic headache disorders is calcitonin gene-related peptide (CGRP), a neuropeptide that has emerged as one of the most important molecular targets in contemporary headache research and therapy. CGRP is abundantly expressed within neurons of the trigeminal ganglion and is released from both peripheral and central trigeminal nerve terminals. Following its release at peripheral nerve endings, CGRP stimulates increased production of nitric oxide, promotes vasodilation of cerebral and dural blood vessels, and contributes to neurogenic inflammation through activation of inflammatory pathways [15][16]. In addition to its vascular effects, CGRP enhances trigeminal nerve sensitization and facilitates transmission of nociceptive signals from intracranial vessels to the central nervous system. Sustained elevation of CGRP activity is believed to perpetuate headache frequency and intensity, providing the biological rationale for the development of monoclonal antibodies and receptor antagonists targeting the CGRP signaling pathway in chronic migraine prevention. Medication overuse headache (MOH) represents a unique form of secondary chronic headache that shares numerous pathophysiological mechanisms with chronic migraine and chronic tension-type headache. Persistent overuse of analgesic medications induces both functional and structural alterations within the central nervous system, resulting in maladaptive neuroplastic changes that perpetuate headache recurrence even after the original headache disorder has resolved [7]. Neuroimaging studies have demonstrated abnormalities involving several brain regions responsible for pain processing, cognitive function, emotional regulation, and reward mechanisms, including the hippocampus, periaqueductal gray matter, posterior cingulate cortex, thalamus, cerebellum, orbitofrontal cortex (OFC), and components of the mesocorticolimbic reward system [17][18]. These alterations are accompanied by dysregulation of serotonergic neuromodulatory pathways, increased expression of vasoactive and pro-inflammatory mediators, enhanced susceptibility to cortical spreading depression, amplification of central sensitization, and expansion of nociceptive receptive fields [19]. Collectively, these neurobiological changes establish a self-perpetuating cycle of chronic pain and medication dependence that complicates treatment and contributes to high relapse rates following medication withdrawal.

Emerging evidence also suggests that genetic susceptibility may influence the development of medication overuse headache and other chronic headache disorders. Genetic polymorphisms affecting neurotransmitter systems, inflammatory pathways, pain modulation, and neuronal plasticity have been proposed as contributing factors. Among the mechanisms under investigation, the renin-angiotensin system has attracted considerable interest because of its recognized role in regulating synaptic plasticity, neuronal signaling, and central nervous system homeostasis [20]. Although additional research is required to clarify these associations, genetic factors are increasingly recognized as important determinants of individual vulnerability to headache chronification. The trigeminal autonomic cephalalgias, including chronic cluster headache, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA), and hemicrania continua, possess distinctive yet overlapping pathophysiological mechanisms. These disorders are characterized by activation of the trigeminal autonomic reflex, which links nociceptive trigeminal pathways with cranial parasympathetic outflow. Intense unilateral pain results from activation of trigeminal nociceptive afferents, while associated autonomic manifestations such as lacrimation, conjunctival injection, nasal congestion, rhinorrhea, and facial sweating arise through parasympathetic activation mediated by the superior salivatory nucleus and related autonomic pathways [21]. Functional neuroimaging studies have additionally demonstrated hypothalamic activation during attacks, suggesting that hypothalamic dysfunction may contribute to the characteristic periodicity, circadian rhythmicity, and autonomic features observed in these headache syndromes. Collectively, these findings underscore the intricate neurobiological mechanisms responsible for chronic headache disorders and provide the scientific foundation for the development of increasingly targeted therapeutic interventions.

History and Physical

A comprehensive clinical history and detailed physical examination are fundamental components of the evaluation of patients presenting with chronic headache and remain essential for establishing an accurate diagnosis. Chronic headache is generally defined as headache occurring on at least 15 days per month for a minimum duration of three consecutive months. Clinical assessment should carefully characterize headache frequency, duration, intensity, location, quality, associated symptoms, precipitating and relieving factors, and the degree of functional impairment. Particular attention should be directed toward identifying ipsilateral cranial autonomic manifestations, including lacrimation, conjunctival injection, conjunctival edema, ptosis, miosis, nasal congestion, and rhinorrhea, as these findings may suggest specific primary headache syndromes. A meticulous medication history is equally important, particularly regarding the use of prescription and over-the-counter analgesics. Patients with medication overuse

headache frequently have an underlying primary headache disorder and often consume excessive amounts of nonsteroidal anti-inflammatory drugs (NSAIDs), triptans, ergotamine derivatives, opioids, or combination analgesics [22]. Historical features suggestive of medication overuse include early morning headaches, headache recurrence when medication intake is delayed, and temporary symptom relief following analgesic administration [23].
The evaluation should also include assessment of medical comorbidities, sleep disorders, psychosocial factors, and family history of headache disorders. Excluding secondary headache causes is a primary objective during clinical assessment. Particular attention should be given to headache "red flags," including age over 50 years, sudden alteration in headache pattern, thunderclap headache, fever or other systemic manifestations, underlying conditions such as malignancy or human immunodeficiency virus (HIV) infection, focal neurological symptoms, and headaches precipitated by Valsalva maneuvers [24]. Physical examination should include a comprehensive neurological assessment, with particular attention to focal neurological deficits, papilledema, visual field abnormalities, reduced visual acuity, or headache exacerbation during Valsalva maneuvers, all of which may indicate secondary intracranial pathology. In contrast, primary chronic headache disorders generally demonstrate normal neurological findings, although cranial autonomic activation or tenderness involving the cervical and occipital musculature may be present.

Evaluation

The evaluation of chronic headache is guided by the clinical presentation and the likelihood of an underlying secondary cause. In patients with a typical history and normal neurological examination consistent with a primary chronic headache disorder, extensive diagnostic investigations may not be necessary. Nevertheless, many clinicians recommend baseline laboratory tests and neuroimaging to exclude potentially treatable secondary etiologies. A comprehensive assessment should obtain detailed demographic information, including age, sex, ethnicity, and occupation, followed by careful characterization of headache onset, anatomical location, radiation, intensity, quality, duration, timing, frequency, progression, triggering and relieving factors, associated symptoms, relationship to sleep, and the impact of medications, including the type, dosage, and frequency of analgesic use. Initial laboratory investigations commonly include a complete blood count to identify evidence of infection or hematological abnormalities, erythrocyte sedimentation rate (ESR) to evaluate for giant cell arteritis and other vasculitides, and a comprehensive metabolic panel to detect metabolic disturbances. Endocrine investigations may also be indicated when pituitary or other hormonal disorders are suspected. Magnetic resonance imaging (MRI) of the brain is the preferred imaging modality because of its superior sensitivity for detecting structural abnormalities, with contrast-enhanced studies often providing additional diagnostic value [25]. Vascular imaging should be considered when cerebrovascular pathology is suspected. Selected patients may require advanced investigations such as positron emission tomography (PET), magnetic resonance spectroscopy (MRS), tissue biopsy, or lumbar puncture, particularly when central nervous system infection or idiopathic intracranial hypertension is suspected. Medication overuse headache should also be evaluated according to established diagnostic thresholds. Overuse is defined as the use of ergotamines, triptans, opioids, combination analgesics, or multiple drug classes on at least 10 days per month for more than three months, whereas acetylsalicylic acid (ASA), nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen (paracetamol) are considered overused when taken on at least 15 days per month for more than three months [22].

Treatment / Management

The management of chronic headache disorders requires an individualized, evidence-based approach tailored to the underlying diagnosis, headache severity, associated comorbidities, and patient-specific risk factors. Optimal care frequently involves an interprofessional team including neurologists, primary care physicians, pain specialists, psychologists, physical therapists, and pharmacists. Patients should be encouraged to maintain a headache diary documenting headache frequency, duration, intensity, associated symptoms, medication use, and potential triggers, as this facilitates diagnosis, monitors treatment response, and identifies modifiable precipitating factors. Lifestyle optimization, including adequate sleep, regular physical activity, stress reduction, hydration, and limitation of caffeine intake, forms an essential component of long-term management. For chronic migraine, treatment should focus on reducing headache frequency, severity, and disability rather than complete elimination of attacks. Patients should receive education regarding the adverse effects of sleep deprivation, excessive caffeine consumption, analgesic overuse, and uncontrolled comorbid conditions on headache progression. Preventive pharmacotherapy is recommended for most patients, with beta-blockers, anticonvulsants, and tricyclic antidepressants serving as first-line options. Commonly prescribed agents include propranolol, topiramate, and amitriptyline [26]. Botulinum toxin type A is approved for patients with chronic migraine who require additional preventive therapy, while monoclonal antibodies targeting calcitonin gene-related peptide (CGRP), including erenumab, fremanezumab, and galcanezumab, have demonstrated significant efficacy in patients who fail conventional treatments [26]. Acute migraine attacks may be managed with triptans, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or opioids when appropriate; however, frequent use should be avoided because of the risk of medication overuse headache. Psychological counseling, cognitive behavioral interventions, manual therapy, trigger-point treatment, occipital nerve

block, sphenopalatine ganglion block, and selected neuromodulation techniques, including deep brain stimulation in highly refractory cases, may provide additional benefit [27-29].

Chronic tension-type headache is primarily managed with preventive therapy, and amitriptyline remains the first-line pharmacological treatment because of its ability to modulate serotonin and noradrenaline pathways while reducing pericranial muscle tenderness. Cardiovascular assessment, including electrocardiography in patients older than 40 years or those with cardiac risk factors, is recommended before initiating tricyclic antidepressants. Alternative preventive agents include topiramate and gabapentin. Non-pharmacological interventions, including physical therapy, acupuncture, trigger-point injections, spinal manipulation, relaxation techniques, biofeedback, and cognitive behavioral therapy, are particularly valuable in patients with musculoskeletal dysfunction or coexisting anxiety and depression [30]. Management of medication overuse headache centers on patient education, withdrawal of the offending medication, and initiation of appropriate preventive therapy. Withdrawal symptoms such as nausea and anxiety commonly persist for 2 to 10 days. Temporary bridge therapy may include long-acting NSAIDs, prednisone, dihydroergotamine, or antiemetics, provided these agents do not belong to the same medication class responsible for the overuse [31]. Long-term prophylaxis should be individualized using agents such as topiramate, amitriptyline, valproic acid, or beta-blockers according to the underlying primary headache disorder and associated comorbidities [32]. Treatment of chronic autonomic cephalalgias varies according to the specific syndrome. Indomethacin remains the treatment of choice for paroxysmal hemicrania, hemicrania continua, primary stabbing headache, hypnic headache, and Valsalva-induced headaches. Verapamil is the preferred preventive therapy for chronic cluster headache, with corticosteroids or dihydroergotamine used during acute exacerbations. Refractory cluster headache may benefit from non-invasive vagus nerve stimulation or sphenopalatine ganglion stimulation [11]. Lamotrigine is considered first-line preventive therapy for chronic short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA), while topiramate and gabapentin represent effective alternative treatment options [33].

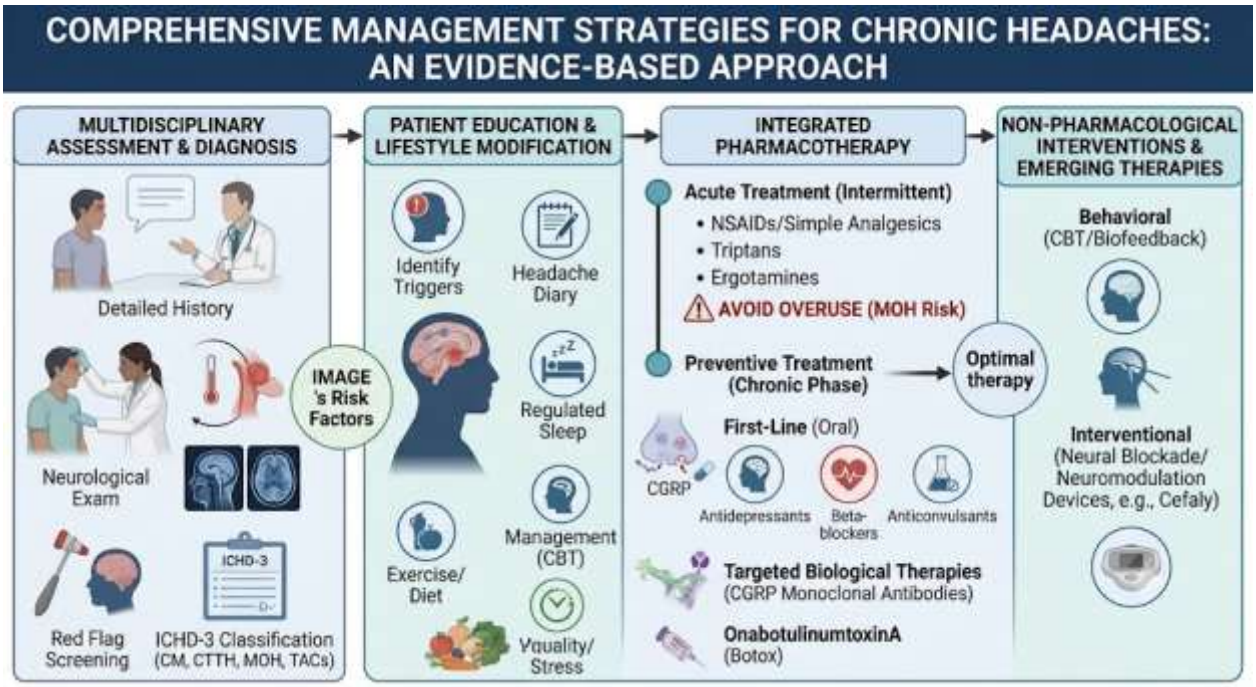

Fig. 2: Management and Treatment of Chronic Headache.

Conclusion

Chronic headache disorders comprise a diverse group of neurological conditions that impose a substantial burden on individuals, healthcare systems, and society. Their development results from complex interactions among genetic susceptibility, neurobiological mechanisms, environmental influences, and modifiable lifestyle factors. Although chronic migraine and chronic tension-type headache account for most cases, clinicians must remain vigilant for secondary headache disorders that require prompt investigation and targeted treatment. Comprehensive history taking, careful neurological examination, recognition of clinical red flags, and appropriate diagnostic investigations remain the cornerstones of accurate diagnosis. Advances in understanding the roles of central sensitization, trigeminovascular activation, serotonin, and calcitonin gene-related peptide have significantly improved therapeutic options, particularly through the introduction of targeted biological agents. Successful management extends beyond pharmacological

therapy and incorporates patient education, lifestyle modification, behavioral interventions, and multidisciplinary care tailored to individual patient needs. Preventive strategies, early intervention, and avoidance of medication overuse are essential to reduce disease progression and improve long-term outcomes. Continued research into the molecular mechanisms and personalized treatment approaches for chronic headache disorders will further enhance diagnostic precision, therapeutic effectiveness, and quality of life for affected patients.

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