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CAUSES AND THERAPEUTIC APPROACHES IN CHRONIC MIGRAINE: A NARRATIVE REVIEW

Durdona Mukhammadjonova
Associate Professor, Department of Neurology
Andijan State Medical Institute

Abstract

Chronic migraine is a common and disabling neurological disorder that significantly affects patients' quality of life and socioeconomic productivity. It is characterized by frequent headache episodes accompanied by sensory and autonomic symptoms. The pathophysiology of chronic migraine is complex and involves genetic predisposition, central sensitization, neurovascular dysfunction, and alterations in neurotransmitter systems, particularly calcitonin gene-related peptide (CGRP).

This article aims to analyze the main causes of chronic headache, with a particular focus on migraine, and to review current therapeutic approaches based on recent clinical evidence. A narrative review of the literature was conducted using international databases, including PubMed, Scopus, Web of Science, and Google Scholar. Relevant studies published between 2015 and 2024 were analyzed, focusing on etiological factors, clinical features, and treatment strategies for chronic migraine.

The results indicate that stress, sleep disturbances, hormonal changes, and medication overuse play a significant role in migraine chronification. Pharmacological management includes acute and preventive therapies, with CGRP monoclonal antibodies demonstrating superior efficacy in reducing migraine frequency and improving quality of life. Non-pharmacological interventions, such as lifestyle modification and behavioral therapy, were shown to enhance treatment outcomes when combined with medical therapy.

In conclusion, effective management of chronic migraine requires a comprehensive and individualized approach that integrates pharmacological and non-pharmacological strategies. Further research is needed to develop cost-effective and personalized treatment options to improve long-term disease control.

Keywords

Chronic migraine; Headache disorders; Pathophysiology; CGRP; Preventive therapy; Non-pharmacological treatment

Introduction

Chronic headache disorders represent one of the most prevalent and disabling neurological conditions worldwide, significantly affecting patients' quality of life and productivity [1]. Among them, migraine is a common primary headache disorder characterized by recurrent attacks of moderate to severe head pain, often accompanied by nausea, vomiting, photophobia, and phonophobia [2]. According to epidemiological studies, migraine affects approximately 12–15% of the global population, with a higher prevalence among women and individuals of working age [3]. The chronic form of migraine, defined as headache occurring on 15 or more days per month for at least three months, poses a serious medical and socioeconomic challenge [4].

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The pathophysiology of migraine is complex and multifactorial, involving genetic predisposition, neurovascular dysregulation, central sensitization, and alterations in neurotransmitter systems, particularly serotonin and calcitonin gene-related peptide (CGRP) [5]. Various internal and external triggers—such as stress, sleep disturbances, hormonal changes, dietary factors, and environmental stimuli—play a crucial role in initiating and perpetuating migraine attacks [6]. Despite extensive research, the exact mechanisms underlying the transition from episodic to chronic migraine remain incompletely understood [7].

Effective management of chronic migraine requires a comprehensive and individualized approach. Modern treatment strategies include acute (abortive) therapy aimed at relieving headache attacks and preventive therapy focused on reducing attack frequency and severity [8]. Pharmacological treatments, such as nonsteroidal anti-inflammatory drugs (NSAIDs), triptans, beta-blockers, antiepileptic drugs, antidepressants, and recently developed CGRP monoclonal antibodies, have demonstrated varying degrees of efficacy [9]. In addition, non-pharmacological interventions—such as lifestyle modification, stress management, cognitive behavioral therapy, and physiotherapy—are increasingly recognized as essential components of migraine management [10].

The aim of this article is to analyze the main causes of chronic headache, particularly migraine, and to review current therapeutic approaches based on recent clinical evidence. Understanding the underlying mechanisms and available treatment options is essential for optimizing patient outcomes and improving long-term disease control [11].

Methods

This study was designed as a narrative review of the scientific literature focusing on the causes and treatment approaches of chronic migraine. Relevant publications were identified through a comprehensive search of international electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar.

The literature search covered articles published primarily between 2015 and 2024 to ensure the inclusion of up-to-date clinical evidence. The following keywords and their combinations were used: *chronic headache*, *migraine*, *pathophysiology*, *risk factors*, *pharmacological treatment*, *preventive therapy*, and *non-pharmacological management*. Only articles published in English were considered.

Inclusion criteria comprised original research articles, systematic reviews, meta-analyses, and international clinical guidelines addressing chronic migraine in adult populations. Studies focusing on secondary headaches, pediatric migraine, or non-clinical experimental models were excluded. Additionally, publications lacking clear methodology or outcome data were not considered.

Data extraction was performed by analyzing study objectives, patient characteristics, diagnostic criteria, etiological factors, and therapeutic strategies. Special attention was given to evidence related to pharmacological interventions, including acute and preventive treatments, as well as non-pharmacological approaches such as lifestyle modification and behavioral therapy.

The collected data were qualitatively synthesized to identify common etiological factors and evaluate the effectiveness of various treatment modalities. The analysis was conducted in accordance with current international recommendations for migraine management and evidence-based medicine principles [8–11].

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Results

The analysis of the selected literature revealed that chronic migraine is associated with multiple interrelated etiological factors and requires a multimodal treatment approach. Most reviewed studies reported that chronic migraine was more prevalent among women and individuals aged 20–50 years. Stress, sleep disorders, and hormonal fluctuations were consistently identified as the most common triggering factors contributing to the chronification of migraine [3,6].

Neurobiological findings demonstrated that patients with chronic migraine exhibited increased central sensitization and elevated levels of calcitonin gene-related peptide (CGRP), which were strongly correlated with headache frequency and severity [5,7]. Genetic predisposition and a history of episodic migraine were also found to significantly increase the risk of developing chronic migraine.

Pharmacological treatment outcomes varied depending on the class of medication. Acute treatment with NSAIDs and triptans was effective in relieving pain during migraine attacks; however, excessive use was associated with medication-overuse headache in a substantial proportion of patients [8]. Preventive therapies, including beta-blockers, antiepileptic drugs, and antidepressants, resulted in a moderate reduction in headache days per month [9]. Recent studies highlighted that CGRP monoclonal antibodies demonstrated superior efficacy in reducing monthly migraine days and improving patients' quality of life compared to conventional preventive agents [10].

Non-pharmacological interventions showed additional benefits when combined with drug therapy. Lifestyle modification, stress management, and cognitive behavioral therapy contributed to improved treatment adherence and a reduction in migraine frequency, particularly in patients with comorbid anxiety and sleep disturbances [11].

Table 1. Main etiological factors and treatment outcomes in chronic migraine

Factor / Treatment Approach	**Key Findings**	**Clinical Impact**
Stress and sleep disorders	Most frequently reported triggers	Increased migraine frequency
Hormonal fluctuations	Higher prevalence in women	Chronification risk
Central sensitization	Elevated pain sensitivity	Severe and persistent attacks
NSAIDs and triptans	Effective for acute attacks	Risk of overuse headache
Preventive medications	Moderate reduction of headache days	Long-term control
CGRP monoclonal antibodies	Significant reduction in migraine days	Improved quality of life

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Factor / Treatment Approach	Key Findings	Clinical Impact
Non-pharmacological therapy	Enhanced treatment adherence	Reduced attack frequency

Discussion

The findings of this review confirm that chronic migraine is a multifactorial neurological disorder influenced by a combination of biological, psychological, and environmental factors. The high prevalence of chronic migraine among women and individuals of working age observed in the reviewed studies is consistent with previously published epidemiological data, highlighting the significant burden of this condition on both healthcare systems and society [3,4].

One of the key mechanisms identified in the progression from episodic to chronic migraine is central sensitization. Increased neuronal excitability and dysregulation of pain processing pathways contribute to the persistence and severity of migraine attacks [5,7]. Elevated levels of calcitonin gene-related peptide (CGRP) have been strongly associated with migraine pathophysiology, supporting the rationale for targeting CGRP in preventive treatment strategies [10].

The results also emphasize the importance of careful use of acute migraine medications. While NSAIDs and triptans remain effective for abortive therapy, their excessive use increases the risk of medication-overuse headache, which may further exacerbate chronic migraine [8]. This finding underscores the necessity of patient education and close monitoring during treatment.

Preventive pharmacological therapies demonstrated varying degrees of efficacy. Traditional agents such as beta-blockers, antiepileptic drugs, and antidepressants provided moderate benefits but were often limited by side effects and poor adherence [9]. In contrast, CGRP monoclonal antibodies showed superior effectiveness and better tolerability, representing a significant advancement in chronic migraine management [10]. However, their high cost and limited availability may restrict widespread use, particularly in low- and middle-income countries.

Non-pharmacological interventions played a crucial complementary role in migraine management. Lifestyle modification, stress reduction techniques, and cognitive behavioral therapy were associated with improved treatment outcomes and reduced migraine frequency, especially in patients with comorbid psychological conditions [11]. These findings support a multidisciplinary and individualized approach to chronic migraine treatment.

Despite the valuable insights provided by this review, several limitations should be considered. The reliance on published literature may introduce publication bias, and differences in study design and outcome measures may affect the generalizability of the results. Future research should focus on long-term comparative studies and the integration of personalized treatment strategies to optimize chronic migraine management.

Conclusion

Chronic migraine represents a complex and disabling neurological disorder with a significant impact on patients' quality of life and socioeconomic well-being. The findings of this review highlight that the development and persistence of chronic migraine are driven by a combination

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of genetic susceptibility, neurobiological mechanisms such as central sensitization, and various internal and external triggering factors.

Effective management of chronic migraine requires an individualized and comprehensive treatment strategy. While acute therapies remain essential for controlling migraine attacks, their inappropriate or excessive use may contribute to medication-overuse headache and disease chronification. Preventive pharmacological treatments play a key role in reducing headache frequency and severity, with CGRP monoclonal antibodies emerging as a promising and targeted therapeutic option.

In addition to pharmacological approaches, non-pharmacological interventions—including lifestyle modification, stress management, and behavioral therapies—are crucial components of long-term migraine control. A multidisciplinary approach that combines medical treatment with patient education and behavioral support may lead to improved clinical outcomes and enhanced quality of life. Further research is needed to better understand the mechanisms underlying migraine chronification and to develop cost-effective, personalized treatment strategies. Strengthening evidence-based clinical practice will contribute to more effective prevention and management of chronic migraine in diverse patient populations.

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