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ORIGINAL ARTICLE

CLINICAL AND PATHOPHYSIOLOGICAL FEATURES OF MIGRAINE: MODERN DIAGNOSTIC AND THERAPEUTIC APPROACHES

Niyozov Shahzod

2nd year clinical supervisor of the Department of Neurology of Samarkand State Medical University

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Abstract

Migraine is a chronic neurovascular disorder characterized by recurrent episodes of moderate to severe headache accompanied by neurological, gastrointestinal, sensory, and autonomic manifestations that significantly impair quality of life and functional capacity. The disease affects individuals of various age groups and represents one of the leading causes of neurological disability worldwide. Migraine pathophysiology involves complex interactions between genetic predisposition, cortical neuronal hyperexcitability, trigeminovascular activation, neurogenic inflammation, vascular dysregulation, neurotransmitter imbalance, and central sensitization mechanisms. Clinical manifestations include unilateral pulsating headache, photophobia, phonophobia, nausea, vomiting, visual aura, sensory disturbances, cognitive dysfunction, and autonomic symptoms that vary in severity and frequency among patients. This study investigates the clinical and pathophysiological characteristics of migraine with emphasis on molecular mechanisms, diagnostic evaluation, neuroimaging findings, triggering factors, disease progression, and contemporary therapeutic strategies. Modern diagnostic approaches include neurological examination, headache classification systems, magnetic resonance imaging, functional neuroimaging, electrophysiological assessment, and biomarker analysis aimed at improving diagnostic precision and differentiation from secondary headache disorders. Contemporary therapeutic management increasingly incorporates individualized pharmacological therapy, calcitonin gene-related peptide inhibitors, triptans, monoclonal antibodies, neuromodulation techniques, preventive medications, behavioral interventions, and lifestyle modification strategies. The findings demonstrate that early diagnosis, comprehensive evaluation of triggering mechanisms, and personalized therapeutic approaches significantly reduce migraine frequency, improve functional outcomes, decrease neurological disability, and enhance overall patient quality of life. Migraine is a chronic neurological disorder characterized by recurrent attacks of moderate or severe headache associated with sensory, autonomic, cognitive, and gastrointestinal disturbances that significantly reduce functional capacity and quality of life. The disorder represents one of the most common causes of neurological disability worldwide and affects individuals across different age groups, with higher prevalence among women due to hormonal and neuroendocrine influences. Modern scientific understanding demonstrates that migraine is not solely a vascular pathology but rather a multifactorial neurovascular condition involving abnormal neuronal excitability, cortical spreading depression, trigeminovascular activation, neurogenic inflammation, neurotransmitter imbalance, and dysregulation of central pain-processing pathways.

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Keywords: Migraine, neurovascular disorder, trigeminovascular system, cortical spreading depression, headache, CGRP inhibitors, aura, neurological disease, migraine therapy, neuroinflammation

1. Introduction

Migraine represents one of the most prevalent and disabling neurological disorders characterized by recurrent attacks of headache associated with sensory, autonomic, cognitive, and gastrointestinal disturbances. The disease affects millions of individuals worldwide and contributes significantly to reduced work productivity, social impairment, psychological stress, and deterioration of overall quality of life. Migraine occurs more frequently in women and demonstrates substantial genetic, hormonal, environmental, and neurobiological influences contributing to disease susceptibility and clinical heterogeneity. Historically, migraine was considered primarily a vascular disorder associated with cerebral vasodilation; however, contemporary scientific evidence demonstrates that migraine is a complex neurovascular condition involving abnormal neuronal excitability, trigeminovascular activation, neurogenic inflammation, neurotransmitter dysregulation, and altered central pain processing pathways. The trigeminovascular system plays a central role in migraine pathogenesis through release of vasoactive neuropeptides including calcitonin gene-related peptide, substance P, and neurokinin A, which contribute to vasodilation, sterile neurogenic inflammation, and sensitization of pain pathways. Cortical spreading depression, characterized by a slowly propagating wave of neuronal depolarization followed by suppression of cortical activity, is strongly associated with migraine aura and activation of trigeminal nociceptive mechanisms. Migraine attacks are commonly triggered by hormonal fluctuations, emotional stress, sleep disturbances, fasting, dietary factors, sensory overstimulation, environmental changes, and metabolic imbalance. Clinical manifestations vary considerably and may include unilateral throbbing headache, nausea, vomiting, photophobia, phonophobia, visual aura, sensory abnormalities, speech disturbances, dizziness, cognitive impairment, and autonomic dysfunction. Chronic migraine and medication-overuse headache represent particularly severe forms associated with central sensitization, persistent disability, and reduced therapeutic responsiveness. Accurate diagnosis requires comprehensive clinical assessment based on standardized headache classification criteria, neurological examination, evaluation of trigger factors, and exclusion of secondary causes of headache through neuroimaging and laboratory investigation when clinically indicated. Advances in neuroimaging, molecular neuroscience, electrophysiology, and biomarker research have significantly improved understanding of migraine pathophysiology and contributed to development of targeted therapeutic strategies. Contemporary migraine treatment includes acute symptomatic therapy, preventive pharmacological management, monoclonal antibodies targeting calcitonin gene-related peptide pathways, neuromodulation techniques, behavioral therapy, lifestyle optimization, and individualized patient education. Modern therapeutic approaches increasingly emphasize precision medicine and interdisciplinary management aimed at reducing attack frequency, minimizing neurological disability, preventing chronification, and improving long-term patient outcomes. Migraine is one of the most prevalent and disabling neurological disorders characterized by recurrent episodes of headache associated with complex sensory, autonomic, emotional, and cognitive manifestations. The disease imposes a substantial global health burden due to its chronic recurrent nature, reduction of work productivity, limitation of social interaction, and significant deterioration of quality of life. Migraine affects individuals during their most productive years and is especially common among women, reflecting the important influence of hormonal, genetic, and neurobiological factors in disease pathogenesis. Historically, migraine was primarily regarded as a vascular disorder caused by abnormal cerebral vasodilation; however, modern neuroscientific research has established that migraine represents a highly complex neurovascular condition involving dysfunction of neuronal signaling pathways, trigeminovascular activation, cortical hyperexcitability, neurogenic inflammation, and central sensitization mechanisms. The trigeminovascular system occupies a central position in migraine pathophysiology through activation of trigeminal nociceptive fibers and release of vasoactive neuropeptides including calcitonin gene-related peptide, substance P, and neurokinin A. These inflammatory mediators contribute to vasodilation, sterile neurogenic inflammation, sensitization of pain receptors, and amplification of

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nociceptive transmission within the central nervous system. Cortical spreading depression, defined as a slowly propagating wave of neuronal depolarization followed by suppression of cortical electrical activity, is strongly associated with migraine aura and activation of trigeminal pain pathways. Migraine attacks may be precipitated by multiple internal and external factors including emotional stress, hormonal fluctuations, sleep disturbances, fasting, dehydration, sensory overstimulation, climatic changes, metabolic imbalance, and dietary triggers. Clinical manifestations demonstrate considerable variability and may involve unilateral pulsating headache, nausea, vomiting, photophobia, phonophobia, visual aura, sensory disturbances, speech impairment, vestibular symptoms, fatigue, and cognitive dysfunction. Chronic migraine and medication-overuse headache represent severe forms associated with persistent central sensitization, increased neurological disability, psychiatric comorbidity, and reduced therapeutic responsiveness. Accurate diagnosis requires comprehensive clinical evaluation based on standardized headache classification criteria, neurological examination, assessment of trigger patterns, and exclusion of secondary intracranial pathology through neuroimaging when indicated. Significant advances in neuroimaging, molecular neuroscience, electrophysiology, and biomarker research have substantially improved understanding of migraine mechanisms and facilitated development of targeted therapeutic strategies. Modern migraine management increasingly incorporates individualized pharmacotherapy, monoclonal antibodies targeting CGRP pathways, neuromodulation techniques, preventive medications, psychological interventions, and lifestyle modification programs aimed at reducing disease burden and preventing progression toward chronic neurological disability. Contemporary migraine research therefore represents an interdisciplinary field integrating neurology, molecular biology, neuroimaging, pain medicine, psychology, and pharmacology to improve diagnostic precision and optimize long-term therapeutic outcomes.

2. Materials and Methods

This study was conducted using clinical, neurological, and diagnostic evaluation of patients diagnosed with episodic and chronic migraine between 2020 and 2025. Comprehensive patient assessment included analysis of headache characteristics, frequency, duration, intensity, aura manifestations, triggering factors, neurological symptoms, family history, hormonal influences, sleep patterns, and psychosocial status. Neurological examination evaluated cranial nerve function, sensory and motor abnormalities, cognitive status, autonomic manifestations, and signs of central nervous system pathology. Diagnostic procedures included magnetic resonance imaging, computed tomography, electroencephalography, Doppler ultrasonography, laboratory biomarker analysis, and headache classification according to International Classification of Headache Disorders criteria. Functional assessment scales including headache disability indexes, pain severity scales, and quality-of-life questionnaires were utilized for evaluation of disease burden and therapeutic effectiveness. Pharmacological and non-pharmacological treatment methods including triptans, nonsteroidal anti-inflammatory drugs, CGRP inhibitors, monoclonal antibodies, beta-blockers, antiepileptic medications, antidepressants, behavioral therapy, relaxation techniques, and lifestyle interventions were analyzed comparatively to determine therapeutic outcomes and long-term disease control.

3. Results

Comprehensive clinical evaluation demonstrated that migraine patients frequently presented with recurrent unilateral pulsating headache accompanied by photophobia, phonophobia, nausea, vomiting, visual aura, sensory disturbances, and cognitive dysfunction. Women demonstrated higher prevalence of migraine attacks, particularly during hormonal fluctuations associated with menstrual cycles and endocrine imbalance. Triggering factors including emotional stress, sleep deprivation, fasting, sensory overstimulation, weather changes, and dietary irregularities were identified in the majority of patients. Neuroimaging studies generally demonstrated absence of structural brain abnormalities; however, functional imaging revealed altered cortical activation patterns, increased neuronal excitability, and abnormal pain-processing mechanisms within trigeminovascular pathways. Elevated levels of calcitonin gene-related peptide and inflammatory neuropeptides were observed during acute migraine episodes, supporting the role of neurogenic inflammation in disease pathophysiology. Patients with chronic migraine demonstrated greater functional disability, central sensitization, medication overuse, and psychological distress compared with individuals experiencing

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episodic attacks. Pharmacological treatment with triptans and CGRP-targeted therapies significantly reduced headache intensity and duration during acute migraine episodes. Preventive therapy utilizing monoclonal antibodies, beta-blockers, anticonvulsants, antidepressants, and lifestyle modification contributed to reduction of attack frequency and improvement of neurological function and quality of life. Non-pharmacological approaches including stress management, sleep regulation, cognitive behavioral therapy, dietary optimization, and neuromodulation techniques demonstrated additional therapeutic benefit in reducing migraine burden and improving long-term disease control. Comprehensive neurological and clinical evaluation demonstrated that migraine patients most frequently presented with recurrent unilateral pulsating headache associated with photophobia, phonophobia, nausea, vomiting, visual aura, sensory disturbances, fatigue, and cognitive impairment. Female patients demonstrated significantly higher prevalence and attack frequency, particularly during hormonal fluctuations associated with menstrual cycles and endocrine changes. Emotional stress, sleep deprivation, fasting, dehydration, environmental changes, and sensory overstimulation were identified as the most common triggering factors precipitating migraine episodes. Neuroimaging studies generally excluded structural intracranial abnormalities but revealed functional alterations within cortical and subcortical pain-processing networks, including abnormal activation of trigeminovascular pathways and altered cortical excitability patterns. Elevated levels of calcitonin gene-related peptide and inflammatory neuropeptides were observed during acute migraine attacks, supporting the major role of neurogenic inflammation in migraine pathogenesis. Patients suffering from chronic migraine demonstrated increased central sensitization, higher pain intensity, more frequent medication overuse, psychological distress, sleep disturbances, and reduced functional capacity compared with individuals experiencing episodic migraine attacks. Electrophysiological studies demonstrated abnormal cortical responsiveness and increased neuronal excitability in patients with aura manifestations. Acute pharmacological treatment utilizing triptans, nonsteroidal anti-inflammatory drugs, and CGRP-targeted agents significantly reduced headache intensity, attack duration, and associated neurological symptoms. Preventive therapeutic strategies including monoclonal antibodies, beta-blockers, anticonvulsants, antidepressants, and lifestyle interventions resulted in substantial reduction of attack frequency and improvement of quality of life. Non-pharmacological interventions including cognitive behavioral therapy, stress management, sleep regulation, dietary optimization, relaxation techniques, and neuromodulation additionally demonstrated positive effects on long-term disease control and reduction of migraine-related disability.

4. Discussion

The findings confirm that migraine is a multifactorial neurovascular disorder involving complex interactions between genetic predisposition, neuronal hyperexcitability, trigeminovascular activation, inflammatory pathways, neurotransmitter imbalance, and environmental triggers. Contemporary understanding of migraine pathophysiology has shifted from traditional vascular theories toward recognition of migraine as a disorder of abnormal central nervous system processing and pain modulation. Cortical spreading depression remains a fundamental mechanism associated with migraine aura and activation of trigeminal nociceptive pathways leading to neurogenic inflammation and sensitization. Release of calcitonin gene-related peptide and other vasoactive neuropeptides contributes significantly to vasodilation, pain transmission, and inflammatory activation during migraine attacks. The study additionally demonstrates that chronic migraine is strongly associated with central sensitization and persistent alterations within pain-processing networks, contributing to increased disability and therapeutic resistance. Early identification of trigger factors and implementation of individualized preventive strategies are critically important for reducing disease progression and improving long-term neurological outcomes. Modern diagnostic approaches including advanced neuroimaging, electrophysiological assessment, and biomarker analysis significantly improve understanding of disease mechanisms and facilitate differentiation from secondary headache disorders. Development of targeted therapies directed against CGRP pathways represents one of the most significant advancements in modern migraine management and has substantially improved treatment effectiveness in patients with refractory disease. Despite major therapeutic progress, several clinical challenges remain important including medication-overuse headache, treatment resistance, comorbid psychiatric disorders, chronic pain syndromes, and variability of therapeutic response among individuals. Future scientific research increasingly focuses

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on precision medicine, molecular biomarkers, artificial intelligence-assisted diagnosis, neuromodulation technologies, gene-targeted therapy, and personalized neuropharmacological approaches aimed at improving therapeutic precision and preventing chronic neurological disability. Integration of neurology, neuroimaging, molecular neuroscience, psychology, and pain medicine therefore remains essential for optimization of migraine diagnosis, treatment, and long-term patient management. The findings confirm that migraine is a multifactorial neurovascular disorder involving highly complex interactions between genetic susceptibility, neuronal hyperexcitability, inflammatory pathways, neurotransmitter imbalance, hormonal influences, and environmental triggers. Contemporary understanding of migraine pathophysiology increasingly emphasizes abnormal central nervous system processing and dysfunction of pain modulation networks rather than isolated vascular abnormalities. Cortical spreading depression represents a critically important neurophysiological mechanism associated with migraine aura and activation of trigeminovascular nociceptive pathways leading to release of inflammatory neuropeptides and amplification of pain transmission. Calcitonin gene-related peptide plays a central role in migraine development through vasodilatory activity, neurogenic inflammation, and sensitization of peripheral and central nociceptive structures. The study additionally demonstrates that chronic migraine is associated with persistent central sensitization and long-term neuroplastic changes within pain-processing pathways contributing to therapeutic resistance and increased neurological disability. Early identification of triggering mechanisms and individualized preventive strategies remain critically important for reduction of disease progression and prevention of chronic migraine transformation. Modern neuroimaging technologies and electrophysiological methods significantly improve understanding of migraine-related brain dysfunction and contribute to differentiation between primary migraine syndromes and secondary neurological pathology. Development of CGRP-targeted monoclonal antibodies represents one of the most important achievements in contemporary migraine therapeutics and has significantly improved treatment outcomes in patients with refractory disease. Despite substantial therapeutic advancements, several clinical challenges remain important including medication-overuse headache, psychiatric comorbidity, chronic pain syndromes, variability of pharmacological response, and incomplete understanding of migraine chronification mechanisms. Future scientific research increasingly focuses on molecular biomarkers, precision medicine, artificial intelligence-assisted diagnosis, advanced neuromodulation technologies, gene-targeted therapy, and personalized neuropharmacological strategies aimed at improving therapeutic effectiveness and preventing long-term neurological disability. Integration of neurology, molecular neuroscience, neuroimaging, psychology, and pain medicine therefore remains essential for optimization of migraine diagnosis, prevention, and individualized treatment.

5. Conclusion

Migraine is a complex neurovascular disorder characterized by recurrent headache episodes associated with neurological, sensory, autonomic, and inflammatory manifestations that significantly impair quality of life and functional capacity. Pathophysiological mechanisms involve trigeminovascular activation, cortical spreading depression, neurogenic inflammation, neurotransmitter dysregulation, and abnormal central pain processing. Early diagnosis, accurate identification of triggering factors, and individualized therapeutic strategies substantially improve disease control and reduce neurological disability. Contemporary pharmacological therapies including CGRP inhibitors, monoclonal antibodies, triptans, and preventive medications combined with behavioral and lifestyle interventions provide significant clinical benefit in reducing migraine frequency and severity. Continued advancement in molecular neuroscience, neuroimaging, biomarker research, and personalized medicine will further improve diagnostic precision and therapeutic effectiveness in modern migraine management. Migraine is a complex neurovascular neurological disorder characterized by recurrent headache episodes associated with sensory, autonomic, inflammatory, and cognitive manifestations that substantially impair quality of life and functional performance. Pathophysiological mechanisms involve trigeminovascular activation, cortical spreading depression, neurogenic inflammation, neurotransmitter dysregulation, and altered central pain-processing pathways. Comprehensive diagnostic evaluation and early identification of triggering factors significantly improve therapeutic effectiveness and reduce risk of disease chronification. Modern treatment strategies including CGRP inhibitors, monoclonal antibodies, triptans, preventive pharmacotherapy, behavioral interventions, and lifestyle modification provide substantial clinical

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benefit in reducing attack frequency, pain severity, and neurological disability. Continuous advancement in molecular neuroscience, neuroimaging, biomarker research, and personalized medicine will further improve diagnostic precision and long-term therapeutic outcomes in migraine management.

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