

NARRATIVE REVIEW

PAIN MEDICINE

The link between migraine and eye pain: a review of current evidence

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ABSTRACT

Eye pain is a frequent and distressing symptom in individuals with migraines, yet it remains an underexplored aspect of migraine pathology. This review consolidates current knowledge on the association between eye pain and migraines, covering pathophysiological mechanisms, clinical features, differential diagnoses, and management approaches. A thorough analysis of existing literature indicates that migraine-related eye pain is multifactorial, involving neural, vascular, and sensory pathways. Additionally, this review underscores the need for further research to refine diagnostic criteria and enhance treatment strategies for patients experiencing ocular discomfort during migraine episodes.

Key words: Eye Pain; Migraine; Cluster Headache; Pathophysiology; Diagnostic Challenges; Ocular Manifestations; Trigeminal Neuralgia; Dry Eye Disease; Quality of Life

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1. INTRODUCTION

Migraine is a widespread and debilitating neurovascular disorder that affects millions globally.¹⁻⁴ It is primarily defined by recurrent, moderate to severe headaches, often accompanied by various neurological symptoms.⁵ Among these, eye pain is a common yet underexplored feature, which can be distressing and challenging to distinguish from other ocular conditions.^{6,7}

Migraine-related eye pain may manifest as sharp, throbbing, or aching discomfort, typically localized around the eyes or periorbital region. Its pathophysiology is complex and involves neural, vascular, and sensory pathways. Despite its prevalence, the exact mechanisms underlying migraine-associated eye pain remain insufficiently understood, leading to diagnostic and therapeutic challenges.

This review examines the connection between migraines and eye pain, emphasizing pathophysiology, clinical presentation, differential diagnosis, and

management strategies. A thorough evaluation of existing literature underscores the need for further research to refine diagnostic criteria and enhance treatment approaches for patients experiencing ocular pain during migraine episodes.

2. APPLIED PATHOPHYSIOLOGY

The mechanisms underlying migraines and associated eye pain are intricate, involving vascular, neuronal, and inflammatory processes.⁸ Recent research has extensively explored the relationship between migraines and eye pain, shedding light on their underlying mechanisms, clinical presentations, and potential therapeutic approaches. The following is a detailed review of current evidence to enhance our understanding of this complex interaction.

2.1. Role of the Trigeminal Nerve in Migraine-Related Eye Pain:

The trigeminal nerve, the largest cranial nerve, is pivotal in the pathophysiology of migraines and associated ocular pain. During a migraine attack, activation of the trigeminal nerve leads to the release of neuropeptides, including calcitonin gene-related peptide (CGRP), substance P, and neurokinin A.⁹ These neuropeptides induce vasodilation and inflammation in the meningeal blood vessels, contributing to pain in the eyes and surrounding regions. Additionally, the trigeminal-autonomic reflex plays a role in ocular symptoms such as tearing, conjunctival injection, and periorbital pain.¹⁰

Functional MRI (fMRI) studies have demonstrated increased activity in the trigeminal ganglion and trigeminal nucleus caudalis during migraine attacks, correlating with reports of eye pain in affected patients. These findings underscore the significance of the trigeminal system in migraine-related ocular pain and suggest that targeting this pathway could offer therapeutic benefits.¹¹⁻¹²

2.2. Inflammation and Vascular Changes in Migraines and Eye Pain:

Inflammatory processes in the blood vessels surrounding the brain and eyes are another crucial factor in migraine-related eye pain. Studies indicate that migraine attacks are linked to increased levels of pro-inflammatory cytokines and inflammatory markers, contributing to pain pathway sensitization. One study found that patients experiencing migraines with pronounced eye pain had increased levels of C-reactive protein (CRP) and interleukin-6 (IL-6) in their blood samples.¹⁴ These markers were linked to greater pain intensity and longer attack duration, suggesting that anti-inflammatory treatments could be beneficial for managing migraine-related ocular pain.

2.3. Visual Cortex Hyperexcitability and Eye Pain:

The visual cortex, responsible for processing visual stimuli, has been implicated in migraine-related ocular symptoms. Research suggests that individuals with migraines often exhibit hyperexcitability in the visual cortex, potentially contributing to both visual disturbances (such as aura) and eye pain.¹⁵ A study assessing brain activity in migraine patients with and without eye pain revealed significantly higher levels of visual cortex activation in those experiencing ocular pain during migraine episodes. This hyperexcitability may explain the frequent co-occurrence of photophobia and eye pain in migraine sufferers.¹⁶

2.4. Ocular Migraines and Retinal Blood Flow:

Ocular migraines, or retinal migraines, are a subtype characterized by transient vision loss or visual disturbances in one eye, often accompanied by eye pain. Recent research has examined the role of retinal blood flow in these migraines. Optical coherence tomography angiography (OCTA) studies have demonstrated a significant reduction in retinal blood flow during ocular migraine attacks, correlating with the severity of eye pain. This reduction in perfusion is believed to result from vasospasm in the retinal arteries, potentially explaining the visual symptoms and discomfort experienced by patients.¹⁷⁻¹⁹

2.5. The Role of CGRP in Migraine-Related Eye Pain:

Calcitonin gene-related peptide (CGRP), a neuropeptide integral to migraine pathophysiology, has been a key target in recent migraine treatment advances. Emerging therapies aimed at inhibiting CGRP have shown promise in reducing both migraine severity and associated eye pain, further emphasizing its role in migraine-related ocular symptoms.²⁰⁻²¹

2.6. Dry Eye Syndrome and Migraine-Related Eye Pain:

Dry eye syndrome (DES) is a common comorbidity in migraine sufferers and may exacerbate ocular discomfort during migraine episodes. Studies investigating the link between DES and migraines have found that patients with both conditions report significantly higher levels of eye pain compared to those without DES. Researchers suggest that managing DES could help alleviate migraine-related ocular pain in these individuals.²²⁻²⁴ Additionally, the involvement of the visual cortex in migraine-related visual symptoms, such as photophobia and aura, may contribute to or intensify eye pain in light-sensitive individuals.²⁵

3. Common Ocular Manifestations in Migraine

Eye pain in migraine sufferers varies in intensity and character, ranging from mild discomfort to severe, throbbing, or aching sensations. It is typically unilateral, localized around the eye or periorbital region, though it may radiate to the forehead or temples and, in some cases, occur bilaterally. The pain often worsens with physical activity or eye movement, further intensifying the distress of a migraine attack. Ocular symptoms frequently accompany migraine headaches, along with nausea, vomiting, and heightened sensitivity to light and sound.²⁶⁻²⁷ The most common ocular manifestations include:

3.1. Eye Pain:

Migraine-related eye pain is often described as throbbing, pressure-like, or deep-seated, typically centred around the orbit or behind the eyes. This discomfort may intensify with physical exertion or eye movement, contributing to significant distress during an attack.

3.2. Photophobia:

Light sensitivity, or photophobia, is a hallmark symptom of migraines. Bright light can intensify eye discomfort, prompting many migraine sufferers to seek dark, quiet environments for relief.

3.3. Visual Disturbances:

Migraines are frequently associated with visual symptoms, including auras, blurred vision, and scotomas (blind spots). Visual auras, occurring before or during a migraine, may manifest as flickering lights or geometric patterns, sometimes exacerbating eye pain.

3.4. Eye Redness and Tearing:

Some migraine patients experience ocular redness and excessive tearing during an attack, likely due to neurogenic inflammation affecting the ocular region.

3.5. Pressure Behind the Eyes:

A deep, pressure-like sensation behind the eyes is commonly reported, causing a feeling of heaviness and strain. This symptom can be particularly bothersome during migraine episodes, adding to the overall discomfort.

4. Diagnostic Challenges

Diagnosing migraine-related eye pain can be complex due to symptom overlap with various ocular and neurological conditions. While eye pain is a common

migraine symptom, distinguishing it from other causes of ocular discomfort is essential for accurate diagnosis and effective management.

Several eye-related pathologies must be excluded, including acute angle-closure glaucoma, optic neuritis, and dry eye syndrome, as these conditions can mimic migraine-associated eye pain.²⁸⁻³⁰ Additionally, tension-type headaches and other headache disorders may contribute to eye strain and discomfort, further complicating the differential diagnosis.³¹⁻³³ In some cases, migraine treatments such as triptans may induce secondary ocular symptoms like dry eye, emphasizing the need for a thorough medication history.

The primary diagnostic challenge lies in differentiating migraine-related eye pain from other conditions with similar presentations, such as:

4.1. Cluster Headaches:

Like migraines, cluster headaches cause severe unilateral eye pain, often described as sharp and burning, and may be accompanied by tearing and redness. However, cluster headaches are typically shorter in duration (lasting 15–180 minutes) and are associated with autonomic symptoms such as nasal congestion and ptosis.

4.2. Sinusitis:

Inflammation of the sinuses can result in facial pain and pressure, often localized around the eyes, leading to confusion with migraine-related eye pain. However, sinusitis is usually associated with nasal congestion and lacks the characteristic throbbing headache seen in migraines.

4.3. Glaucoma:

Acute angle-closure glaucoma can present with severe eye pain and visual disturbances, resembling migraine symptoms. However, glaucoma-related pain is often accompanied by elevated intraocular pressure, along with nausea and vomiting, which are not typically seen in migraines.

4.4. Trigeminal Neuralgia:

This condition involves sudden, severe, shock-like pain along the trigeminal nerve, frequently affecting the eye region. Although it shares some characteristics with migraine-related eye pain, it is a distinct disorder requiring different therapeutic approaches.

A thorough clinical history, comprehensive physical examination, and, when necessary, imaging or ophthalmologic evaluation are essential for distinguishing migraine-related eye pain from other conditions. Recognizing key distinguishing features aids in accurate diagnosis and ensures appropriate management for patients experiencing ocular discomfort in the context of migraines.

5. Management Strategies

The treatment of eye pain in migraines follows general migraine management principles, incorporating both acute and preventive approaches.³⁴⁻³⁶ The primary goal is to relieve ocular pain during an attack while also reducing the frequency and severity of migraines over time.

5.1. Pharmacological Approaches

5.1.1. Acute Treatment Medications: Triptans (e.g., sumatriptan, rizatriptan) are first-line treatments for moderate to severe migraines. They work by constricting blood vessels and inhibiting neuropeptide release, effectively relieving both headache and eye pain.

5.1.2. NSAIDs (e.g., ibuprofen, aspirin) help reduce inflammation and pain, including ocular discomfort associated with migraines.

5.1.3. CGRP Inhibitors (e.g., erenumab) target calcitonin gene-related peptide, a key molecule in migraine pathophysiology, reducing both the frequency and intensity of migraines and their associated eye pain.

5.2. Preventive Therapies

5.2.1. Beta-blockers (e.g., propranolol), calcium channel blockers, and anticonvulsants (e.g., topiramate) are commonly prescribed for migraine prevention.

5.2.2. Botulinum toxin injections have been explored as a preventive option for chronic migraine sufferers, particularly those experiencing significant ocular involvement.

5.3. Non-Pharmacological Strategies³⁷⁻⁴⁰

5.3.1. Lifestyle Modifications: Maintaining a consistent sleep schedule, staying hydrated, and avoiding known migraine triggers (e.g., bright lights, stress, and dietary factors) can significantly reduce the occurrence of migraines and associated eye pain.

5.3.2. Stress Management: Meditation and mindfulness like approaches and cognitive behavioural therapy (CBT) can be effective in reducing stress-related migraine triggers.

5.3.3. Rest and Eye Care: A dark, quiet environment provides relief during migraine attacks. The use of artificial tears can help alleviate dry eye symptoms, a common comorbidity in migraine

patients. Additionally, cool compresses applied around the eyes may reduce pressure and discomfort.

By integrating pharmacological treatments, lifestyle modifications, and supportive therapies, individuals experiencing migraine-related eye pain can achieve better symptom control and an improved quality of life.

6. Impact of Migraine⁴¹⁻⁵¹

Chronic migraines, particularly those accompanied by frequent ocular symptoms, can have profound effects on both ocular health and overall quality of life. The persistent strain associated with migraine-related eye pain can contribute to long-term complications that extend beyond episodic discomfort.

6.1. Effects on Ocular Health

6.1.1 Chronic Dry Eye Syndrome: Individuals with frequent migraines often experience photophobia, leading them to avoid bright environments by squinting or reducing blinking frequency. This habitual reduction in blinking can contribute to tear film instability, exacerbating dry eye symptoms. Studies have shown that migraine sufferers have a higher prevalence of dry eye disease (DED) compared to the general population. Inflammation, trigeminal nerve dysfunction, and the use of certain migraine medications (e.g., triptans) have also been linked to tear film disruption and ocular surface discomfort. Left untreated, chronic dry eye can lead to ocular surface damage, foreign body sensation, and worsening eye pain, further intensifying the burden of migraines.

6.1.2. Visual Disturbances and Functional Vision Impairment: Migraine-related visual auras and transient vision loss can disrupt daily activities, especially tasks requiring prolonged visual focus such as reading, driving, or screen work. Repeated exposure to visual disturbances may lead to long-term visual fatigue, reduced contrast sensitivity, and difficulty maintaining focus. In some cases, patients with frequent migraine auras report persistent visual symptoms even between migraine episodes, a condition known as persistent visual aura without infarction.

6.2. Psychosocial and Quality of Life Implications

6.2.1. Emotional and Psychological Impact: Chronic migraines and associated eye pain have been linked to increased anxiety, depression, and emotional distress. The unpredictability of migraine attacks, combined with the disabling impact of photophobia and visual disturbances, can limit social interactions, workplace productivity, and daily functioning. Many migraine sufferers report avoidance behaviours, where they restrict social outings or certain activities due to

the fear of triggering an attack, leading to social isolation and decreased quality of life.

6.2.2. Occupational and Academic Challenges: Recurrent migraines with eye pain can interfere with work performance and academic productivity, particularly in professions requiring extensive screen time or detailed visual tasks. In students, frequent ocular migraines may impact reading efficiency, concentration, and exam performance, necessitating academic accommodations or modifications in study habits.

6.2.3. Sleep Disruptions: Many migraine sufferers experience poor sleep quality, often due to nocturnal headaches, sensitivity to light, or discomfort from dry eyes. Sleep disturbances, in turn, are recognized as a major trigger for migraine attacks, creating a vicious cycle that exacerbates both the frequency and intensity of migraines.

The impact of migraines extends beyond headache episodes, significantly affecting ocular health, emotional well-being, and daily functioning. Addressing both the physical symptoms (such as dry eye and visual fatigue) and the psychosocial burden (such as anxiety and workplace challenges) is essential for a comprehensive management approach. A combination of targeted migraine therapy, ocular surface care, lifestyle adjustments, and psychological support can help mitigate the long-term effects of migraine-related eye pain and enhance overall quality of life.

7. Future Directions and Research

Although significant strides have been made in understanding the complex relationship between migraines and eye pain, several gaps in knowledge remain. Future research should focus on refining pathophysiological insights, improving diagnostic accuracy, and developing more targeted treatment approaches for migraine-associated eye pain.

7.1. Understanding the Mechanisms of Ocular Pain in Migraines: While the trigeminal nerve is well recognized as a key player in migraine pathophysiology, its specific role in ocular pain remains an area of active research. Future studies utilizing functional neuroimaging (e.g., fMRI, PET scans) could help map real-time trigeminal activation during migraine episodes, providing deeper insight into how the trigeminal-autonomic reflex contributes to eye pain and associated ocular symptoms.

7.2. Neurogenic Inflammation and CGRP: The role of calcitonin gene-related peptide (CGRP) in migraine-associated eye pain warrants further investigation, particularly in identifying how CGRP inhibitors affect ocular symptoms in migraine.

Research on novel CGRP-blocking agents or combination therapies specifically designed for migraine-related eye pain could offer new therapeutic options.

7.3. Visual Cortex Hyperexcitability and Photophobia:

Studies have suggested that migraine sufferers experience hyperexcitability of the visual cortex, contributing to photophobia and visual disturbances. Advanced electrophysiological studies (e.g., visual evoked potentials) may help clarify how cortical excitability influences eye pain, potentially guiding the development of light-filtering technologies or neuromodulatory interventions to alleviate migraine-related photophobia.

7.4. Improving Diagnosis and Early Detection:

There is a growing need to identify objective biomarkers that can differentiate migraine-related ocular pain from other causes of eye discomfort, such as glaucoma, optic neuritis, or trigeminal neuralgia. Research into inflammatory markers (e.g., C-reactive protein, interleukins) and genetic predispositions could enhance diagnostic precision and facilitate personalized treatment strategies.

7.5. Artificial Intelligence (AI) and Digital Tools in Migraine Diagnosis:

AI-driven wearable technology or smartphone applications that track migraine triggers, ocular symptoms, and neurovascular changes could revolutionize migraine management. Machine learning algorithms analyzing patient-reported data may help in predicting onset patterns, optimizing preventive therapy, and individualizing treatment plans.

7.6. Advancements in Optical Coherence Tomography Angiography (OCTA):

Retinal blood flow changes have been observed during ocular migraines, and emerging OCTA imaging techniques may provide valuable insight into vasospasm-related ocular ischemia. Further research on OCTA as a diagnostic tool could help in detecting early retinal changes in migraine patients and assessing vascular health in chronic sufferers.

The future of migraine research lies in a multidisciplinary approach integrating neurology, ophthalmology, and advanced imaging techniques to enhance our understanding of migraine-associated eye pain. Expanding clinical trials and collaborative research efforts will be key to unlocking more effective, personalized treatments for individuals suffering from migraine-related ocular symptoms.

8. CONCLUSION

Eye pain is a common yet often underrecognized symptom in individuals with migraines. The complex interaction of vascular, neuronal, and sensory

pathways contributes to the development of ocular discomfort during migraine attacks. Understanding the pathophysiology of this symptom and distinguishing it from other potential causes of eye pain is crucial for appropriate management. Treatment strategies should focus on both acute relief and long-term prevention, with an individualized approach tailored to the patient's specific needs. Further research into the mechanisms and treatment of eye pain in migraines will improve outcomes for individuals affected by this debilitating symptom.

Understanding the relationship between migraines and eye pain is essential for clinicians and patients alike. Migraine-induced ocular pain can be debilitating, and its identification and management require a comprehensive approach. With appropriate treatment and lifestyle modifications, patients can experience significant relief from the ocular manifestations of migraines. Further research into the pathophysiology and management of migraine-related eye pain will be instrumental in developing more targeted therapies and improving the quality of life for those affected by this condition.

9. STRENGTHS AND LIMITATIONS

The review provides a well-rounded discussion on the link between migraines and eye pain, addressing pathophysiology, clinical features, differential diagnoses, and management strategies. This holistic approach enhances its value for both clinicians and researchers. By highlighting gaps in current knowledge and suggesting areas for future investigation, the article encourages further exploration of migraine-related eye pain, which could lead to improved diagnostic and therapeutic strategies.

While the review covers differential diagnoses and management, it may not sufficiently discuss emerging imaging techniques or biomarkers that could aid in distinguishing migraine-related eye pain from other ocular or neurological conditions. Expanding this aspect could strengthen the article's clinical relevance.

10. Data availability

The numerical data generated during this research is available with the authors.

11. Conflict of interest

All authors declare that there was no conflict of interest.

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13. Authors' contribution

All authors contributed to conception, design, writing and reviewing of the manuscript. All authors have approved the final version to be published.

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