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## **The Burden of Menstrual Migraine: Advances in diagnosis, treatment, and understanding of pathogenesis**

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## **Abstract**

Menstrual migraine is a debilitating neurological condition linked to hormonal fluctuations during the menstrual cycle. It disproportionately affects women of reproductive age, imposing significant personal and societal burdens. Characterized by intense, prolonged headaches often resistant to standard treatments, menstrual migraines are primarily triggered by estrogen withdrawal and further influenced by prostaglandins and neurotransmitter dysregulation. This review synthesizes current knowledge on the pathophysiology of menstrual migraine, emphasizing hormonal and genetic factors, and highlights diagnostic criteria distinguishing pure menstrual migraine from menstrually related migraine.

The review examines both acute and chronic treatment approaches. Pharmacological options such as triptans, NSAIDs, and the emerging use of CGRP inhibitors and lasmiditan show varying levels of efficacy, while hormonal therapies aim to stabilize estrogen fluctuations. Non-pharmacological strategies, including lifestyle modifications, cognitive-behavioral therapy, and acupuncture, offer complementary relief and improve quality of life. Despite advancements, significant challenges remain, including variability in treatment response and a lack of biomarkers for precise diagnosis and management.

Furthermore, this review highlights gaps in current research, such as the need to better understand hormonal sensitivity and long-term treatment safety. Future directions emphasize the development of personalized therapies, innovative diagnostic tools, and more inclusive studies addressing the socioeconomic burden of menstrual migraines. By bridging these gaps, the medical community can advance care for affected women, reducing disability and improving overall well-being.

Key words: menstrual migraine; acute treatment; prevention; triptans; CGRP antibodies; hormonal therapy; acupuncture

## **Introduction**

Migraine is one of the most common neurological disorders, affecting approximately 18% of women and 6% of men worldwide [1,2]. Among young women, it represents the leading cause of years lived with disability (YLD), significantly impacting their daily functioning, although it does not reduce life expectancy [3]. A typical migraine attack involves severe headache, heightened sensitivity to light and sound, as well as gastrointestinal symptoms such as nausea and vomiting [4]. These episodes are often accompanied by transient and reversible neurological disturbances [5].

The markedly higher prevalence of migraines in women points to a significant role of female sex hormones in the pathophysiology of the disease. Menstruation is one of the most commonly reported triggers of migraine attacks. In this context, two types of menstrual migraine are distinguished: pure menstrual migraine and menstrually related migraine—both of which can occur with or without aura [6]. The exact prevalence of these migraine subtypes remains unclear due to a limited number of population-based studies and variability in diagnostic criteria and research methodologies [7]. It is estimated, however, that menstrual migraine may affect between 18% and 25% of individuals suffering from migraines [8].

To standardize diagnosis, specific criteria for menstrual migraine have been developed and included in the third edition of the International Classification of Headache Disorders (ICHD-3) [9]. This classification identifies two subtypes: pure menstrual migraine and menstrually related migraine—each of which can present with or without aura [10].

The treatment of menstrual migraines tends to be more challenging than that of classic migraine forms, as the attacks are often longer and less responsive to conventional therapies [11]. Management strategies are divided into acute treatment during an attack and preventive

measures aimed at reducing the frequency of episodes. The most commonly used medications are triptans—selective 5-HT<sub>1B/1D</sub> receptor agonists that cause vasoconstriction and inhibit the release of neuropeptides [12,13]. In recent years, new and promising therapies have emerged, such as monoclonal antibodies targeting CGRP and lasmiditan—a 5-HT<sub>1F</sub> receptor agonist that acts without causing vasoconstriction [14,15]. Given the hormonal basis of these migraines, some therapeutic approaches include estrogen and progesterone supplementation. Additionally, non-pharmacological strategies, such as lifestyle modifications, acupuncture, and psychotherapy, are gaining increasing attention as supportive methods to enhance patients' overall well-being [16,17].

This review aims to provide a comprehensive overview of menstrual migraines—from their underlying mechanisms and diagnostic criteria to available therapeutic options. Particular emphasis will be placed on evaluating the effectiveness and limitations of both pharmacological and non-pharmacological treatments, with a specific focus on interventions used for acute episodes and short-term prevention.

## **Pathophysiology**

### **Pathogenesis of Menstrual Migraine: Main Hypotheses and Possible Mechanisms**

Currently, researchers propose two main hypotheses to explain the development of menstrual migraine. The first emphasizes the role of a sudden drop in estrogen levels, while the second focuses on increased prostaglandin production. There is also ongoing research into genetic factors that may predispose individuals to this condition.

#### **Hormonal Fluctuations – Estrogen and Progesterone**

In the days leading up to menstruation, women experience a significant decline in both estrogen and progesterone levels. This hormonal shift correlates with a higher incidence of headaches, suggesting that estrogen withdrawal may trigger menstrual migraines in susceptible individuals [18]. To test this theory, researchers conducted hormonal intervention studies. Administration of estradiol helped delay the estrogen drop and postponed migraine onset, whereas progesterone delayed menstruation but did not prevent headaches [19].

Interestingly, no consistent link was found between absolute estrogen levels and the exact timing of migraine onset [20].

Estrogen levels drop twice during the menstrual cycle – once after ovulation and again before menstruation. However, only the premenstrual decline has been clearly associated with migraine attacks [21]. The reasons behind this pattern are still not fully understood but may include prolonged estrogen exposure, progesterone's effects during the luteal phase, or increased prostaglandin levels [22].

Some studies suggest that progesterone might help alleviate headache intensity. During the mid-luteal phase – when progesterone peaks – women report the lowest severity of migraine symptoms [23]. Both estrogen and progesterone influence neurotransmitters involved in pain perception and migraine development. A drop in estrogen is linked to decreased serotonin levels, which may increase pain sensitivity [24]. Estrogen also modulates the  $\mu$ -opioid system, and its reduction may make individuals more vulnerable to pain around menstruation [25].

Moreover, progesterone and its metabolite allopregnanolone enhance GABAergic transmission, potentially providing pain relief [26]. Research has shown that allopregnanolone may reduce activity in the trigeminal nucleus caudalis by positively modulating GABA-A receptors [27]. In contrast, estrogen promotes glutamatergic activity and inhibits GABA signaling, which may heighten pain sensitivity [28]. Animal studies also suggest that estrogen stimulates the release of analgesic neuropeptides such as ghrelin, neuropeptide Y, and galanin [29].

### **The Role of CGRP in Migraine**

Calcitonin gene-related peptide (CGRP) plays a central role in migraine pathophysiology by contributing to pain signaling and vasodilation. As a result, CGRP has become a major focus of therapeutic strategies for migraine [30–32]. Higher CGRP levels have been observed in pregnant women and in those using hormonal contraceptives [33,34], while postmenopausal women typically show lower concentrations [35,36].

### **Prostaglandins and Migraine**

Although prostaglandins have not been extensively studied in the context of migraine, it is known that their secretion increases significantly during the early menstrual phase,

particularly from the endometrial lining [37]. Elevated prostaglandin levels are closely associated with menstrual pain [38], and women who suffer from dysmenorrhea are more likely to experience migraines [39]. Additionally, prostaglandin injections can trigger migraine-like headaches in individuals with a history of migraine, indicating a potential role in its pathogenesis [40].

### **Genetic Factors in Menstrual Migraine**

To date, no significant relationship has been found between menstrual migraine and polymorphisms in genes involved in estrogen metabolism (COMT, CYP1A1, CYP19A1) or the estrogen receptor ESR1 [41]. However, specific genetic variants in TNF $\alpha$  and SYNE1 (a gene located near ESR1) have been linked to menstrual migraine. TNF $\alpha$ , a pro-inflammatory cytokine, may mediate the interaction between sex hormones and inflammatory responses implicated in migraine [42]. SYNE1 is also associated with other estrogen-related processes. Furthermore, the neuropilin 1 gene (NRP1), which is involved in neurovascular mechanisms, has shown a significant association with menstrual migraine, suggesting its role in the disorder's pathophysiology [43].

### **Diagnostic criteria**

Table 1. Diagnostic criteria of menstrual migraine. International Classification of Headache Disorders, third edition [44].

- **Pure menstrual migraine with or without aura**

Migraine attacks during or occurring -2 and +3 days of menstruation, in at least 2 of 3 consecutive cycles, with no migraine attacks in other days of menstrual cycle.

- **Menstrually related migraine with or without aura**

Migraine attacks, which are similar to pure menstrual migraine but also occur on other days of the menstrual cycle.

## **Differential diagnosis**

It is essential to distinguish menstrual migraines from other headache disorders for effective treatment since many conditions exhibit similar symptoms. In contrast to tension-type headaches that feature mild to moderate, non-pulsating pain without nausea or photophobia and phonophobia, menstrual migraines are usually more severe, one-sided, and recurring, closely tracking the menstrual cycle [45,46]. Chronic migraines, while they may happen around the time of menstruation, vary in frequency, typically appearing on 15 or more days each month, necessitating a detailed headache diary to confirm the diagnosis [47].

Hormone-associated, non-migraine headaches serve as another differential, often absent the traditional migraine features of throbbing pain, nausea, and heightened sensory sensitivities. Likewise, secondary headaches resulting from underlying health problems, like sinus infections or cervical spine conditions, may resemble migraines but typically present additional unusual characteristics that necessitate further examination [48, 49].

Cluster headaches should also be considered; although they result in severe pain, their brief duration, regular occurrence in groups, and autonomic symptoms (like tearing and nasal congestion) distinguish them from menstrual migraines. This particular headache is mainly seen in men [50].

Finally, medication overuse headache (MOH) is a significant differential diagnosis for patients who often utilize headache medication, as it can increase headache frequency without adhering to a consistent menstrual pattern [51].

## **Impact of quality of life**

Menstrual migraines significantly affect both personal and societal aspects, frequently interrupting daily activities, work efficiency, and overall life quality. On an individual basis, the crippling symptoms can result in decreased productivity and absenteeism, affecting career advancement and financial security. Research indicates that migraines rank as the second primary cause of disability globally, with menstrual migraines playing a substantial role in this issue [52]. The unpredictability and intensity of symptoms can also lead to increased stress and anxiety, heightening the risk of mental health issues like depression and low self-

esteem as individuals struggle with the limitations imposed by recurrent pain. Socially, the condition can strain relationships, as those affected may feel isolated due to frequent missed family or social events, creating misunderstandings among peers [53]. At a societal level, the economic consequences of menstrual migraines encompass rising healthcare expenses for appointments, therapies, and possible hospital stays, alongside significant reductions in productivity; in the U.S. alone, migraines account for an estimated 13-17\$ billion every year in lost work productivity [54]. These effects highlight the necessity for greater awareness, supportive interventions, and more effective treatments to tackle the significant personal and societal impact of menstrual migraines.

### **Acute pharmacotherapy**

Acute pharmacological treatment for menstrual migraines involves medications aimed at relieving pain and reducing associated symptoms, with a focus on timely administration to maximize efficacy.

Nonsteroidal anti-inflammatory drugs (NSAIDs), like naproxen and ibuprofen, are frequently the initial treatment choice for menstrual migraines, especially when administered in advance. Naproxen alleviates pain and inflammation by blocking cyclooxygenase (COX) enzymes that are involved in the mechanisms of pain and inflammation. It addresses both migraine pain and related symptoms such as menstrual cramps. This combined effect can be beneficial for patients experiencing both migraine and menstrual pain. Therapy, specifically, has shown effectiveness in decreasing the occurrence and intensity of menstrual migraines [55,56].

Triptans, which are serotonin receptor agonists, are frequently very effective for menstrual migraines because of their targeted mechanism of action on migraine pathways, such as the constriction of dilated cranial blood vessels and the inhibition of neurogenic inflammation [57]. Frovatriptan and naratriptan are favored for menstrual migraines among triptans due to their extended half-lives, which provide prolonged relief and lower chance of recurrence [58]. Other triptans, including rizatriptan and sumatriptan, can also be used acutely, however, their shorter half-lives may necessitate redosing or the addition of other treatments to avert recurrence [59]. Meta-analyses indicate that sumatriptan 100 mg had the highest effectiveness

in 2-hour pain relief in migraineurs [60].

In some cases, when single drug treatment is not sufficient, a combination of pharmaceuticals may also be considered. A combination that works well is triptans together with NSAIDs. They are used to achieve additive effects, with the NSAID providing anti-inflammatory benefits and the triptan offering targeted migraine relief [61]. Moreover, antiemetics like metoclopramide or prochlorperazine can be used alongside to manage nausea and vomiting, which are frequent symptoms of menstrual migraines [62].

Lasmiditan is a new drug which is a selective 5-HT<sub>1F</sub> agonist that targets the 5-HT<sub>1F</sub> receptors in the brain, which play a role in regulating pain and migraine pathways while avoiding effects on blood vessels. For this reason, its use may be considered in case of patients with cardiovascular risk and hypertension [63].

Calcitonin gene-related peptide (CGRP) receptor antagonists are the latest discovery of acute treatment. It has been demonstrated that CGRP levels rise during migraine attacks, and CGRP antagonists, like ubrogepant and rimegepant, have been shown to alleviate migraine symptoms by inhibiting this pathway. Although research is still in progress, initial studies suggest that CGRP antagonists could provide an alternative acute treatment option for patients who are unable to tolerate or do not respond effectively to conventional medications [64, 65]. Moreover, monitoring for potential medication overuse is crucial, as regular use of acute treatments may cause rebound headaches or medication-overuse headaches. Patients suffering from frequent or particularly severe menstrual migraines may need to consider preventive approaches, such as hormonal treatments or continuous triptan regimens.

### **Prevention therapy**

The objective of preventive therapy for menstrual migraines is to minimize the frequency, intensity, and duration of migraine attacks by giving medications during the high-risk times of a woman's menstrual cycle or continuously, depending on the selected strategy and the patient's needs. Preventive measures can be very advantageous, especially for individuals who suffer from frequent or severe migraines.

Short-term preventive therapy (mini-prophylaxis) consists of giving medication during the days before menstruation and maintaining it throughout the high-risk timeframe. This method typically uses NSAIDs and triptans. For instance, naproxen is often advised to begin one to

two days prior to menstruation and to carry on for five to seven days, aiding in the alleviation of menstrual migraines by addressing inflammation. Frovatriptan has shown significant effectiveness in short-term prevention among triptans, owing to its prolonged half-life and lasting impact, which can reduce the frequency of migraine occurrences during menstruation. Research indicates that frovatriptan 2.5 mg, administered twice a day for 6 days during the perimenstrual phase, can decrease both the frequency and severity of menstrual migraines. Naratriptan 2.5 mg taken twice daily for 5 days during the perimenstrual phase and zolmitriptan 2.5 mg taken three times daily for 7 days are also effectively used for short-term prevention, although frovatriptan is frequently favored due to its longer duration of action [66, 67, 68].

Monoclonal antibodies targeting CGRP (calcitonin gene-related peptide) are a new choice for preventing menstrual migraines. Medications such as erenumab and galcanezumab focus on the CGRP pathway, which is crucial in the pathophysiology of migraines. Interest is increasing in their potential effectiveness for menstrual migraines as well, especially for patients who do not respond to or cannot tolerate alternative preventive treatments. While data specifically related to menstrual migraines are not wide, CGRP monoclonal antibodies show promise for individuals with a significant level of migraine-related disability [69,70,71].

Regular hormonal treatments can deliver preventive benefits by maintaining stable estrogen levels across the menstrual cycle, which helps decrease hormonal changes that lead to menstrual migraines.

For those patients who do not have contra-indications, combined hormonal contraceptives (CHCs) are usually prescribed to provide continuous or extended-cycle dosing, enabling patients to skip the hormone-free interval or to have a reduced number of menstrual cycles each year. This method aids in preventing the start of menstrual migraines by avoiding the decrease in estrogen levels that usually happens prior to menstruation [72]. CHCs, such as oral contraceptive pills, transdermal patches, and vaginal rings, integrate estrogen and progesterone to inhibit ovulation and regulate hormone levels during the menstrual cycle. By keeping estrogen levels stable, CHCs can lower the occurrence and intensity of menstrual migraines for numerous women. Extended-cycle regimens consist of using active pills for an extended time (e.g., 84 days) before a short hormone-free interval. Continuous-use regimens skip the placebo week entirely, leading to the absence of withdrawal bleeding, which may

decrease the chances of migraine onset [73]. While CHCs work well for many individuals, they are not appropriate for all patients, especially those who experience migraine with aura, as they raise the stroke risk in this group. Women who have cardiovascular risk factors (such as smoking, hypertension, or a history of thromboembolic events) are similarly advised not to use CHCs [74].

Progesterone-only hormonal therapy could be considered in patients who cannot use preparation containing estrogen. However the impact of progesterone-only methods on menstrual migraines is less consistent compared to CHCs. Certain patients find that their migraine frequency and severity improve, whereas others may not experience any meaningful changes [75].

Estradiol alone during the hormone-free period can aid in alleviating estrogen withdrawal. Low-dose estrogen supplementation can assist women who experience migraines during the hormone-free interval of CHC use or the luteal phase of their natural menstrual cycle by maintaining stable estrogen levels and decreasing the probability of migraines caused by estrogen withdrawal. Transdermal application of low-dose estrogen patches (e.g., 0.1 mg/day estradiol) or estrogen gels can be utilized during the final few days of the CHC cycle or the luteal phase. Certain patients begin estrogen supplementation a few days prior to the anticipated onset of menstruation and maintain it through the hormone-free interval, reducing the likelihood of menstrual migraines. The limitation of this therapy is people who have contraindications to the use of estrogens and experience migraines with aura [76,77].

Moreover, daily preventive treatments typically used for general migraine control, including beta-blockers (e.g., propranolol), antidepressants (e.g., amitriptyline), and antiepileptic medications (e.g., topiramate), may also be an option for women suffering from menstrual migraines, especially if migraines occur at times other than during the menstrual cycle. These drugs might assist in lowering the overall frequency of migraines and are advantageous for patients with mixed or chronic migraine patterns [78].

### **Alternative treatment**

Acupuncture, a technique from traditional Chinese medicine used for thousands of years, has shown encouraging outcomes in lowering the frequency of migraines and the intensity of pain during acute episodes. This method includes the placement of fine, sterile needles into designated areas of the body, referred to as acupoints, which are thought to activate the body's

natural energy circulation, or Qi [79]. Through focusing on these points, acupuncture seeks to re-establish balance within the body's systems, which may assist in controlling migraine symptoms. Acupuncture is believed to operate through various mechanisms specifically for menstrual migraines. Firstly, it can trigger the release of endorphins and other natural pain-relieving substances, aiding in the modulation of the pain response and diminishing the overall experience of pain [80,81]. Furthermore, acupuncture might affect the body's hormonal regulation systems, aiding in the reduction of the hormonal changes that commonly cause migraines during menstruation [82]. Studies, for example, have demonstrated that consistent acupuncture sessions can enhance the balance of estrogen and various reproductive hormones, potentially preventing or reducing the intensity of migraines associated with the menstrual cycle.

Several clinical trials and reviews have explored its role. A multicenter randomized controlled trial found that acupuncture could reduce the number of migraine days during the perimenstrual period compared to sham acupuncture and standard medication (e.g., naproxen). The effects appeared to be sustained over multiple cycles, indicating potential benefits for long-term management [83]. Studies indicate that acupuncture can serve as a preventive method for menstrual migraines, demonstrating decreases in migraine frequency, duration, and intensity with regular treatment over time. To achieve the best outcomes, professionals might suggest consistent weekly sessions, placing greater emphasis on treatments during the days prior to menstruation, when hormonal changes are most pronounced. These combined effects indicate that acupuncture may serve as a beneficial, non-drug alternative for individuals looking to manage menstrual migraines holistically [84]. However, acupuncture has demonstrated mixed efficacy in the management of menstrual migraines, with studies reporting variable results regarding its effectiveness as a preventive or acute treatment option. While acupuncture is considered a safe and non-invasive therapy, evidence regarding its ability to consistently reduce migraine frequency, severity, or duration remains inconclusive [85].

Cognitive-Behavioral Therapy (CBT) can serve as an effective resource for those experiencing menstrual migraines, as it instructs individuals on how to handle negative thoughts and stress reactions that may exacerbate migraine symptoms. With CBT, individuals acquire techniques to manage migraine pain, tackle mood issues (like anxiety or depression), and cultivate healthier responses to stress, which is a frequent trigger for migraines [86].

Biofeedback is a method that employs electronic monitoring to assist patients in gaining control over physiological functions, including muscle tension, heart rate, and skin temperature. Patients can learn to alleviate the physical tension and stress that frequently come with menstrual migraines by practicing relaxation techniques and noticing their body's reactions. Studies have indicated that biofeedback is especially beneficial in diminishing both the frequency and severity of migraines [87].

Changing the current lifestyle may also prove beneficial. Keeping a consistent sleep routine is vital, since changes in sleep patterns are recognized as migraine triggers. Women susceptible to menstrual migraines gain from maintaining regular bedtimes and wake-up times, since even slight variations can affect hormonal rhythms and heighten migraine risk [88]. Recognizing and minimizing dietary triggers like caffeine, alcohol, processed foods, and certain additives may help lower the frequency of migraines. Maintaining a food and migraine journal can be beneficial for pinpointing personal triggers. It is important to stay hydrated, as dehydration can worsen migraines [89]. Engaging in regular exercise, like moderate aerobic activities, has been linked to a decrease in migraine frequency. Engaging in exercise can aid in hormone regulation, boost mood, and improve sleep quality, collectively contributing to the prevention of migraines. Nevertheless, patients need to be cautious about overexerting themselves, since intense physical stress can occasionally provoke migraines [90].

Table 2. Summary of Treatment and Prevention Methods.

Category	Examples	Mechanism of Action	Efficacy
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<b>Acute Pharmacological Treatment</b>	<b>Triptans</b> (e.g., sumatriptan, frovatriptan)	5-HT <sub>1B/1D</sub> receptor agonists; promote vasoconstriction and inhibit pain signaling pathways.	High efficacy for rapid relief; sumatriptan had the highest effectiveness in 2-hour pain relief; frovatriptan preferred for long-lasting relief.
	<b>NSAIDs</b> (e.g., naproxen, ibuprofen)	Inhibit COX enzymes, reducing prostaglandin production and inflammation.	Effective for pain relief and reducing inflammation during attacks.
	<b>Lasmiditan</b>	5-HT <sub>1F</sub> receptor agonist; reduces pain transmission without causing vasoconstriction.	Effective for acute treatment, especially for patients with cardiovascular risks.
	<b>CGRP antagonists</b> (e.g., ubrogepant, rimegepant)	Block CGRP pathways	Promising results for acute relief in resistant migraines.

<b>Pharmacological Prevention</b>	<b>Triptans</b> (eg., frovotriptan, naratriptan)	Similar to acute triptans but used preemptively in the perimenstrual phase.	Reduces frequency and intensity of menstrual migraines when used prophylactically.
	<b>Hormonal Therapy</b> (e.g., estrogen patches)	Stabilizes hormonal fluctuations by supplementing estrogen.	Effective in reducing perimenstrual migraine onset.
	<b>Beta-blockers</b> (e.g., propranolol)	Inhibit adrenergic activity, stabilizing vascular tone and reducing migraine frequency.	Effective for general migraine prevention; less specific for menstrual migraines.
	<b>Antiepileptics</b> (e.g., topiramate)	Modulates neuronal excitability to prevent migraine triggers.	Effective in reducing migraine frequency; broader preventive option.

<b>Non-pharmacological Treatment</b>	<b>Lifestyle Changes</b> (e.g., sleep hygiene, exercise, stress reduction)	Improves resilience to hormonal and environmental triggers.	Beneficial as a supportive approach; results vary individually
	<b>Cognitive Behavioral Therapy (CBT)</b>	Addresses stress and maladaptive thought patterns to reduce migraine frequency.	Demonstrated efficacy for stress-related triggers.
	<b>Acupuncture</b>	Stimulates energy flow and modulates pain pathways.	Mixed evidence; some find significant relief with regular sessions.

### Unanswered questions

A major unresolved question is why certain women suffer from menstrual migraines while others do not, even with comparable hormonal changes. Research on personal sensitivity to hormonal fluctuations, especially changes in estrogen and progesterone levels, is still scarce. Comprehending these distinctions might result in more tailored treatment choices that cater to individual hormonal sensitivities.

Despite the widespread use of hormonal therapies (such as oral contraceptives and hormone replacement therapies), there is a lack of data regarding the long-term effects of these treatments specifically for managing menstrual migraines. Issues encompass possible cardiovascular dangers, stroke in individuals with migraine with aura, and the prolonged

effects on reproductive health and bone density. Research focused on these long-term risks and benefits is required to elucidate the safety profile of hormonal therapies.

At present, there are no trustworthy biomarkers for forecasting who will experience menstrual migraines or for evaluating migraine intensity based on hormonal levels. Detecting biomarkers (e.g., blood estrogen levels and inflammatory markers) could lead to early diagnosis, better insight into menstrual migraine patterns, and support the customization of treatment plans.

Another crucial gap relates to why various patients have differing responses to identical treatments, especially concerning non-hormonal and lifestyle interventions. Grasping the biological and lifestyle elements that affect treatment responses may enhance therapy results and minimize trial-and-error methods.

### **Perspectives for future research**

Creating more specific diagnostic criteria and tools to distinguish menstrual migraines from other types of migraines could enhance early detection and management. Tools may involve hormonal profiling or imaging methods to evaluate vascular alterations linked to migraines. It is essential to undertake long-term research that observes hormonal changes and migraine rates over time to uncover the mechanisms that contribute to menstrual migraines. These studies may elucidate the effects of hormonal treatments on the frequency and intensity of migraines, while also identifying trends or factors related to age that could predict the beginning or end of menstrual migraines. It is worth expanding knowledge about environmental and lifestyle factors, which can be easy and beneficial for patients to change (e.g., dietary, exercise, sleep routine). This type of research could deliver practical and easy-to-follow recommendations for patients wanting non-medication solutions. Future research on treatments such as CGRP inhibitors or other non-hormonal medications aimed at menstrual migraines could offer new, safer alternatives for patients who cannot tolerate hormonal therapies.

### **Conclusion**

Menstrual migraines represent a unique subtype of migraine conditions, where hormonal changes, especially estrogen withdrawal, play a main role in their initiation. Menstrual migraines have a greater effect on women's quality of life, resulting in considerable personal,

social, and economic challenges. Even with greater awareness and enhanced diagnostic standards, menstrual migraines continue to be difficult to treat, as there are few therapies specifically designed for this hormone-sensitive issue.

The existing therapeutic landscape features a range of pharmacological choices, including triptans, NSAIDs, CGRP monoclonal antibodies, and the new serotonin 5-HT<sub>1F</sub> receptor agonist, lasmiditan. These treatments have demonstrated effectiveness in acute management, although patient response and tolerability can differ significantly. Interventions based on hormones, such as estrogen supplementation, have provided extra alternatives; however, they come with complications arising from individual differences in hormonal sensitivity and possible side effects from prolonged use. In addition, non-pharmacological methods such as acupuncture, cognitive-behavioral therapy, and lifestyle changes are crucial for support, though additional research is needed to completely determine their effectiveness.

While improvements have occurred, considerable gaps are still present. A deeper understanding of hormonal sensitivity mechanisms, more effective long-term prevention strategies, and personalized treatment approaches that consider individual variations in migraine patterns and responses is necessary. Finding predictive biomarkers for menstrual migraines might optimize diagnosis and support individualized treatment strategies, decreasing the reliance on the trial-and-error approach used today. Longitudinal studies examining hormonal effects throughout various life stages may offer insights into the changing nature of menstrual migraines and guide age-specific treatments.

Future studies ought to keep investigating innovative therapies, encompassing new hormonal and non-hormonal agents, as well as the impact of lifestyle interventions. Broadening treatment choices and comprehension will facilitate more comprehensive, patient-focused care that enhances long-term results and quality of life for women impacted by menstrual migraines. These initiatives provide optimism for improved and sustainable management of this debilitating condition, giving affected women a way to regain control over their everyday lives.

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