

# Overcoming obstacles to effective treatment of patients with migraine

## (Statement of the expert group on optimizing treatment of patients with migraine)



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Despite the development of basic principles and a wide arsenal of therapeutic and preventive agents, the effective treatment of migraine patients in daily practice is associated with some well-identified obstacles. Among many obstacles to effective treatment, several key factors can be identified: low patients' awareness of the nature of the disease, its course and prognosis, methods of treatment and prevention, low rate of patients' referral for medical care and unsatisfactory level of diagnosis in clinical practice, inadequate training of physicians in the field of headache, nonoptimal use of symptom management and preventive treatment strategies. The article discusses the most common problems and strategies to optimize treatment of migraine patients.

**Keywords:** headache; migraine; relief of migraine attacks; preventive therapy of migraine.

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In 2015, all Member States of the United Nations adopted the Ensure Healthy Lives and Promote Well-Being for All at All Ages 2030 Agenda for Sustainable Development (ASD-2030), which lists measures that aim to reduce mortality and the burden of disease as one of the most important goals [1]. The prospect of achieving these goals in the area of headache management, as stated by the Expert Panel of Specialists [2], should focus on overcoming barriers to effective patient care. Headache is one of the most significant public health problems that must be adequately addressed at the global level [2]. According to the latest estimates by the Global Burden of Disease (GBD) study, there were 793.8 million cases of primary headache in 2019 alone, with a prevalence of 2.6 billion cases and a total of 46.6 million years lost due to disability (YLDs) [3]. In terms of YLDs, headache ranks 3rd in

the world, and in the 15–49 age group, it ranks 1st and accounts for 8% of total YLDs [3]. Migraine holds a leading position not only because of its high prevalence, but also because of its significant burden on patients and society as a whole. According to the GBD 2021 study, the global burden of migraine increased markedly between 1990 and 2021, with a 58.15% increase in prevalence, from 732.56 million to 1.16 billion cases, and a 42.06% increase in the incidence. The number of disability-adjusted life years (DALYs) also increased by 58.27% [3], with incidence and prevalence increasing four to five times faster in men, and adolescents (under 20 years of age) showing the fastest increase in prevalence and DALYs. Prognostic analysis suggests that the prevalence of migraine will continue to increase until 2050, especially among men and adolescents [4].

Effective management of patients with migraine remains a significant issue in clinical practice, as it is associated with a number of challenges that can be overcome with modern strategies of specialized care. This article discusses the most frequent and common issues in the practical management of patients with migraine and identifies ways to optimize care for these patients.

### **Barriers to the management of patients with migraine**

#### ***Prevalence and burden of migraine***

According to GBD 2019 data, migraine affects more than one billion people worldwide and its prevalence in the population is about 14% (18.9% in women and 8.9% in men) [5]. The global burden of migraine is determined by a combination of factors that lead to a reduced quality of life of patients, disruption in social, occupational, and daily functioning, as well as the financial costs associated with the disease [6, 7].

Although migraine has a generally favorable prognosis, it is characterized by a significant impact on the ability to work. On average, patients with episodic migraine (EM) lose about 2 weeks of work time per year, which corresponds to a loss of about 3.5 h per week; thus, migraine ranks first among all diseases in this respect [8]. Among working patients with migraine compared to those without migraine, there are higher rates of both absenteeism and days with decreased productivity («presenteeism») [8, 9].

#### ***Care seeking in patients with migraine and the level of its diagnosis in clinical practice***

Timely access to medical care is a prerequisite for effective patient functioning and maintaining quality of life. In this aspect, both adequate diagnosis of the disease and the use of optimal therapeutic approaches are important. The rate of initial presentation of patients with headache is consistently low in all populations. Overall, approximately 60–70% of people with migraine never seek medical attention [8]. It has been suggested that lack of awareness about headaches contributes to the low rate of consultation with a physician [10].

On the one hand, timely care seeking is necessary to exclude potentially dangerous causes and any form of secondary headache, and on the other hand, it is necessary to confirm the diagnosis of migraine, which will allow to develop individualized strategies for its treatment based on the possibility of applying the latest advances in the field of its effective treatment. The low level of individuals' awareness of the nature of their headache has been demonstrated in a number of dedicated studies. Thus, in a large population-based study in Italy, P. Brusa et al. [11] found that about 1/3 of all headache sufferers and 1/3 of migraine sufferers were unaware of their diagnosis and did not see a doctor. Similar data were obtained in a large Russian Internet study [12]. In the Russian population, 1490 out of 1598 respondents experienced headache and 937 participants reported migraine symptoms, but only 542 (58.4%) patients were diagnosed with migraine [12]. Among 405 patients with chronic headache, 37% of individuals met the criteria for migraine; however, only 40% of them were diagnosed with migraine, indicating a low rate of migraine diagnosis in the Russian population as well [12].

An important problem of suboptimal patient management is low quality of diagnosis, even when consulting special-

ists. In diagnosing the form of headache, 30% of physicians do not always use the criteria of the International Classification of Headache Disorders 3rd edition (ICHD-3), and 7% do not use them at all [13]. One significant barrier to seeking care for patients with even frequent migraine attacks may be a lack of trust in practicing physicians and overall dissatisfaction with medical care. Thus, a recent Wellcome Trust report on attitudes towards healthcare globally showed that in Europe, Australia, and New Zealand 65% of respondents trust doctors and nurses; in North America – 52%, and in Japan only 26% [14]. One of the most frequent reasons why patients with migraine avoid seeing a doctor is the long waiting time for an appointment, especially with a specialist/neurologist. Among young patients who are not sufficiently aware of their disease, doubts about the right specialist for consultation also play a role [15]. Another likely cause is stigmatization, a social problem of negative attitudes towards people suffering from various diseases [16]. Stigma is experienced by 31.7% of people with migraine [17].

#### ***Problems of effective pain management for migraine in clinical practice***

The strategy of migraine attack management implies the possibility of choosing a drug not only on the basis of its efficacy and safety, but also taking into account the individual characteristics and preferences of the patient. Drugs with proven efficacy for migraine include both over-the-counter and prescription medications and can be grouped into five commonly used drug classes: 5-HT<sub>1B-1D</sub> serotonin receptor agonists (i.e., triptans); nonsteroidal anti-inflammatory drugs (NSAIDs); opioids; barbiturate containing analgesics; and ergot alkaloids [18]. Antiemetics, myorelaxants, simple analgesics, analgesic combinations, neurostimulation techniques, and behavioral therapies may also be used as symptomatic treatment. Despite the wide choice of drugs, patient satisfaction with effective attack control remains low in real-world practice [19]. Analyzing the reasons for poor attack control and patient preferences is key to building an individualized approach to selecting the attack management strategy.

In general, studies of migraine symptom therapy patterns and effects have shown clear evidence of low patient satisfaction [20]. According to the American Migraine Prevalence and Prevention Study (AMPP), nearly 40% of patients are dissatisfied with current attack control [21]. Surveys of patients about their attitudes toward migraine control show that the most important characteristics in selecting a medication are rapid onset of pain relief, complete relief, few or no side effects (SEs), and no headache recurrences [22–24]. Patients most commonly report that pain relief takes too long or is intermittent, that pain often returns even after relief, or that medications cause adverse events (AEs) [23]. At the same time, it is well known that poor efficacy of attack management in patients with EM is associated with an increased risk of developing chronic migraine (CM) [25].

The MAST study (Migraine in America Symptoms and Treatment Study) analyzed unmet patient needs for symptomatic treatment among individuals using oral prescription migraine medications [19]. Of the 15,133 respondents, 26.0% reported current use of prescription drugs. Three areas of unmet need were identified: inadequate response to treatment (i.e., inadequate 2-h pain relief, relapse within 24 h of initial

relief), complex attack characteristics (rapid attack onset, sleep-related headache), and unique patient characteristics (excessive opioid or barbiturate use, cardiovascular comorbidities). The vast majority of participants (95.8%) had at least one area of unmet need. At the same time, problems related to the attacks themselves were reported by almost 90% of respondents, while unmet needs related to inadequate response to treatment were reported by  $\frac{3}{4}$  of them (74.1%) [19].

### ***Problems of preventive therapy for migraine in clinical practice***

The strategy of preventive (prophylactic) therapy for migraine is not only of great importance in terms of reducing the frequency and severity of headache attacks, improving the response to analgesics and reducing their use, reducing the need for medical care, but it also affects the course of migraine in general and improves the quality of life of patients. Currently, there is a trend towards an increasing use of preventive therapy for migraine, given the expanding arsenal of preventive drugs [26–28]. The expansion of preventive treatment options is associated with the emergence of new highly effective targeted drugs, in particular, monoclonal antibodies against calcitonin gene-related peptide (anti-CGRP mAbs), which best meet the needs of patients: they have good tolerability, rapid onset of effect, and high efficacy [15]. However, there are significant unmet needs for current migraine preventive treatment that limit its efficacy and accessibility [29].

*Inadequate coverage of those in need of preventive treatment and limited awareness of its benefits among patients with migraine* are significant barriers to effective care. The frequency of preventive treatment remains insufficient and ranges from 16% to 26% among patients with migraine requiring such treatment [30, 31]. The reasons are underestimation by patients and even physicians of the severity of the disease and the negative impact of migraine on daily life as well as lack of awareness of modern preventive treatment options. For example, according to the EPISCOPE study, even among patients with CM, 48% have never tried prophylactic treatment [15].

*The lack of efficacy and treatment dissatisfaction*, especially with regard to traditional oral drugs (beta-blockers, anti-convulsants, antidepressants, angiotensin II receptor antagonists, etc.) are well known. Up to 33% of patients are dissatisfied with the preventive therapy provided [15]. The reasons are insufficient efficacy, a large number of AEs and contraindications, and difficulty in selecting dosages [15]. Thus, the efficacy of preventive treatment with tablets does not exceed 45–50% on average [29], and it is not effective in 24% of patients [30].

*Resistance (refractoriness) to preventive therapy* is a complex and not fully solved problem in the management of patients with migraine [32]. These patients that account for 5% to 10% of the patient population with this disease suffer from debilitating headache for more than 8 days per month with no effect, intolerance or contraindications to three or more classes of preventive drugs (resistant migraine) or all classes of drugs (refractory migraine) [33].

*The limited understanding of predictors of efficacy* is related to the traditional use of «trial and error» approach in selection of

drugs for migraine prophylaxis: starting with the first-line drugs, and then, if necessary, using the second- and third-line drugs or a combination of drugs of different classes [34]. This is related to the lack of reliable biomarkers to predict the efficacy of therapy in a particular patient.

*AEs and low adherence to therapy* is a common problem in clinical practice. Conventional preventive treatment for migraine with oral drugs is often accompanied by AEs, including somnolence, body weight change, cognitive impairment, erectile dysfunction, hepato- and cardiotoxicity [35]. AEs undermine patient's trust in the physician, cause patients to refuse therapy or change the recommended treatment regimen, and as a consequence less than 30% of patients with migraine take their medications correctly [36], which increases the risk of painkiller abuse, migraine chronicity, and development of medication-overuse headache (MOH) [36]. Seventy-five percent of patients discontinue prophylactic treatment with oral drugs within six months, with the majority discontinuing within the first 2 months [37].

*The limited availability of modern therapies* is a significant barrier for a wide range of patients requiring preventive treatment. Modern highly effective preventive drugs, such as anti-CGRP mAbs, gepants, and botulinum toxin type A (BTA), are often unavailable. The main reasons for this are the high cost of drugs and/or lack of their approval in some countries [35]. For example, of the six targeted drugs affecting the CGRP pathway (four mAbs and two gepants) developed for the preventive treatment of migraine in adults, only two antibodies (fremanezumab and erenumab) and one gepant (atogepant) are approved in Russia [38]. On the other hand, some non-pharmacological methods remain insufficiently accessible [39, 40].

### **Ways to optimize care for patients with migraine**

#### ***General principles***

Strategies for optimal care of patients with migraine involve consideration of several important approaches, each of which requires evaluation in terms of feasibility in real-world clinical practice.

*Raising awareness of patients with migraine* is a prerequisite for its timely diagnosis, development of strategies for its self-management, increased adherence to therapy and, finally, adequate evaluation of the effectiveness of treatment in general. The main problem of low awareness of migraine and consequently low patient utilization of health care is related to the lack of information, services, and culture regarding migraine. Many patients do not have satisfactory knowledge of the disease, its course and prognosis, symptoms, and treatment options. Some studies demonstrate that among patients with migraine there is a clear discrepancy between the effort in finding an effective treatment strategy and the degree of satisfaction with its control in general [41].

*Training general practitioners, internists, and neurologists* using educational programs on headache is key to improving the quality of care for patients with migraine. The main challenges of effective management of patients with migraine are related to the lack of personal training of health professionals, especially at the primary care stage, as revealed by large studies in real clinical practice [42]. The need for increased education regarding migraine is primarily determined by the low level of

its diagnosis, as adequate diagnosis is achieved in no more than 40% of cases. In addition, a significant contribution is made by the factor of late diagnosis even with repeated referrals of patients with headaches to various specialists. A migraine patient receives a correct diagnosis about 10 years after the disease onset and visits at least four medical centers before an optimal therapy strategy is found [43]. The organization of specialized care and specialized headache centers can ensure effective management of the most diagnostically and therapeutically challenging patients.

*Building an effective dialog* with the patient is a key strategy to ensure a partnership and trusting relationship, which will build the patient's understanding of the disease and self-management strategies as well as provide opportunities for long-term follow-up and increased adherence to pharmacologic and non-pharmacologic treatments. The most important step is to communicate the diagnosis of migraine using four principles: clarity of the presentation (in language understandable to the patient), relevance (taking into account the patient's characteristics), a positive attitude (communicating in terms that do not evoke negative emotions), and reinforcement (repeating the most important aspects with changes in wording) [44]. An integral aspect of communication should be discussing with the patient all available treatment options and their suitability in the individual case. It is also necessary to inform the patient about the importance of developing adequate behavioral strategies, compliance with all recommendations, the regimen, and duration of therapy, the principles of attack control, and monitoring the course of the disease against the background of treatment.

*Patient-centered approach* is the basic prerequisite for successful migraine therapy. Explaining the nature of the disease, its favorable prognosis in general, support, and discussing realistic treatment options and expectations are key to effective patient management. Given the considerable interindividual variability in migraine manifestations, strategies for selecting therapy may vary. Consideration of such important factors as sex, age, lifestyle, personality traits, presence of comorbidities, concomitant therapy, previous migraine treatment experience, known triggers and form of migraine, as well as excessive consumption of analgesics and other drugs may serve as additional factors that predetermine priorities in choosing a treatment strategy.

*The patient's adherence* to pharmacological and non-pharmacological treatment recommendations, on the one hand, provides conditions for effective treatment and, on the other hand, indicates motivation to achieve effective disease control. The implementation of the above-mentioned general principles of migraine management, as well as the provision of feedback with the possibility of continuous patient follow-up, contribute to increased adherence.

*Trigger control* is an important part of non-pharmacologic preventive treatment of migraine [45]. It is known that some migraine attacks can be provoked by various factors (sleep disorders, hunger, menstrual cycle, stress, excessive caffeine intake, etc.). Identification and elimination of these factors in a number of patients may provide a preventive effect and result in some reduction in attack frequency.

*Assessment of therapy efficacy and monitoring the patient* are key to effective therapy. Response to migraine preventive therapy should be properly evaluated after 2P3 months from the start or

change of the treatment; if therapy is effective, follow-up should be performed at intervals of 3P6 months [46]. It is important to use a headache diary for convenience and objective evaluation of treatment results. Evaluation of the therapy results should be done by carefully analyzing the data from the patient interview and headache diary. The efficacy of preventive treatment can build up gradually, quite slowly, 2P3 months after the treatment initiation.

*Confirmation and treatment of comorbidities and MOH* is one of the most important factors predetermining the effectiveness of patient management, and at the same time a condition for determining the priority treatment strategy for the category of patients with the most severe headaches, including those with resistant forms of the disease. In order to improve treatment efficacy and adherence to therapy, an important step is the active identification and correct treatment of comorbidities, as well as identification of overuse of analgesics.

### *Optimizing the diagnosis of migraine*

Diagnosis of migraine is based on a clinical interview with collection of complaints, history, and assessment of specific clinical manifestations of migraine according to ICHD-3 [34, 47]. Neuroimaging is not indicated for patients with recurrent headaches and with typical signs of migraine, normal neurological examination findings, and no «red flags» [34, 47]. In addition to neuroimaging, routine tests such as electroencephalography, magnetic resonance and/or CT scan of the cervical spine, ultrasonography of the brachiocephalic arteries, and examination of the nasal sinuses are also unnecessary [34].

A prerequisite for correct diagnosis of migraine is the use of the ICHD-3 diagnostic criteria [34, 47]. Migraine is classified into several forms: without aura and with aura (develops in  $\frac{1}{3}$  of patients), by frequency of attacks C into EM (<15 days per month) and CM ( $\geq 15$  days per month) [47]. In addition, frequent EM (10–14 days per month) is distinguished, because migraine at this frequency has a high potential for chronicity and is closer to the chronic form than to the episodic form in terms of clinical manifestations. The use of the ID Migraine test [48] is recommended for screening diagnosis in the setting of limited admission time.

Meanwhile, making a diagnosis requires taking into account many features of migraine manifestations. First of all, it is known that the unilateral character of pain is not a mandatory criterion for the diagnosis of «migraine». Because the interpretation of pain intensity is subjective and varies from patient to patient, the most valid question for determining pain severity is the degree of maladaptation during an attack. When clarifying the relationship between the physical activity and the headache aggravation, it is necessary to find out whether the headache does not increase when bending over, climbing stairs, whether there is a feeling of need to avoid head movements. A common symptom of an attack is neck pain in combination with other migraine manifestations. As for the manifestations of photo- and phonophobia, it is not always a matter of severe intolerance of external stimuli, and it is necessary to ask the patient clarifying questions: whether there is a need to stay in a dark, quiet room, avoiding social contacts, during an attack, and whether there is increased sensitivity to normal light and sounds. Diagnosing migraine



with aura also has specific features. It should be differentiated with prodromal symptoms of migraine such as light or sound hypersensitivity, thirst, neck pain, fatigue, emotional agitation, thought disturbances, dizziness, yawning, or flashes in the eyes [34, 49, 50].

In addition to determining whether the diagnostic criteria are met, additional history information such as experience with triptans for the management of headache attacks, family history, association with the menstrual cycle in women, and the presence of specific pain triggers can be evaluated. The most relevant triggers are: emotional stress, hormonal changes in women, skipping meals, weather changes, sleep disturbances, odors, alcohol, heat, exercise, and sexual activity [51].

Thus, the diagnosis of migraine is complex and includes both the correct construction of a clinical interview to assess whether the headache meets the diagnostic criteria of the ICHD-3, as well as the evaluation of associated symptoms and the exclusion of secondary causes of headache.

### ***Optimization of symptomatic therapy for migraine attacks***

The goals of migraine attack treatment were defined in the American Headache Society (AHS) 2019 Consensus Position Statement [52]: 1) rapid and permanent relief from pain and related symptoms without relapse; 2) restoration of ability to function; 3) minimal need for repeat medication or additional pain relief; 4) optimal self-care and reduced subsequent resource utilization (emergency department visits, diagnostic imaging, physician and outpatient infusion center visits, etc.); and 5) no or minor SEs.

Unfortunately, these goals are not always achieved due to the ineffectiveness of drugs or the presence of SEs [35]. For example, NSAIDs have many SEs (nephrotoxicity, bleeding tendency, gastrointestinal disorders), triptans are effective in 18–50% of patients but should be prescribed with caution in patients with cardiovascular risk factors and are not recommended for patients with a history of cerebrovascular disease and established cardiovascular disease due to vasoconstriction as the basis of their pharmacologic action [35]. Among EM patients, 19.1% of men and 18.6% of women have three or more cardiovascular risk factors (hypertension, smoking, diabetes mellitus, obesity, dyslipidemia), 73.4% and 69.5%, respectively, have at least one of them [21]. Thus, a significant proportion of patients with migraine have difficulty managing their attacks and tend to abuse other categories of medications that are not safe or may not be effective.

Some hope lies in the use of new drugs that could overcome these limitations. CGRP receptor antagonists (gepants) and 5-HT<sub>1F</sub> receptor agonists (ditans) are thought to have at least comparable efficacy, with no reported risks of abuse and apparently no cardiovascular contraindications [53, 54]. As these new drugs have been recently approved and are not yet widely used, longer clinical experience is needed to accurately establish AEs, mainly in people with cardiovascular diseases and during pregnancy.

For more than 30 years, the traditional treatments for migraine attacks in clinical practice have been NSAIDs, triptans, and ergotamine preparations [55]. Based on specific clinical studies, three main approaches to the selection of symptomatic drugs depending on the severity of migraine attacks have been identified: the stratified, the step-care-

across-attacks, and the step-care-within-attacks [56]. Stratified drug selection is based on the severity of attacks and is considered the most effective approach. The severity of a headache attack in patients with migraine is assessed cumulatively based on its intensity and impaired functional activity. If the attacks are mild to moderate in severity, one can start with acetaminophen or NSAIDs. If this proves unsuccessful, one can try using specific drugs. However, for patients with severe disabling attacks, their use is preferred if there are no contraindications [34]. Even when stratification of migraine attacks is used, their effective control is not always achieved and additional strategies to optimize headache management may be required.

### ***Optimization of migraine preventive therapy***

The goals of migraine preventive treatment are to reduce the frequency, severity, duration of attacks and restore the patient's functioning, as well as to improve the response to attack control and minimize the use of symptomatic drugs [57]. Preventive treatment is recommended for patients who have three or more severe disabling headache attacks per month with adequate relief or 18 days with headache per month, as well as for patients with prolonged aura, even with a low frequency of attacks [34]. It should also be considered when drugs for attack control are ineffective or poorly tolerated, in cases of CM or MOH, in patients with migraine subtypes that pose a risk of stroke (the history of migraine infarction or migraine status, migraine with trunk aura, hemiplegic migraine), and in the presence of severe comorbidities (depression, anxiety, phobias, dyssomnia), and taking into account patient's preference [34].

A holistic approach to migraine therapy involves consideration of lifestyle modification and the use of non-pharmacologic methods [39, 57]. Many patients can obtain marked relief of the course of the disease with lifestyle modifications, including sleep hygiene, exercise and diet, keeping a headache diary, and utilizing stress management techniques. Many modalities of non-pharmacological methods have also been found to be effective in migraine prevention and are recommended for use. These include cognitive behavioral therapy, biofeedback, and relaxation training [39].

When choosing pharmacologic preventive treatment, drugs with a high level of efficacy should be considered first [57]. However, the choice of treatment is influenced by comorbidities, individual patient preferences, adverse effects, and availability of drugs [52].

According to the Russian national clinical guidelines for the diagnosis and treatment of migraine [34], first-line drugs include beta-adrenoblockers (metoprolol and propranolol), antiepileptic drugs (topiramate), BTA-hemagglutinin complex (only for the treatment of CM), and anti-CGRP mAbs (fremanezumab and erenumab). Second-line drugs include beta-adrenoblockers (atenolol), anticonvulsants (valproic acid), antidepressants (amitriptyline and venlafaxine), and angiotensin II receptor antagonists (candesartan) [34]. If monotherapy is not successful, simultaneous use of drugs of different classes (combination or polytherapy) may be useful, which allows affecting complex and diverse pathophysiologic mechanisms of migraine [58].

New methods (BTA, anti-CGRP mAbs, low molecular weight CGRP receptor antagonists C gepants) have expanded

the possibilities of preventive therapy and have shown higher response rates (by 50, 75 and even 100% compared to placebo), as well as good tolerability [59–61]. The combination of novel methods targeting the CGRP pathway is one of the most promising current strategies in achieving high and sustained efficacy of preventive migraine treatment [62, 63]. However, the high cost of combinations of drugs targeting the CGRP pathway, such as BTA, anti-CGRP mAbs, and gepants, prevents the widespread use of this approach in real-world clinical practice.

The effectiveness of preventive treatment varies considerably depending on individual patient characteristics such as genetic features, clinical and demographic characteristics, comorbidities, and lifestyle. This makes it difficult to choose the best treatment for each patient. Therefore, personalized preventive therapy remains a key unmet need in the treatment of migraine.

Genetic factors can determine not only predisposition to migraine, but also the features of clinical manifestations of the disease, association with comorbidities and personality traits, sensitivity or resistance to treatment and development of MOH [64]. Genetic characteristics also predetermine the pharmacokinetics and pharmacodynamics of a therapeutic agent in a particular patient, which affects the success of treatment [65].

Clinical and demographic factors such as sex, age, form of migraine, comorbidities, personality traits, trigger factors, and lifestyle largely determine differences in the efficacy of preventive therapy. Migraine is more common in women, and hormonal changes (e.g., related to the menstrual cycle) alter the response to treatment [66]. For example, severe menstrual-associated migraine attacks are not prevented well with traditional prevention options, requiring the use of special therapeutic strategies: «short-term» prevention or the use of hormone therapy.

Comorbidities may alter pain perception and contribute to migraine chronicity [67], and comorbid psychiatric disorders (anxiety disorders, stress-related depressive disorders, and somatoform disorders) as well as personality accentuations (anxious/hypochondriacal, hysteroid types) may worsen the course of migraine, increase the risk of painkiller abuse and the risk of developing MOH [68]. CM is associated with persistent central sensitization, which may reduce the efficacy of most conventional preventive therapies and requires long-term (at least 12 months) treatment with drugs with proven efficacy in this form of migraine (BTA, anti-CGRP mAbs, topiramate) [34].

Traditional preventive drugs such as beta-blockers, antidepressants, and antihistamines cause various AEs that may lead to problems with treatment adherence: in daily practice, only 10% of migraine patients adhere to preventive therapy [69]. This often leads to overuse of analgesics, polypragmasia, which can result in disease chronification and resistance to therapy [30]. Treatment with anti-CGRP mAbs and BTA may be the optimal approach in these cases, which is well tolerated and patients rarely refuse treatment [15]. For example, 94% of migraine patients have long-term adherence to anti-CGRP mAbs therapy [70].

The treatment of patients with migraine that is resistant to conventional therapy is particularly challenging [71]. According to experts, distinguishing refractory migraine is

important in terms of better understanding the nature of the disease, developing new treatments, creating patient-centered approaches to therapy, and indications for the use of polypharmacotherapy and invasive neurostimulation techniques [33, 72].

In general, regardless of the prevention strategy chosen, preventive treatment should be initiated early in the course of the disease to preclude decreased quality of life and reduce the burden of migraine.

## Conclusion

Migraine is a common yet severe disease with a long, chronic course that involves significant maladaptation.

Despite the development of fundamental principles and a wide arsenal of therapeutic and preventive options, the problem of effective care for these patients is due to a number of obstacles that can be overcome with modern disease management strategies. Large-scale clinical and epidemiologic studies demonstrated that among the many barriers to effective care for patients with migraine, several key aspects can be identified:

1. Low awareness of patients about the nature of the disease, its course and prognosis, methods of treatment and prevention.
2. Low level of patients seeking medical care and low level of its diagnosis in clinical practice.
3. Inadequate training of physicians in the area of headache management.
4. Non-optimal use of symptomatic treatment strategies for migraine attacks.
5. Insufficient or non-optimal preventive measures.

Analysis of these problems of practical management of patients with migraine helps identify potential solutions. Educational efforts to improve patient awareness and educational programs for physicians, as well as the organization of specialized care at different levels, fully contribute to the optimization of patient care. Diagnosis of migraine is available at the level of clinical examination, based on a detailed analysis of the patient's complaints and history, and in most cases does not require additional examination of the patient. Optimization of diagnosis should follow the path of complex analysis of clinical data, the use of formal diagnostic criteria, but with mandatory analysis of the nature of the course of the disease, heredity, triggers, identification of factors that aggravate the course of the disease and affect the efficacy of symptomatic and preventive treatment.

Clinical polymorphism of migraine, i.e. different forms and types of its course requires the development of personalized strategies, in which patients with CM, MOH, comorbidities, as well as patients with therapeutically resistant forms should be considered separately. Some measures to optimize symptomatic therapy are proposed, considering the patient profile, personal characteristics and comorbidities. The concept of «preventive treatment» should imply a comprehensive use of available strategies, including lifestyle modification, non-pharmacological approaches, and the development of personalized prevention programs. The arsenal of these possibilities has significantly expanded in recent years due to the introduction of new targeted drugs into clinical practice. Facilitating access to modern therapies can significantly improve overall disease outcomes.

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