

Migraine management in adolescents: treatment requires a multimodal approach

Licia Grazzi,¹ Paul B. Rizzoli,² Danilo Antonio Montisano,¹ Alberto Raggi³

¹Headache Center, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; ²John Graham Headache Center, Brigham & Women's Faulkner Hospital, Harvard Medical School, Boston, MA, USA; ³Neurology, Public Health and Disability Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

ABSTRACT

Background: Migraine is associated with a reduced quality of life, even in young patients. Despite this, there is no convincing evidence supporting the efficacy of pharmacological treatments for children and adolescents. New anti-calcitonin gene-related peptide (CGRP) medications, life-changing for many adult patients, are not yet available for pediatric use. There is a growing hypothesis that effective management of migraine during adolescence may reduce the risk of developing chronic migraine in adulthood.

Methods: Over the past two decades, increasing evidence has highlighted the benefits of non-pharmacological treatments, especially those within the "third wave" of behavioral approaches, such as mindfulness-based protocols and Acceptance and Commitment Therapy (ACT). A therapeutic strategy based solely on pharmacological treatment is likely to be ineffective. Instead, a multimodal approach that integrates various elements, such as behavioral ones, education on health habits, nutraceuticals, and medical prophylaxis when needed, is recommended.

Results: Based on our findings, the use of mindfulness-based internet protocols in young migraine patients showed promising results, with a significant decrease in headache frequency both in the short term and up to one year.

Conclusions: A treatment approach based solely on pharmacological therapies is likely to be ineffective in pediatric migraine. Instead, a multimodal strategy, integrating behavioral and educational components along with pharmacological support when needed, appears more effective. Such programs may help modify the disease course, enhance the efficacy of medications, and promote a broader culture of care centered on brain health.

Key words: migraine, adolescents, cognitive behavioral therapy, mindfulness.

Introduction

A recent meta-analysis showed that 11% (95% CI: 9-14) of children and adolescents aged 8-18 suffer from migraine, 8% have migraine without aura, and 3% have migraine with aura. (1) The impact is also significant in terms of associated years lived with disability (YLDs), accounting for approximately 5.2% of all-cause YLDs among individuals aged 5-14, and 8.9% among those aged 15-19, highlighting its current and future public health relevance. (2) Besides known and common symptoms – head pain, nausea, vomiting, and photo-phonophobia – migraine exhibits a heterogeneous presentation, varying in headache frequency, presence of aura, response to acute and preventive treatments, and comorbidities. Such variability likely reflects a heterogeneous genetic and molecular basis, and a biopsychosocial perspective is needed to address migraine at all ages. (3)

Pediatric migraine significantly impacts patients and their families, particularly affecting quality of life, school performance, and social interactions. This impact is especially pronounced when school absences are frequent, leading to loss of workdays for parents. (4) It is particularly relevant in high-frequency migraine forms, such as high-frequency episodic and chronic migraine, which strongly impact sleep, daily functioning, and school activities, as well as increase anxiety and depression. (5-7)

Here, we aim to discuss the issue of treatment for this specific group of patients, with particular focus on the possibility that early intervention during this age could help reduce

the risk of developing chronic migraine and medication over-use headache (MOH) in adulthood.

Efficacy of migraine pharmacological prophylaxis in adolescents

When migraine episodes in adults occur weekly or more frequently and are disabling, pharmacologic prevention is usually recommended. However, in young patients, this approach remains debated, as there is limited convincing evidence of the effectiveness of pharmacological treatments in adolescents. The significance and impact of the placebo effect were highlighted in a network meta-analysis. (8) These authors reported that, in young populations, pharmacologic prophylaxis for migraine was generally no more effective than placebo (except for the short-term use of propranolol and topiramate). They concluded that, due to safety and acceptability concerns, non-pharmacological targets should be prioritized and further explored. (8) The lack of superiority in a trial might be attributable either to the inefficacy of the compound tested or to a genuine placebo effect. It is important to note that placebo-related improvements can result from several factors, including regression to the mean, unidentified parallel treatments, and spontaneous improvement. Additionally, the timing of follow-up assessments, such as periods coinciding with holidays, may influence observed outcomes. (9)

The pharmacological prophylaxis for migraine is at a piv-

otal point. For many years, we relied on repurposed medications, such as antidepressants or anti-epileptics, but now new targeted agents that inhibit the calcitonin gene-related peptide (CGRP) pathway are transforming patient outcomes. These agents have demonstrated high efficacy and safety in numerous randomized controlled trials (RCTs) and real-life studies. While these compounds may also be safe and effective for younger patients, more time is needed before they become routinely available for pediatric use. In the meantime, a biopsychosocial and family-centered approach is, in our view, among the most effective strategies to enhance clinical care for youth with headache disorders for the reasons outlined below.

A biopsychosocial view of migraine treatment: non-pharmacological treatments

Migraine is a condition in which biological, social, and psychological aspects are intimately interconnected. (10) Non-pharmacological approaches, and particularly behavioral interventions, have shown a 34-78% reduction in headache frequency from baseline, (9) often with a synergistic effect when combined with pharmacological treatments. For instance, the combination of amitriptyline and cognitive behavioral therapy led to greater reductions in headache days and migraine-related disability compared to amitriptyline combined with patient education. (11)

Evidence from available studies on non-pharmacological treatments not only supports improvements in primary clinical outcomes (headache frequency) but also indicates benefits in disability, quality of life, depression, and anxiety. This information should facilitate the implementation of comprehensive, multimodal therapeutic programs that incorporate these approaches, which are particularly helpful in managing pain and decreasing the reliance on symptomatic medications in young patients. (9) In particular, mindfulness has gained popularity over the past 20 years as a technique for treating different pain conditions, including migraine. Its core feature involves developing patients' ability to intentionally focus on the present moment, employing techniques such as breathing exercises, guided imagery, and other practices aimed at relaxing the body and mind. (12-14) To the best of our knowledge, only two RCTs have been published so far, but they were conducted in adult populations. (12,15)

The two RCT studies conducted on adults included patients with episodic migraine and patients with chronic migraine and medication overuse. (14,15) Both studies employed a mindfulness based on the Mindfulness-Based Stress Reduction program; in particular, in one study, (15) the program was modified and a shorter version was used: six weekly sessions with two final booster sessions.

The other study (14) reported that education and mindfulness-based stress reduction therapy produced a similar reduction in headache frequency, with mindfulness showing a superior improvement in disability and quality of life confirmed at one-year follow-up. The larger RCT (15) showed that adding mindfulness to standard treatment was associated with superior improvements in headache frequency, quality of life, disability, headache impact, loss of productive time, medication intake, and overall disease-related costs. The improvement was also associated with increased connectivity in the salience network and in cingulate cortical thickness, which are thought to enhance body awareness of painful sensations and the cognitive processing of nociception. (16)

Moreover, another investigation (17) conducted on ado-

lescents suffering from chronic migraine and high-frequency migraine without aura reported a significant reduction at one-year follow-up in terms of a decrease in migraine days per month. The mindfulness program consisted of 8 weekly sessions, each lasting 75 minutes. This pilot study involved a small group of young patients and incorporated some skills derived from Acceptance and Commitment Therapy (ACT). Adherence to the program was high, with patients regularly participating in and practicing at home through short home exercises. Although neuroimaging findings are more extensively characterized in adults, recent evidence suggests that mindfulness practice can influence activity within specific brain networks involved in pain perception in young patients as well. (18)

There is no one-size-fits-all approach to migraine management. (3) Patients live in different contexts and engage in different activities, and their lifestyle habits are not always optimal for controlling migraine. Therefore, a multimodal approach that includes tailored patient education is essential to address lifestyle factors that might interfere with migraine management. This is particularly important in pediatric populations, given the limited efficacy of pharmacological prophylaxis. Key targets include diet habits and sleep hygiene, with specific attention to electronic device use close to bedtime. (19)

In recent years, the "third wave" of cognitive behavioral approaches, including mindfulness-based approaches and ACT, (20) has been applied to young patients suffering from various kinds of pain and headache, with some initial evidence indicating clinical benefits. (21) At our center, we developed a protocol for mindfulness-based treatment that incorporates different skills from ACT, consisting of six weekly sessions and a final booster session, to be delivered in small groups of 5-6 patients. As mentioned, our pilot study showed a significant reduction in headache frequency (from an average of 21.3 to 9.6 days per month) that was observed at six months and maintained at 12 months. Additionally, improvements were seen in medication use, disability, symptoms of anxiety and depression, and pain catastrophizing. (17)

Recent literature confirms that mindfulness practice can modulate cerebral patterns involved in pain perception, (18) and recent findings suggest that changes in brain connectivity in young patients may reflect increased flexibility in transition between mental states. This flexibility could help explain the well-established link between higher mindfulness and lower anxiety. (17,18) Unfortunately, this area of research is in its early stages, with evidence limited to a few pilot studies. Currently, studies on behavioral approaches for young headache sufferers treated have some limitations: aside from the large sample size of one study (11) on CBT in chronic migraine, most clinical experiences involved small patient cohorts (17) or have short follow-up durations. These factors reduce the robustness of the clinical findings. Consequently, larger studies with longer follow-up periods and, if possible, the use of biomarkers to validate clinical outcomes are needed to strengthen the evidence base.

Managing different forms of migraine in young patients will continue to pose challenges in clinical practice. It is essential for neurologists involved in this field to be aware that behavioral strategies exist and they can be valuable in helping patients manage pain while minimizing acute medication use, especially during the early stages of their clinical course. Patients should be encouraged to adopt lifestyle measures that can effectively reduce the frequency of migraine attacks. The clinical management of this population should therefore include education and support.

Recommendations such as maintaining good sleep hygiene, following a balanced diet, and engaging in regular physical activity are significant and should be integrated into a comprehensive therapeutic strategy. Additionally, establishing strong collaborations among headache centers and developing programs that deliver behavioral interventions remotely are crucial. Such approaches can facilitate greater patient participation, making these interventions more accessible and effective.

Finally, for young patients, the possibility of using innovative medications such as anti-CGRP drugs, currently under clinical investigation, should be considered in the near future. Preliminary data suggest that these agents may be promising in terms of efficacy and safety during the most critical phases of the disease. At the same time, traditional medications can still be considered in certain cases and may be particularly helpful to enhance the effectiveness of symptomatic treatments. (22,23)

Conclusions

The management of migraine in adolescents is inherently challenging, and, in our view, there is no single optimal approach. A multimodal strategy is, therefore, the most appropriate. Relying exclusively on a pharmacological treatment is likely to be ineffective: pharmacotherapy should be primarily reserved for acute attacks, while preventive medications should be considered as a second-line or in specifically selected cases. Conversely, education on lifestyle issues is fundamental and should focus on dietary habits, such as consuming adequate meals, particularly breakfast, and maintaining proper hydration. Additionally, it should emphasize sleep hygiene, including maintaining a regular sleep schedule and avoiding smartphone and tablet use before bedtime. Addressing risk factors such as smoking, alcohol consumption, and physical inactivity is also crucial. Education should focus on the proper use of medications, restricting them to severe headache episodes and possible MOH.

Clearly, a collaborative effort involving clinicians, patients, and caregivers is essential, as addressing lifestyle factors requires a comprehensive, family-centered approach. Establishing such multimodal programs can empower patients' outcomes and improve their pain-coping strategies and resilience, potentially altering the course of the disease and fostering the culture of brain health. This issue is of urgent importance, as today's adolescents are the adults of tomorrow.

References

1. Onofri A, Pensato U, Rosignoli C, Wells-Gatnik W, Stanyer E, Ornello R, et al. Primary headache epidemiology in children and adolescents: a systematic review and meta-analysis. *J Headache Pain* 2023;24:8.
2. Steiner TJ, Husøy A, Stovner LJ. GBD2021: headache disorders and global lost health - a focus on children, and a view forward. *J Headache Pain* 2024;25:91.
3. Raggi A, Leonardi M, Arruda M, Caponnetto V, Castaldo M, Coppola G, et al. Hallmarks of primary headache: part 1 - migraine. *J Headache Pain* 2024;25:189.
4. Canfora M, Pallotto IK, Davis JK, Farley S, Khayata MJ, Hornik CP, et al. More Than a Headache: Lived Experience of Migraine in Youth. *Pediatr Neurol* 2023;146:79-84
5. Genizi J, Guidetti V, Arruda MA. Primary Headaches and School Performance-Is There a Connection? *Curr Pain Headache Rep* 2017;21:31.
6. Jafari E, Kazemizadeh H, Togha M, Haghghi S, Salami Z, Shahamati D, et al. The influence of anxiety and depression on headache in adolescent migraineurs: a case-control study. *Expert Rev Neurother* 2022;22:1019-23.
7. Onofri A, Ferilli MAN, Tozzi E, Ursitti F, Sforza G, Olivieri L, et al. How to Assess the Headache-Sleep Disorders Comorbidity in Children and Adolescents. *J Clin Med* 2021;10:5887.
8. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine Prophylaxis: A Systematic Review and Network Meta-analysis. *JAMA Pediatr*. 2020;174:341-349.
9. Hróbjartsson A, Kaptchuk TJ, Miller FG. Placebo effect studies are susceptible to response bias and to other types of biases. *J Clin Epidemiol* 2011;64:1223-9.
10. Rosignoli C, Ornello R, Onofri A, Caponnetto V, Grazi L, Raggi A, et al. Applying a biopsychosocial model to migraine: rationale and clinical implications. *J Headache Pain* 2022;23:100.
11. Powers SW, Kashikar-Zuck SM, Allen JR, LeCates SL, Slater SK, Zafar M, et al. Cognitive behavioral therapy plus amitriptyline for chronic migraine in children and adolescents: a randomized clinical trial. *JAMA* 2013;310:2622-30.
12. Aemaz Ur Rehman M, Waseem R, Habiba U, Fahad Wasim M, Alam Rehmani S, Alam Rehmani M, et al. Efficacy of mindfulness-based intervention for the treatment of chronic headaches: a systematic review and meta-analysis. *Ann Med Surg (Lond)* 2022;78:103862.
13. Andrasik F, Grazi L, D'Amico D, Sansone E, Leonardi M, Raggi A, Salgado-García F. Mindfulness and headache: a "new" old treatment, with new findings. *Cephalalgia* 2016;36:1192-205.
14. Wells RE, O'Connell N, Pierce CR, Estave P, Penzien DB, Loder E, et al. Effectiveness of Mindfulness Meditation vs Headache Education for Adults With Migraine: A Randomized Clinical Trial. *JAMA Intern Med* 2021;181:317-28.
15. Grazi L, D'Amico D, Guastafierro E, Demichelis G, Erbetta A, Fedeli D, et al. Efficacy of mindfulness added to treatment as usual in patients with chronic migraine and medication overuse headache: a phase-III single-blind randomized-controlled trial (the MIND-CM study). *J Headache Pain* 2023;24:86.
16. Fedeli D, Ciullo G, Demichelis G, Medina Carrion JP, Bruzzone MG, Ciusani E, et al. Longitudinal neurofunctional changes in medication overuse headache patients after mindfulness practice in a randomized controlled trial (the MIND-CM study). *J Headache Pain* 2024;25:97.
17. Grazi L, Grignani E, Raggi A, Rizzoli P, Guastafierro E. Effect of a Mindfulness-Based Intervention for Chronic Migraine and High Frequency Episodic Migraine in Adolescents: A Pilot Single-Arm Open-Label Study. *Int J Environ Res Public Health* 2021;18:11739.
18. Marusak HA, Elrahal F, Peters CA, Kundu P, Lombardo MV, Calhoun VD, et al. Mindfulness and dnmic functional neural connectivity in children and adolescents. *Brain Behav Res* 2018;336:211-8.
19. Suh H, Kavouras SA. Water intake and hydration state in children. *Eur J Nutr*. 2019;58:475-496. doi: 10.1007/s00394-018-1869-9.
20. Hayes SC. Acceptance and commitment therapy, relational frame theory, and the third wave of behavioral and cog-

- native therapies—republished article. Behav Ther 2016;47: 869-85.
21. Lovas DA, Pajer K, Chorney JM, Vo DX, Howlett M, Doyle A, Huber A. Mindfulness for adolescent chronic pain: a pilot feasibility study. J Child Adolesc Ment Health 2017;29: 129-36.
 22. Frattale I, Ferilli MAN, Ursitti F, Sforza G, Monte G, Proietti Checchi M, et al. Unsatisfactory response to acute med-ications does not affect the medication overuse headache development in pediatric chronic migraine. J Head Pain 2024; 25:61
 23. Papetti L, Ursitti F, Moavero R, Ferilli MAN, Sforza G, Tarantino S, et al. Prophylactic treatment of pediatric migraine: Is there anything new in the last decade? Front Neurol 2019;10:1-8.

Correspondence: Licia Grazzi, MD, Neuroalgology Unit and Headache Center, Fondazione IRCCS Istituto Neurologico Carlo Besta, Via Celoria 11, 20133 Milan, Italy.

E-mail: licia.grazzi@istituto-besta.it

Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: not applicable.

Received: 1 April 2025. Accepted: 20 May 2025.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Confinia Cephalalgica 2025; 1:15782. doi:10.4081/cc.2025.15782

©Copyright: the Author(s), 2025. Licensee PAGEPress, Italy

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0).