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Mindfulness meditation.

What clinical utility in migraine and headache patients?

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Mindfulness meditation. What clinical utility in migraine and headache patients?

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Abstract

Background. Mindfulness is an Oriental practice based on knowing how to listen to oneself and accept the reality of that moment without judgment. Over time this practice has become a real treatment in the medical field with benefits in the treatment of chronic pain of various conditions, particularly low back pain. Two main approaches emerge from the literature, MBSR (Mindfulness-Based Stress Reduction) and MBCT (Mindfulness-Based Cognitive Therapy) that differ in the type of purpose pursued, the first helps to manage one's emotions (especially stress), the second to avoid depressive relapses. Based on these results, this review tries to evaluate the effects of mindfulness programmes on treat headache disorders.

Purpose. The purpose of this review was to map the existing literature relating to mindfulness clinical application as a therapeutic approach in the treatment of headache and migraine attacks, to evaluate its effectiveness on the perception of disability, intensity and frequency of attacks.

Methods. This study follows the PRISMA statement. Searches were based on PubMed, Cochrane Library and PEDro databases for studies that explicitly claimed to use mindfulness programme in adult with headache disorders. Study design, characteristics, outcome and results were extracted, and quality of randomized controlled trials (RCT) and non-RCT was assessed using the Quality Index.

Results. Six articles were included. Four studies applied MBSR, one study MBCT and the remaining study applied a non-specific programme called mindfulness therapy. Heterogeneity of approaches and outcomes not allowed to perform a meta-analysis.

Discussion. From the analysis of literature has emerged that mindfulness programmes used as treatment of headache disorders improves psychological aspects, frequency of attacks and disability.

Conclusion. Mindfulness could be a new frontier in rehabilitation. It is important to standardize programmes and outcomes to allow quantitative analyses.

Keywords. mindfulness; mbsr; mbct; headache disorders; rehabilitation

1. Background

Primary headache is the most common pain syndrome [1] which causes widespread and debilitating problems. Particularly, the last Global Burden of Disease study, has rated headache disorders as the sixth cause of disability [2]. Tension-Type Headaches (TTH) have been reported as the second common disorders [3]; and Migraine Headaches (MH) have been reported, in people under age 50, as the third common disorders worldwide [3, 4] and they affect about 10-18% of the overall population [5]. Cluster Headache is a type of headache which has a lower prevalence rate than TTH and MH. Cervicogenic Headache (CgH), is a secondary headache type, which impacts for 3% according to IHS [6] and 4.1-8% according to Sjaastad [7].

1.1 Classification of headaches

Headaches were classified as primary and secondary headaches. Headache diagnosis criteria were defined by the International Headache Society (IHS) [6], and by the Sjaastad group [7] which proposed modified diagnostic criteria for Cervicogenic Headache.

The IHS defines among the primary headaches:

- *Migraine (MH)*

A. At least 5 attacks meeting criteria B-D

B. Duration of untreated headache of 4–72 hours

C. At least 2 of the following characteristics

1. One-sidedness
2. Button quality
3. Moderate to severe pain
4. Worsens with physical activity (walking, climbing stairs)

D. During the headache at least one of the following:

1. Nausea and/or vomiting
2. Photophobia and phonophobia

E. Not best attributed to another ICHD-3 headache

- *Tension-Type headache (TTH)*

A. At least 10 attacks with frequency (for the infrequent one)

<1 day per month and on average

<12 days a year that meet the B-D criteria

B. Headache duration from 30 minutes to 7 days

C. At least 2 of the following characteristics

1. Bilateralism
2. Bite pain (non-throbbing) (+)
3. Mild to moderate pain
4. Not aggravated by physical activity (+++)

D. Both of the following:

1. No vomiting/nausea
2. Not more than one of the following: photophobia or phonophobia

E. Not best attributed to another ICHD-3 headache

- *Cluster headache*

A. At least 5 attacks meeting criteria B and D

B. Severe or Very Severe unilateral orbital, supra-orbital and/or temporal pain that lasts 15'-180 ' (when untreated)

C. Headache has one or both of the following characteristics:

1. At least one of the following ipsilateral symptoms or signs:
   a) Conjunctival injection and/or lacrimation
   b) Nasal congestion and/or rhinorrhea
   c) Eyelid edema
   d) Facial and frontal sweating
   e) Miosis and/or ptosis
2. Sense of restlessness or agitation

D. Frequency ranging from 1-2 per day to 8 per day for more than half the time the disorder is active

E. Not better described by other ICHD-3 diagnostic classifications

Among the secondary headaches the IHS includes *Cervicogenic Headache (CgH)*:

A. All headaches that satisfy point C

B. Clinical, laboratory and/or imaging evidence of a cervical spine disorder/injury recognized as a possible cause of headache

C. At least two of the following:

1. Temporal relationship between the appearance of headache and cervical disorder

2. Headache significantly improved or disappeared with improvement or resolution of the disorder or cervical injury

3. Cervical ROM is reduced and headache significantly worsens with provocative maneuvers

4. Disappears by anesthetic blockade of a cervical structure or its nerve

D. Not best attributed to another ICHD-3 headache

The Sjaastad group defines *Cervicogenic Headache* with the following diagnostic criteria:

1.Cervical Trauma

2. Moderate pain, usually non-pulsating

3. Strictly Unilateral Pain, without side-shift

4. Caused by non-physiological positions of the neck

5. Provoked by the external pressure of the TrP of the neck/occipital area and by specific movements

6. Reduction of cervical ROM

7. Diffuse pain, in the shoulder/arm ipsilaterally

8. Pain starting posteriorly, radiating anteriorly

9. Diagnostic anaesthetic block

1.2 Impact of headaches

Most of the population suffering from migraine reports a low quality of life and repercussions also on personal and working life [8-11], these aspects are among the main side effects of headaches [1, 12, 13]. These patients show high levels of stress and emotional reactivity [14] both during the attacks and in the pain-free intervals, which leads them to be anxious about the next attacks during the day [15]. This aspect finds an explanation in some pathological studies according to which among the triggering factors of migraine and headache attacks there are biological [16], social and psychological factors [17-21] including stress [18,19, 22, 23], anxiety and depression [24-26], personality traits [27, 28], coping styles [29], cognitive structures [30-32].

1.3 From pharmacological treatments to mindfulness meditation

Drug treatment is one of the first approaches to treat headaches, which can range from simple NSAIDs to up to one third of opioid-using patients [33-35]. If in some cases the results are good, it has been shown that they can increase the chronicity of the headache, and for this reason the American Headache Society does not recommend the use of opioids [33-36]. In fact, two-thirds of migraine patients discontinue medications due to inefficacy or adverse effects [37].

According to the studies which have highlighted an important role of the bio-psycho-social aspect as a trigger of headaches, the therapeutic approach should be multidisciplinary including pharmacological and non-pharmacological therapies [38]. Literature has studied the role of stress as a trigger for headaches [1, 18, 19, 39] and it has looked for ways to reduce it, in particular the first and second generation of behavioral and cognitive therapies have been studied [40-42]. The results of both indicate small results in terms of the reduction of headache generation and disability [43-45]. For this reason, the third generation of behavioral therapies does not focus on the control and management of emotional factors but on the acceptance of these [46].

Mindfulness is a practice based on the conscious acceptance of what is. Born as an Oriental practice/ritual based on knowing how to listen to oneself and how to accept the reality of that moment without judgment, over time this practice has become a real treatment in the medical field so as to be considered a third generation behavioral therapy [47-49] and it has been recently included in rehabilitation programs for chronic pain conditions [50, 51].

Two mindfulness-programs emerge from literature: Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT). According to Jon Kabat-Zinn, the MBSR protocol theorist, this means "paying attention in a particular way: intentionally, in the present moment and in a non-judgmental way". MBCT program is the union of Cognitive-Behaviour Therapy (CBT) with the principles of mindfulness. This approach shifts the relationship between the person and his emotions to a metacognitive level, it is how to have an “observer position” of oneself from the outside and without judgment favouring the acceptance of even painful experiences [52].

Scientific research explored the effects of mindfulness meditation, in particular showing that MBSR improved pain and functional outcomes in chronic back pain [53]. Pilot studies demonstrated the efficacy of MBSR, in patients with primary headaches, on improving quality of life, individual performance, and reducing stress, anxiety and depression [54-57]. Other pilot studies applied MBCT to patients with primary headaches, and found significant improvements in psychological variables like pain acceptance and pain self-efficacy, headache-related outcomes such as frequency, intensity, and disability showed improvements [58, 59].

The working mechanism has not yet been fully understood [60, 61], but mindfulness could be an effective non-drug prevention and treatment strategy in headaches.

The use of mindfulness-based protocols could help patients to reduce the use of medication to a minimum, with the consequent reduction of side effects, like the frequency of headaches [62].

The aim of this review is to map the existing literature relating to mindfulness clinical application as a therapeutic approach in the treatment of headache and migraine attacks, and evaluate its effectiveness on the perception of disability, intensity and frequency of attacks.

2. Methods

This study followed the Preferred Reported Items for Systematic Reviews and Meta-Analyses (PRISMA) [63].

2.1 Eligibility criteria

Participants, interventions, comparisons, outcomes, and the study design (PICOS) model were used to define eligibility criteria.

Participants: Adults with headache or migraine disorders

Interventions: Any intervention defined as “mindfulness”

Comparisons: Any

Outcomes: disability

Study design: Randomized controlled trials and non-randomized controlled trials from the earliest available records to recent publications, excluding posters, abstracts, oral presentation or qualitative studies.

Language: only studies in English have been included.

2.2 Information sources

One author (C.D) developed and conducted the search. Studies were identified by searching electronic databases and scanning reference lists of articles. This search was applied to PubMed, Cochrane and PEDro from October 2021 to March 2022. Studies included run from August 2015 to November 2021.

2.3 Search

The author developed a search strategy to the following search terms: “headache”, “migraine disorders”, “head pain”, “cephalgia”, “mindfulness”, “mindfulness meditation”, “mindfulness-based cognitive therapy”, “mindfulness therapy”, “mindfulness-based stress reduction”, “mbsr”, “disability” (see in appendix *Table 1*).

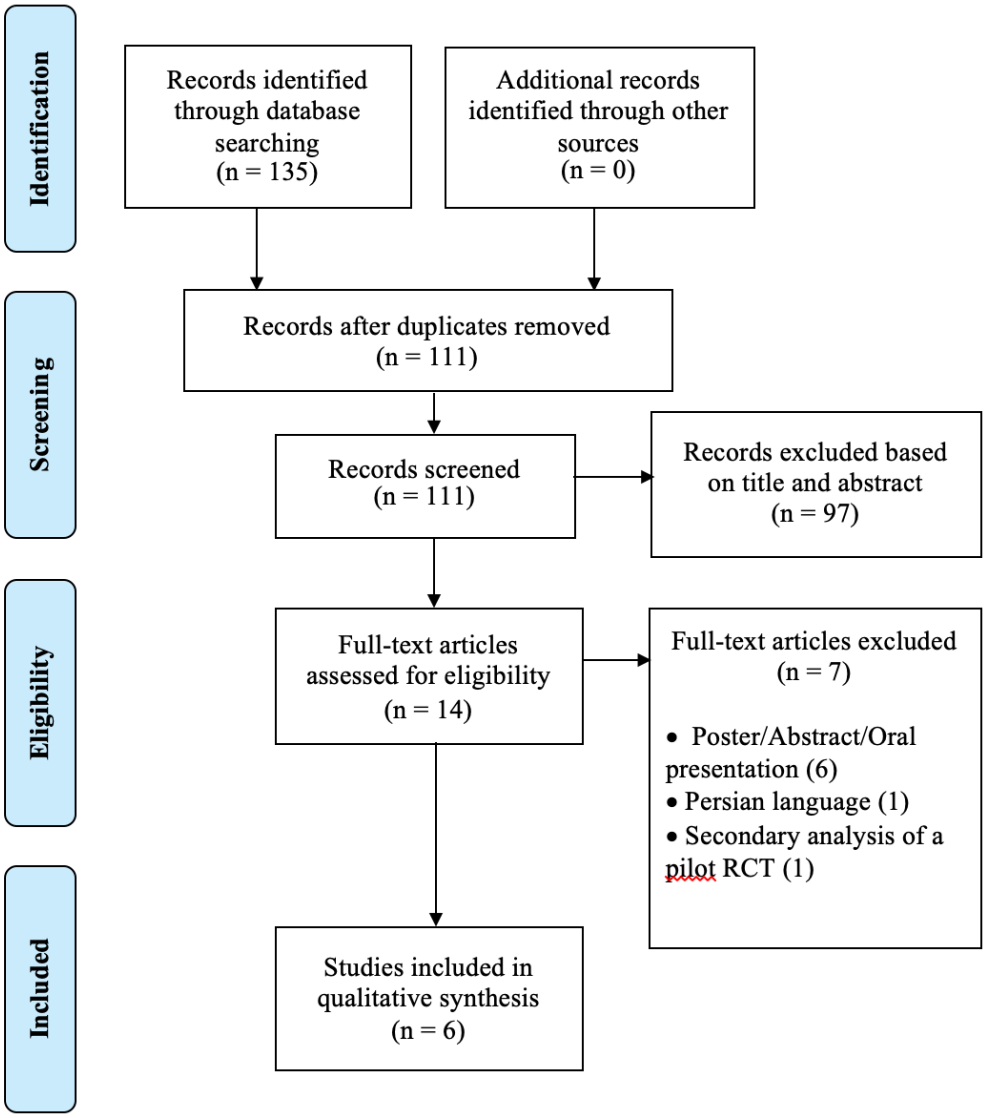
2.4 Study selection

One author (C.D) performed the eligibility assessment using an electronic reference manager tool (Mendeley Desktop), by first screening records by title and abstract, and then checking the full texts of the remaining records (see *Figure 1*). Eventual disagreements were resolved by consulting a second author (S.DL).

2.5 Data collection process

The author developed a data collection form to extract data. After testing the form on a sample of 7 articles, the author extracted data from each one. Information extracted from each study included: (1) characteristics of participants (pathology, sample size, sex, age); (2) type of intervention (type of mindfulness therapy used, dose, duration vs standard care or no treatment); (3) type of outcome measures assessing primary and secondary outcomes and their results (see in appendix *Table 2*).

Figure 1.
Flow diagram



2.6 Quality assessment

In order to compare the quality of both Randomized Controlled Trials (RCTs) and Non-Randomized Controlled Trials (N-RCTs) the Quality Index was used [64] (internal validity sub-scales: items 14-26). For each item a score of 0 was assigned if the answer was 'no' or 'unable to determine' and 1 if the answer was 'yes'. The maximum score is 13 and it indicates a good internal validity of the study.

3. Results

The search strategy identified 135 records (see *Figure 1*). After the removal of duplicates, 111 records were screened by title and abstract. The full texts of the remaining 14 citations were assessed for eligibility. Of these, 7 studies did not meet the inclusion criteria as they were abstracts, posters, oral presentations, one had an English abstract but a Persian text, and one was a secondary analysis of a pilot study. Finally, 6 publications met the inclusion criteria and were included in qualitative synthesis. Due to the heterogeneity of the outcomes a quantitative synthesis could not be carried out (see in appendix "Outcome" *Table 2*).

3.1 Study characteristics

3.1.1 Study design

The 6 included studies were published in English between 2015 and 2021. The study design is the following: 5 RCTs (83,3%), 1 N-RCT (16,7%) (see *Table 3*). Sample sizes ranged from 30 participants to 98 participants. All studies were conducted on patients with headache or migraine disorders. Diagnoses varied in the studies: migraine (3 studies), episodic migraine (1 study), chronic migraine (2 studies), tension-type headache (1 study) (see *Table 3*).

3.1.2 Participants

Sample sizes ranged from 30 participants to 98 participants. All studies were conducted on patients with headache or migraine disorders. Diagnoses varied in the studies: migraine (3 studies), episodic migraine (1 study), chronic migraine (2 studies), tension-type headache (1 study) (see *Table3*).

Table 3.
Characteristics of studies included

Study	Design	Quality Index (*)	n. participants	Pathology	Period of intervention	Type of Mindfulness				Control
						MBSR	MBSR+	MBCT	MT	
Simshäuser, 2021	RCT	9	54	Migraine	8 weeks once a week for 2.5 hours			✓ + **O****		**O****
Wells, 2020	RCT	13	89	Migraine	8 weeks once a week for 2 hours	✓ + **O**				Δ + **O**
Seminowicz, 2020	RCT	12	98	Episodic migraine	4 months 2 hours weekly for 8 weeks then bi-weekly for 8 weeks		✓ + **O**			Δ + **O**
Tavallaei, 2018	RCT	10	30	Migraine	8-week once a week for 30 min	✓ + **O**				**O**
Grazzi, 2017	N-RCT	10	44	Chronic migraine	6 weeks once a week for 45 min				✓	**O**
Bakhshani, 2015	RCT	10	37	Chronic migraine and tension-type headache	8 weeks once a week for 1.5 to 2 hours	✓ + **O**				**O**

RCT = Randomized controlled trial; N-RCT = Non-randomized controlled trial
Quality Index (*) = It is for the assessment of the methodological quality of RCT and N-RCT only
MBSR = Mindfulness-Based Stress Reduction; MBSR+ = Enhanced Mindfulness-Based Stress Reduction; MBCT = Mindfulness-Based Cognitive Therapy; MT = Mindfulness Training
✓ = type of Mindfulness used; **O** = prophylactic medications; Δ = received headache education/information
O ** = in case of a medical prophylaxis maintaining a stable dose for at least 3 months prior to inclusion until the end of the trial.

3.1.3 Intervention

Two thirds of the studies were conducted in the USA, two thirds in Europe and two thirds in Iran. The length of treatment varied from 6 weeks to 4 months.

As far as types of intervention are concerned, four groups of studies were identified. Group 1 is composed of 3 studies (3 RCTs) which used the Mindfulness-Based Stress Reduction protocol (MBSR) managed by therapists with experience in the field of mindfulness [65-67]. The MBSR included 1 therapy session per week in person managed by a psychologist/instructor for 1.5-2 hours, furthermore the participants received technological tools such as electronic audio files, CDs and booklets to carry out meditation homework at home. Topics covered during the therapy sessions included emotion and body senses, stress reaction and stress response, mindful breathing practice, mindful physical exercises, behavioural activation, mindfulness of routine activity, body scan practice, seeing and hearing exercise, sitting meditation, mindful walking, reading poems related to mindfulness, etc. (see "Attachment B"). Group 2 consisted of 1 study (1 RCT), which provided Enhanced Mindfulness-Based Stress Reduction (MBSR+) administered by 2 experienced, certified instructors, first for 8 weeks with a weekly 2-hour session therapy, then bi-weekly for another 8 weeks [68]. The first eight sessions adapted the MBSR program developed by Jon Kabat-Zinn for use at home. Each session included a longer arriving practice, and a loving kindness meditation. The format of the additional four bi-weekly sessions was similar to the original program (MBSR), and enhanced typical MBSR training by encouraging continued mindfulness practice including both didactic content and mindfulness practice, includes body scan, yoga, sitting and walking meditation (see "Attachment B").

Group 3 is composed of 1 study (1 RCT) which used the Mindfulness-Based Cognitive Therapy (MBCT) protocol, the courses were taught by three experienced and certified MBSR / MBCT teachers [69]. MBCT consisted of 8 weekly sessions of 2.5 hours. Program content included: educational elements on the migraine condition, promoting self-monitoring of cascades of bodily thoughts, feelings and reactions, identifying cognitive errors, regulating the level of activity and stress in daily life, and promoting recognition and regulation of early signs of specific stress and overload. Participants

were encouraged to practice at home for 30-45 minutes per day. Additionally, participants received a headache diary to fill out daily (see "Attachment B").

Group 4 consisted of 1 study (1 N-RCT) which used Mindfulness Therapy (MT) for 6 weekly sessions led by an experienced neurologist trained in mindfulness practice [70]. Patients were trained to assume a relaxed position which promoted good and regular breathing, while their eyes remained closed, maintaining a relaxed sitting position. During the meditation, patients were asked to focus their attention on the breath, the present and the silence to increase awareness of the current sensations of the mind and body, accepting their thoughts in a non-judgmental way, protecting themselves from interfering thoughts and concentrating on the present and the sensations they received from their bodies. Patients were encouraged to supplement their training with regular personal home practice of 7-10 minutes per day (see "Attachment B").

3.1.4 Outcomes

Various outcome measures were assessed in each study. Group 1 used outcomes for the assessment of frequency and intensity of headache attacks and psychological outcomes for evaluating participation and quality of life.

Due to the type of study, Group 2 used clinical and imaging outcomes. Clinical outcomes assessed changes in headache frequency and intensity, from baseline to follow-up, using an electronic daily diary. Imaging Outcomes measured brain function with fMRI during cognitive task performance.

Groups 3 and 4 used outcomes for the assessment of headache-related impairment, headache intensity, headache characteristics and psychological outcomes.

A detailed description of the measurement tool is provided in *Table 2*.

3.2 Quality assessment

Quality of RCTs and N-RCT ranged from 9/13 to 13/13 points in the internal validity subscale of Quality Index (QI). A detailed description of the methodological quality is presented in *Table 4*.

Table 4.
Quality Index

QUALITY INDEX (Internal Validity sub-scales)			Simshäuser, 2021	Wells, 2020	Seminowicz, 2020	Tavallaei, 2018	Grazzi, 2017	Bakhshani, 2015
Bias sub-scale	14	Was an attempt made to blind study subjects to the intervention they have received?	1	0	0	0	0	0
	15	Was an attempt made to blind those measuring the main outcome of the intervention?	1	1	0	0	0	1
	16	If any results of the study were based on "data dredging", was this made clear?	1	1	1	1	1	1
	17	In trials and cohort studies, do the analyses adjusts for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?	1	1	1	0	1	1
	18	Were the statistical tests used to assess the main outcome appropriate?	1	1	1	1	1	1
	19	Was compliance with the intervention/s reliable?	1	1	1	1	1	1
	20	Were the main outcome measures used accurate (valid and reliable)?	1	1	1	1	1	1
		Sub-Total (max 7pt)	***4***	***7***	***6***	***5***	***6***	***5***
Confounding sub-scale	21	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	1	1	1	1	1	1
	22	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	1	1	1	1	1	1
	23	Were study subjects randomized to intervention groups?	1	1	1	1	1	0
	24	Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	1	1	0	0	0	0
	25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	1	1	1	1	1	1
	26	Were losses of patients to follow-up taken into account?	1	1	1	1	1	1
		Sub-Total (max 6pt)	***5***	***6***	***6***	***5***	***4***	***5***
		INTERNAL VALIDITY SCORE	**9**	**13**	**12**	**10**	**10**	**10**

3.3 Results of the included studies

The heterogeneity of interventions, patients and outcomes of studies has not allowed a meta-analysis. In the following paragraph the main effects obtained by the groups are reported.

In Group 1 significant results were obtained mainly in the context of psychological status, quality of life and pain. Wells et al. [65] evaluated the effects of MBSR in adults with migraine and found that from baseline at 12 weeks, after 8 weeks of MBSR patients had a reduction of migraine days per month. MIDAS, MSQv2.1, PHQ-9, PCS, HMSE were in favour of an intervention group (all $p< 0.05$).

Tavallaei et al. [66] investigated the effectiveness of mindfulness internet-based bibliotherapy on women with primary headaches. The results demonstrated that pain intensity, distress, disability and mindfulness were all improved (all $p< 0.04$). A subscale of MAAS reported a statistical difference in emotional dimension of pain.

Bakhshani et al. [67] evaluated the effects of MBSR in patients with chronic migraine and tension-type headache and they found a statistical difference in pain intensity. Furthermore, some of the dependent variable of SF-36 were significant: RP, BP, GH, PCS, VT, AH, MCS (all $p< 0.02$).

Group 2 study obtained various results regarding clinical and imaging outcomes. Seminowicz et al. [68] studied the effects of MBSR+ in patients with episodic migraine, and they found a reduction of headache days at 10 and 20 week of follow-up ($p< 0.05$), a decreased anterior mid cingulate volume and decreased connectivity of right dorsal anterior insula to cognitive task network (EMN) at week 20. Results regarding HIT-6 and response to treatment at week 20 of the follow-up were significant. MBSR+ showed a decreased activation in the bilateral cuneus and right parietal operculum during attacks at week 20 compared to the SMH group. Whole brain analyses also revealed a significant interaction of left dorsal anterior insula connectivity to the right posterior parietal cortex and right cuneus.

Group 3 study of Simshäuser et al. [69] evaluated the effects of MBCT in patients with migraine. Results showed improvements in time-per-group and time interaction for the number of headache attacks per days ($p< 0.05$). Psychological Outcomes demonstrate significant improvements in: HADS-D-anxiety, PSQ, DFS-rumination, PRSS-catastrophizing (all $p< 0.05$). Some of these variables remain significant at 7 months

follow-up: headache days, medication days, DFS-rumination, PRSS-catastrophizing, SCS (all $p < 0.02$).

Group 4 study of Grazzi et al. [70] administered Mindfulness Therapy to patients with chronic migraine demonstrating an improvement of HIT, headache frequency, medication intake, MIDAS and BDI-13 (all only for effect of time), only HIT was significant for interaction time-per-group. All 3 follow-up points had significantly improved in comparison with the baseline value.

4. Discussion

This review aims to map the existing literature relating to mindfulness clinical application as a therapeutic approach in the treatment of headache and migraine attacks, and to evaluate its effectiveness on the perception of disability, intensity and frequency of attacks.

Clinical application of mindfulness as a complementary therapy in the treatment of various disorders, such as low back pain [53], is increasingly discussed in the literature. Currently, low back pain seems to be the most studied condition, in particular chronic low back pain (CLBP) as the most common cause of disability in the world in the adult population. It has been seen how psychological factors play an important role in the experience of pain and they can be predictors of the persistence of pain, disability and therefore a low quality of life. Psychological treatments in CLBP have shown to change brain activity by reducing the state of cortical arousal which is the basis for the onset and maintenance of pain [71]. Studies on CLBP have shown how the implementation of non-invasive and non-pharmacological therapies such as MBSR improved low back pain and functional limitations [72], pain intensity and quality of life [73] compared to the usual care. Aspects such as catastrophization and self-efficacy have improved in patients with CLBP who used MBSR as a treatment [74]; even in conditions of Failed Back Surgery Syndrome (FBSS), MBSR is considered a useful clinical intervention [75]. Mindfulness in chronic low back pain reduces negative emotions related to chronic pain, such as the fear of pain, and it improves the awareness of pain itself [76]. Studies on mindfulness programs applied to low back pain also require longer follow-up because improvements in pain intensity,

physical functioning, reduction of depressed mood and greater awareness of the painful condition are often short to medium term [77, 78].

In conclusion, literature is in favour of defining a multimodal intervention as the best in the treatment of CLBP. Pain science education, graded exposure, physical exercise are the elements considered effective in modifying behaviour and the patient's approach to chronic pain in order to have long-term effects [79]. Therefore, multimodal intervention aims not only at treating the biological aspect of a painful condition but also at its social and psychological repercussions.

In line with the bio-psycho-social care approach, mindfulness falls within the "treatment" field of the patient's psychological sphere. Defined as “acceptance of what happens to us in that moment and without judgment”, this practice could especially help the daily management of those with chronic conditions. Even researchers in the field of headache have started to turn their attention to mindfulness training as viable approach for supplementing patient care.

From this study, four groups emerged which differed from each other in the type of mindfulness approach used. Group 1 used the Mindfulness-Based Stress Reduction protocol (MBSR) [65-67] which includes 1 therapy session per week from 30’ to 2 hours for 8 weeks,and participants received technological tools to perform meditation homework at home. Group 2 used an Enhanced Mindfulness-Based Stress Reduction (MBSR+) [68] lasting 4 months, the first 8 weeks with 1 weekly session therapy of 2 hours and the last 8 weeks with a meeting every 2 weeks. In this group, patients were also provided with educational content to enable daily practice at home. Group 3 used the Mindfulness-Based Cognitive Therapy (MBCT) protocol [69], consisting of 8 weekly sessions of 2.5 hours. Participants were also encouraged to practice at home for 30-45 minutes per day and received a headache diary to fill out daily. Group 4 used Mindfulness Therapy (MT) [70] for 6 weekly sessions and patients were encouraged to supplement their training with regular personal home practice of 7-10 minutes per day.

The different mindfulness approaches used by the included studies, differ in the way the therapy sessions are managed and in the way the topics were covered. In particular, the purpose of the MBSR is to improve one's own regulation of emotions, especially

of stress; MBCT aims at preventing depressive falls, it relies more on thinking. So, the heterogeneity of approaches and outcomes did not allow a meta-analysis.

None of the included studies evaluated perceived disability, intensity and frequency of headache attacks together, but all evaluated psychological outcomes demonstrating statistically significant results. From studies by Seminowicz *et al.* [68], at follow-up, and Bakhshani *et al.* [67] the frequency of headache days decreased. Wells *et al.* [65], Tavallaei *et al.* [66] and Grazzi *et al.* [70] showed a significant p-value for disability.

This is the first review concerning clinical application of mindfulness practice in adults with headaches. The Reasons for the lack of studies include the difficulty of finding patients with headaches who agree to practice mindfulness as a therapy even without medication for long periods and of patients who accept mindfulness as a therapy in itself as a non-drug treatment. Choosing a homogeneous population with the same clinical condition allows to conduct a meta-analysis. In this review some studies evaluated adults with Episodic Migraine [68], others with Chronic Migraine [70], and others with Tension-Type Headache [67]. Additionally, there is still a lack of knowledge concerning which aspects of mindfulness practice represent the critical or active ingredients for enhancing brain function that influence headache related outcomes, and the required "dose" of mindfulness is unknown. More good quality research is needed on these components of mindfulness.

5. Limitations

There are some limitations to this review. It was not possible to conduct a quantitative analysis due to the heterogeneity of the studies, both in the type of intervention and in the outcomes used. Even among the studies that used the same mindfulness programme there is not homogeneity in the outcomes, therefore it was not possible to carry out a meta-analysis.

6. Conclusion

This is the first review that gives a general overview of the literature concerning the application of mindfulness programmes for treatment of headaches; although

mindfulness remains a practice which is far from application in the clinical setting. Mindfulness is a new approach which stimulates patients not to be passive when curing their headaches only through drug treatment. It is a way to implement standard care and change the point of view of their condition by looking at it from the outside and accepting it without judgment. Literature findings suggest that various mindfulness-based approaches may be helpful for headache sufferers, so future studies on the clinical application of mindfulness need to be conducted.

This practice could become a self-help method in the treatment of chronic and non-chronic headaches, also through online or self-managed courses, and it could also be used to reduce the intake of drugs.

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Table 1.
Search strategies

PubMed	Records: 75 ((((((((((((headache[MeSH Terms]) OR ("migraine disorders"[MeSH Terms])) OR (headache)) OR ("migraine disorders")) OR (migraine)) OR ("head pain")) OR (cephalgia)) OR (headaches)) OR (cephalgias)) AND (mindfulness[MeSH Terms])) OR (mindfulness)) OR ("mindfulness meditation")) OR (“mindfulness-based cognitive therapy")) OR ("mindfulness therapy”)) OR (“mindfulness-based stress reduction”)) OR (mbsr) AND (disability) Filters: Humans, English, Italian, RCT
Cochrane Library	Records: 57 #1 MeSH descriptor: [Headache Disorders] explode all trees #2 MeSH descriptor: [Migraine Disorders] explode all trees #3 headache* #4 "migraine disorder*" #5 cephalea* #6 "head pain" #7 #1 OR #2 OR #3 #4 OR #5 OR #6 #8 MeSH descriptor: [Mindfulness] explode all trees #9 mindfulness #10 "mindfulness meditation" #11 "mindfulness therapy" #12 "mindfulness-based cognitive therapy” #13 “mindfulness-based stress reduction” #14 #8 OR #9 OR #10 OR #11 OR #12 OR #13 #15 MeSH descriptor: [Disability Evaluation] explode all trees #16 disability #17 #15 OR #16 #18 #7 AND #14 AND #17
PEDro	Records: 3 mindfulness, headache*, migraine*, disability

Table 2.
Detailed description

Study	**Population** Pathology n (male/female) Age, mean (sd)	Mindfulness therapy	Outcome	Results
Simshäuser, 2021	Migraine MBCT group n = 27, 92.6% female 44.4 (8.86) --- Control group n = 27, 85.2% female 46.1 (12.11)	8 weeks + 7 month follow-up only for MBCT group MBCT group Participants received a headache diary with detailed instructions to be filled in daily. 8 weekly 2.5h sessions held by three experienced and certified MBSR/ MBCT teachers. The original MBCT were transformed to headache-specific adaptations. --- Control group (waitlist) Participants received a headache diary with detailed instructions to be filled in daily. Not receive any treatment within that period.	**Primary outcome** **• Headache-related impairment (NRS)** **Secondary outcome** **• Migraine related outcome:** - Headache intensity - Headache-related impairment - Headache characteristics (duration, pain character, aggravation by exercising, presence of the three attendant symptoms aura, sensitivity to light and noise, nausea and sickness) - Medication use **• Psychological Outcomes** - HADS-D - PSQ - PSRS - The scale "dysfunctional self-attention" of the DFS - The scale "catastrophizing" of the PRSS - SCS - FMI Short Version - Treatment satisfaction and homework adherence via questionnaires including Likert scales at the follow-up-assessment	**Secondary outcome** **Migraine related outcome** - Time×group interaction for the number of headache days: p= 0.041 - Time interaction for the number of headache days: p= 0.004 Follow-up: no significant effect **Psychological Outcomes** - HADS-D-anxiety: p< 0.05 - PSQ: p < 0.05 - DFS-rumination: p< 0.01 - PRSS-catastrophizing: p< 0.05 Follow-up: - Headache days p= 0.00002 - Medication days p= 0.002 - DFS-rumination: p= 0.02 - PRSS-catastrophizing: p= 0.0005 - SCS: p= 0.01
Wells, 2020	Adults with migraine MBSR group n = 3/42 44 (12) --- Headache education group n = 4/40 44 (14)	8 weeks + 3 periods follow-up (12, 24, 36 weeks) MBSR group Participants could continue current acute and preventive migraine medications and were requested to maintain stable medications for study duration. 2 hours/week for 8 weeks (with optional retreat day), the MBSR instructor followed the standardized curriculum to teach mindfulness meditation/yoga without migraine modifications. Participants received electronic audio files for home practice and were encouraged to practice at home 30 minutes per day. --- Headache education group Participants could continue current acute and preventive migraine medications and were requested to maintain stable medications for study duration. Received instruction on headaches, pathophysiology, triggers, stress, and treatment approaches 2 hours/week for 8 weeks (with optional retreat day).	**Primary outcome** **• Change in monthly migraine day frequency from baseline to 12 weeks** **Secondary outcome** **• MIDAS-1 month** **• HIT-6** **• MSQv2.1** **• PHQ-9** **• GAD-7** **• PCS** **• HMSE** **• Five-Facet Mindfulness Questionnaire**	**Primary outcome** Participants in both groups demonstrated a reduction of migraine days per month from baseline at 12 weeks, without statistical differences between groups p= 0.5 **Secondary outcome** - MIDAS p< 0.001 - MSQv2.1 p< 0.01 - PHQ-9 p< 0.008 - PCS p< 0.001 - HMSE p< 0.04

Study	**Population** Pathology n (male/female) Age, mean (sd)	Mindfulness therapy	Outcome	Results
Seminowicz, 2020	Episodic migraine MBSR+ group n = 3/47 36 (range 18-65) ---------- SMH group n = 6/42 36 (range 21-63)	4 months (8 weeks + 8 weeks) + 3 follow-up visits (10, 20, 52 weeks) MBSR+ group Participants met 12 sessions of enanched mindfulness based stress reduction. Participants were provided with audio CDs and handouts and a personal copy of Full Catastrophe Living by Jon Kabat-Zinn for home use. For a more detailed description of each session look "Attachment B". ---------- SMH group Participants met 12 sessions of stress management of headache. In addition to educational handouts, participants were provided with a personal copy of The Migraine Brain by Carolyn Bernstein for home use. For a more detailed description of each session look "Attachment B".	**Primary outcome** • **Clinical Outcomes:** Change from baseline to week 20. Headache frequency was measured using an electronic daily diary for 28 days • **Imaging Outcomes:** Brain function was measured as activation during cognitive task performance in left DLPFC and cognitive task network (EMN), and resting state connectivity of right dorsal anterior insula to left DLPFC and cognitive task network (EMN). **Secondary outcome** • **Clinical Outcomes** - HIT-6 - Headache intensity was computed as the average of all headache intensity ratings from the electronic daily diary - Response to treatment as ≥50% reduction in number of headache days from baseline to week 20 • **Imaging Outcomes** - Sandwich estimator toolbox	**Primary outcome** - Headache days (per 28 days calendar) week 10: p= 0.04 week 20: p= 0.04 (Both groups showed decreased anterior mid cingulate volume, p= 0.04 and decreased connectivity of right dorsal anterior insula to cognitive task network (EMN) p= 0.02 at week 20) **Secondary outcome** - At week 20, HIT-6: p= 0.04 - At week 20, 52% of the MBSR+ group were classified as treatment responders: p= 0.004 - MBSR+ group reported fewer migraine days at week 10: p= 0.0008, and week 20: p= 0.004 - MBSR+ group showed decreased activation in the bilateral cuneus and right parietal operculum at week 20 compared to the SMH group. Whole brain analyses also revealed a significant interaction of left dorsal anterior insula connectivity to the right posterior parietal cortex and right cuneus
Tavallaei, 2018	Women with migraine headache referring to headache clinic of Baqiyatallah Hospital in Tehran MBSR group (Mindfulness-Based Stress Reduction) n = 15 all women 34.87 (9.12) ---------- MTAU group (Medical Treatment As Usual) n = 15 all women 32.47 (9.11)	8 weeks MBSR group In addition to the MTAU, the MBSR treatment was performed as bibliotherapy based on an 8-week treatment protocol. The book was given to two psychologists with experience in the field of mindfulness, to be examined in terms of the adaptation of the text to the underlying assumptions of the mindfulness. Participants were followed up weekly in a specific day and time by the support therapist and were questioned about their weekly exercise, and their ambiguities were clarified (30 minutes per week). For a more detailed description of each session look "Attachment B". ---------- MTAU group Only the medical treatment as usual.	• **DASS-21- Short Form** • **MIDAS** • **MPQ-SF** • **MAAS**	Investigate the effectiveness of mindfulness internet-based bibliotherapy on women with primary headaches (tension-type headache and migraine). Pain intensity, distress, disability and mindfulness were all improved. - Distress p< 0.0001 - Disability p< 0.0001 - Pain intensity index p< 0.035 - Mindfulness p< 0.0001 Sub-scale of MAAS: - Emotional dimension of pain p< 0.0001

Study	Population Pathology n (male/female) Age, mean (sd)	Mindfulness therapy	Outcome	Results
Grazzi, 2017	Chronic migraine MT-group (Mindfulness training) n = 22 tot 45.6 (9.3) --- Med-Group (Medication group) n = 22 tot 43.5 (9.2)	6 weekly sessions (on Monday), each of about 45 min duration + 3 periods follow-up (3-6-12 months) MT group Training was provided in small groups (5–6 patients), that met in a relaxed and quiet room. All sessions were guided by an experienced neurologist trained in mindfulness practice. During follow-up patients were instructed to continue their prior treatments and they were strongly recommended to avoid opioids to the extent possible. For a more detailed description of each session look “Attachment B”. --- Med-Group Receiving only prophylactic medications	• **Headache diaries** • **HIT-6** • **MIDAS** • **BDI** • **STAI Y1 and Y2**	<u>Main effect of time</u> - HIT p= 0.002 - Headaches frequency p< 0.001 - Medications intake p< 0.001 - MIDAS p< 0.001 - BDI-13 p< 0.001 <u>Interaction (Time x Group)</u> p= 0.020 All 3 follow-up points as significantly improved with respect to baseline values p< 0.001
Bakhshani, 2015	Patients with chronic migraine and tension-type headache, diagnosed by a neurologist and a psychiatrist using IHS diagnostic criteria Intervention group n = 6/14 30.60 (9.08) --- Control group n = 7/13 31.50 (9.57)	8 weeks Intervention group Therapy sessions (MBSR) were held for 1.5 to 2 hours a week (drug plus MBSR). To do the meditation homework while training participants in sessions, the necessary measures have been provided in a CD and a booklet. Patients also received information about learning how to detect any future relapses as well as strategies and plans on which to base early detection of symptom pain attacks and for being self-directed towards new situations. For a more detailed description of each session look “Attachment B”. --- Control group Continuing usual pharmacotherapy (including specific and nonspecific drugs) by their neurologist until the end of the research.	**Primary outcome** • **Headache log** (to determine the perceived intensity of pain) - 10-point likert-scale ratings - The number of hours of pain per day - Pain frequency during the month **Secondary outcome** • **SF-36**	The main effect of MBSR intervention was significant, p= 0.001, indicating that the pain intensity was lower after MBSR than control group. The covariate (pre-test of pain) was also significant, p= 0.001, indicating that level of pain intensity before MBSR intervention had a significant effect on level of pain intensity. The second hypothesis of this study is the effectiveness of MBSR technique on quality of life in patients with chronic headache. The main effect of MBSR intervention was significant for some of dependent variables including: - RP, role limitations due to physical health: p= 0.025 - BP, bodily pain: p= 0.002 - GH, general health: p= 0.005 - PCS, Physical Component Summary: p = 0.004 - VT, energy and vitality: p= 0.002 - AH, affect health: p= 0.001 - MCS, Mental Component Summary: p = 0.002

HADS-D = Hospital Anxiety and Depression Scale
PSQ = Perceived Stress Questionnaire
PSRS = Perceived Stress Reactivity Scale
PRSS = Pain-Related Self Statements Scale
SCS = Self-Compassion Scale
FMI = Freiburg Mindfulness Inventory
MIDAS = Migraine Disability Assessment
HIT-6 = Headache Impact Test-6
MSQv2.1 = Migraine-Specific quality of Life Questionnaire, version 2.1
PHQ-9 = Patient Health Questionnaire-9
GAD-7 = Generalized Anxiety Disorder-7
PCS = Pain Catastrophizing Scale
HMSE = Headache Management Self-Efficacy Scale
DASS-21 = Depression, Anxiety, Stress Scale - Short Form
MPQ-SF = McGill's Short Form Questionnaire
MAAS = Mindfulness Inventory
BDI = Beck Depression Inventory
STAI = State-Trait Anxiety Inventory
SF- 36 = Short-form 36 questionnaire

Attachment A

Quality Index

QUALITY ASSESSMENT – QUALITY INDEX

K. Simshäuser, R. Pohl, P. Behrens, C. Schultz, C. Lahmann, S. Schmidt; **Mindfulness-Based Cognitive Therapy as Migraine Intervention: a Randomized Waitlist Controlled Trial**, *International Journal of Behavioral Medicine. 2021*

Internal validity – bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

Yes	1
No	**0**
Unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

Yes	1
No	**0**
Unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

Yes	**1**
No	0
Unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

Yes	1
No	**0**
Unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*
For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

Yes	**1**
No	0
Unable to determine	0

<u>Internal validity – confounding (selection bias)</u>
21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

Yes	**1**
No	0
Unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

Yes	**1**
No	0
Unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

Yes	**1**
No	0
Unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

Yes	1
No	**0**
Unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

Yes	**1**
No	0
Unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

Total score 9/13

QUALITY ASSESSMENT – QUALITY INDEX

Rebecca Erwin Wells, MD, MPH; Nathaniel O'Connell, PhD; Charles R. Pierce, MS; Paige Estave; Donald B. Penzien, PhD; Elizabeth Loder, MD, MPH; Fadel Zeidan, PhD; Timothy T. Houle, PhD; **Effectiveness of Mindfulness Meditation vs Headache Education for Adults With Migraine A Randomized Clinical Trial**, *JAMA Intern Med, 2020*

Internal validity – bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

Yes	**1**
No	0
Unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

Yes	**1**
No	0
Unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

Yes	**1**
No	0
Unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

Yes	**1**
No	0
Unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*
For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

Yes	**1**
No	0
Unable to determine	0

<u>Internal validity – confounding (selection bias)</u>
21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

Yes	**1**
No	0
Unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

Yes	**1**
No	0
Unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

Yes	**1**
No	0
Unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

Yes	**1**
No	0
Unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

Yes	**1**
No	0
Unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

Total score 13/13

QUALITY ASSESSMENT – QUALITY INDEX

David A. Seminowicz, PhD1, Shana AB Burrowes, PhD, Alexandra Kearson, BS, Jing Zhang, BS, Samuel R Krimmel, BS, Luma Samawi, BS, Andrew J Furman, MS1, Michael L Keaser, BA, Neda F. Gould, PhD, Trish Magyari, MS, LCP, Linda White, MS, CRN, Olga Goloubeva, PhD, Madhav Goyal, MD, B. Lee Peterlin, DO, Jennifer A. Haythornthwaite, PhD; **Enhanced mindfulness based stress reduction (MBSR+) in episodic migraine: a randomized clinical trial with MRI outcomes**, *Pain. 2020 August; 161(8): 1837–1846*

Internal validity – bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

Yes	1
No	**0**
Unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

Yes	**1**
No	0
Unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

Yes	**1**
No	0
Unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

Yes	**1**
No	0
Unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*
For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

Yes	**1**
No	0
Unable to determine	0

<u>Internal validity – confounding (selection bias)</u>
21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

Yes	**1**
No	0
Unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

Yes	**1**
No	0
Unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

Yes	**1**
No	0
Unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

Yes	**1**
No	0
Unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

Yes	**1**
No	0
Unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

Total score 12/13

QUALITY ASSESSMENT – QUALITY INDEX

Vahid Tavallaei, Yaser Rezapour-Mirsaleh, Peyman Rezaiemaram, Seyed Hassan Saadat **Mindfulness for female outpatients with chronic primary headaches: an internet-based bibliotherapy**, *Eur J Transl Myol, 2018. 28 (2): 175-184*

Internal validity – bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

Yes	1
No	**0**
Unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

Yes	1
No	0
Unable to determine	**0**

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

Yes	**1**
No	0
Unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

Yes	**1**
No	0
Unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*
For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

Yes	**1**
No	0
Unable to determine	0

<u>Internal validity – confounding (selection bias)</u>
21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

Yes	**1**
No	0
Unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

Yes	**1**
No	0
Unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

Yes	**1**
No	0
Unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

Yes	1
No	**0**
Unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

Yes	**1**
No	0
Unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

Total score 10/13

QUALITY ASSESSMENT – QUALITY INDEX

Licia Grazzi, Emanuela Sansone, Alberto Raggi, Domenico D'Amico, Andrea De Giorgio, Matilde Leonardi, Laura De Torres, Francisco Salgado-García, Frank Andrasik, **Mindfulness and pharmacological prophylaxis after withdrawal from medication overuse in patients with Chronic Migraine: an effectiveness trial with a one-year follow-up**, *The Journal of Headache and Pain*. 2017

Internal validity – bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

Yes	1
No	**0**
Unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

Yes	**1**
No	0
Unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

Yes	**1**
No	0
Unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

Yes	**1**
No	0
Unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*
For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

Yes	**1**
No	0
Unable to determine	0

<u>Internal validity – confounding (selection bias)</u>
21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

Yes	**1**
No	0
Unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

Yes	**1**
No	0
Unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

Yes	1
No	**0**
Unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

Yes	1
No	**0**
Unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

Yes	**1**
No	0
Unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

Total score 10/13

QUALITY ASSESSMENT – QUALITY INDEX

Nour-Mohammad Bakhshani, Ahmadreza Amirani, Hamed Amirifard & Mahnaz Shahrakipoor, **The Effectiveness of Mindfulness-Based Stress Reduction on Perceived Pain Intensity and Quality of Life in Patients With Chronic Headache**, *Global Journal of Health Science*. 2015; Vol. 8, No. 4

Internal validity – bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

Yes	1
No	**0**
Unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

Yes	1
No	**0**
Unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

Yes	**1**
No	0
Unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?*
Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

Yes	**1**
No	0
Unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis

has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*
For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

Yes	**1**
No	0
Unable to determine	0

Internal validity – confounding (selection bias)
21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

Yes	**1**
No	0
Unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

Yes	**1**
No	0
Unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.

Yes	**1**
No	0
Unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

Yes	1
No	0
Unable to determine	**0**

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

Yes	**1**
No	0
Unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

Yes	**1**
No	0
Unable to determine	0

Total score 10/13

Attachment B

Data Collection Form

Data Collection Form

Bakhshani N-M, 2015
The Effectiveness of Mindfulness-Based Stress Reduction on Perceived Pain Intensity and Quality of Life in Patients With Chronic Headache
DOI: 10.5539/gjhs.v8n4p142

General Information

Date form completed: 04.04.2022
Name of person extracting data: Carla Difranco

Study Eligibility

Inclusion	Mindfulness as therapy for headache (migraine and/or cephalgia) ☒
Exclusion	Animals ☐; Infants ☐; Psychiatric patients ☐; Healthy subjects ☐; Abstract ☐; Review ☐; Not english ☐

Characteristics of study

Methods

Aim of study	Determine the effectiveness of Mindfulness-Based Stress reduction (MBSR) on perceived pain intensity and quality of life in patients with chronic headache
Design	Randomized controlled trial two-group 'pretest-posttest' study design
Unit of allocation	Intervention group and control group
Duration of participation	8 weeks

Participants

Population description	Patients with chronic migraine and tension-type headache
Inclusion criteria	- Informed consent to participate in the sessions - Minimum age of 18 years - Minimum educational qualification of middle-school degree - The diagnosis of chronic headache (primary chronic migraine and tension-type headache) by the neurologist and according to IHS diagnostic criteria - 15 or more days per month for more than 3 months and least six months history of migraines and tension-type headache
Exclusion criteria	- Subjects who were not willing to continue the participation in the study or leave the study for any reason - Other chronic pain problems - Psychosis, delirium and cognitive disorders - Cases of interpersonal difficulties interfering with teamwork. - Drug and substance abuse - Mood disorder
Method of recruitment of participants	Patients were recruited at the University hospitals of Zahedan University of Medical Sciences, Zahedan-Iran.
Pathology	Chronic migraine and tension-type headache
No.	40 → 37 (3 subject during the therapy were excluded from the study due to lack of a regular presence or exclusion criteria)
Age	30.60(9.08) Intervention group, 31.50(9.57) Control group
Sex, males/females	13/27

Intervention Group

Group name	Intervention group
Duration of treatment period	8 weeks
No. randomised to group	20 (-3 drop-out)
Age mean (SD)	30.60 (9.08)
Sex, males mean (SD)	6 (30)
Type of intervention	Therapy sessions (MBSR) were held for 1.5 to 2 hours a week for the members of the intervention group (drug plus MBSR). To do the meditation homework while training participants in sessions, the necessary measures have been provided in a CD and a booklet. MBSR program and discussions included: understanding pain and its aetiology, discuss about relationship stress, anger and emotion with pain, Understanding negative automatic thoughts, identyfying thoughts and feelings, introducing the concept of acceptance, breathing space, 3-minute breathing space, breath focus exercise, pleasant and unpleasant events daily, behavioral activation, mindfulness of routine activity, body scan practice, seeing and hearing exercise, sitting meditation, mindful walking, reading poems related to mindfulness and also discuss how to keep up what has been developed over the whole course, discuss plans and positive reasons for maintaining the practice. Patients also received information about learning how to detect any future relapses as well as strategies and plans on which to base early detection of symptom pain attacks and for being self-directed towards new situations.

Control Group

Group name	Control group
Duration of treatment period	8 weeks
No. randomised to group	20
Age, mean (SD)	31.50 (9.57)
Sex, males mean (SD)	7 (35)
Type of intervention	Usual pharmacotherapy (including specific and nonspecific drugs) by their neurologist until the end of the research.

Outcomes

Primary	- Headache log was used to determine the perceived intensity of pain
Secondary	- Short-form 36 questionnaire (SF-36)

Results

Primary outcome	**Pain perceived**	The main effect of MBSR intervention was significant, p= 0.001, indicating that the pain intensity was lower after MBSR intervention (Mean= 53.89, SD.E = 2.40) than control group (Mean = 71.94, SD.E= 2.20). The covariate (pre-test of pain) was also significant, p= 0.001, indicating that level of pain intensity before MBSR intervention had a significant effect on level of pain intensity
Secondary outcome	**Quality of life**	Statistically significant difference in the scores of subscales of role limitation due to physical health, bodily pain, general health, energy and vitality, affect health and sum of physical health dimensions and mental health. And also indicates that there was not a statistically significant difference in subscale scores of physical functioning, role limitations due to emotional problems and social functioning in the intervention group. All significant values are reported at $p<0.05$.

Quality Assessment

Quality Index

Item 14-26*	Total score **10**/13

* For further information look at "Attachment A – QI"

Data Collection Form

Grazzi L, 2017

Mindfulness and pharmacological prophylaxis after withdrawal from medication overuse in patients with Chronic Migraine: an effectiveness trial with a one-year follow-up

DOI: 10.1186/s10194-017-0728-z

General Information

Date form completed: 04.04.2022

Name of person extracting data: Carla Difranco

Study Eligibility

Inclusion	Mindfulness as therapy for headache (migraine and/or cephalgia) ☒
Exclusion	Animals ☐; Infants ☐; Psychiatric patients ☐; Healthy subjects ☐; Abstract ☐; Review ☐; Not english ☐

Characteristics of study

Methods

Aim of study	Determine the effectiveness of a mindfulness-based approach would be similar to that of conventional prophylactic treatments.
Design	N-RCT
Unit of allocation	Mindfulness Therapy group (MT) and Medication group (Med-Group)
Duration of participation	6 weeks + 3 follow-up periods (3-6-12 months)

Participants

Population description	Patients with CM-MO (chronic migraine associated with medication overuse)
Inclusion criteria	- Diagnosys of CM-MO (following the international criteria included in point 8.2 of the International Classification of Headache Disorder III edition, beta version (ICHD-3-beta)) - Age between 18 and 65 years - History of CM lasting for at least ten years that was associated with overuse of triptans and non-steroidal anti-inflammatory drugs (NSAIDs) for a minimum of the past five years
Exclusion criteria	- Comorbid major psychiatric disorders (psychotic disorders and personality disorders determined on the basis of clinical history and psychiatric evaluation) - Pregnancy
Method of recruitment of participants	Who presented consecutively for treatment at the Headache Centre of the Neurological Institute C. Besta of Milan, Italy, be- tween February 2014 and June 2015.
Pathology	Chronic migraine
No.	44
Age	44.5 (9.2)
Sex, males/females	/

Intervention Group

Group name	MT-group
Duration of treatment period	6 weeks + 3 follow-up periods (3-6-12 months)
No. randomised to group	22
Age mean (SD)	45.6 (9.3)
Sex, males mean (SD)	/
Type of intervention	Participating in a series of mindfulness training sessions and were not prescribed any form of prophylaxis. Training was provided in small groups (5-6 patients), that met in a relaxed and quiet room every consecutive Monday for 6 weekly sessions, each of about 45 min duration. All sessions were guided by an experienced neurologist trained in mindfulness practice. First, patients were provided a detailed explanation about the treatment protocol. Second, patients were trained to assume a relaxed position that promoted good and regular breathing, while their eyes remained closed, with them maintaining a relaxed sitting position. Third, during the first meditations (approximately up to the second/third session), patients were invited to focus on attention on their breathing, on the present and on silence to enhance awareness of current mind and body sensations. Fourth, once patients learned to focus on the present, they erre requested to enhance awareness of their thoughts (third and fourth session), accepting them in a non-judgmental way. Fifth, in the last sessions (generally the last two), when patients had gathered higher awareness of their thoughts and the capacity to accept them, they were invited to preserve themselves from interfering thoughts, and to focus on the present and on the sensations they received from their bodies. When distractions occurred, patients were informed to resume attention to breathing and body awareness and observe the interfering content in a non-judgmental way. Finally patients were encouraged to supplement their training with regular home self-practice, of 7-10 min per day. During follow-up patients were instructed to continue their prior treatments and they were strongly recommended to avoid opioids to the extent possible.

Control Group

Group name	Med-group
Duration of treatment period	6 weeks + 3 follow-up periods (3-6-12 months)
No. randomised to group	22
Age, mean (SD)	43.5 (9.2)
Sex, males mean (SD)	/
Type of intervention	Receiving only prophylactic medications. The preventive compound was chosen on the basis of clinical history and medical comorbidities, such as done in routine care. During follow-up patients were instructed to continue their prior treatments and they were strongly recommended to avoid opioids to the extent possible.

Outcomes

Primary	- Headache diaries - Headache Impact Test (HIT-6) - Migraine Disability Assessment (MIDAS) - Beck Depression Inventory (BDI) - State-Trait Anxiety Inventory (STAI) Y1 and Y2

Results

Primary outcome	Main effect of time - HIT p= 0.002 - Headaches frequency p< 0.001 - Medications intake p< 0.001 - MIDAS p< 0.001 - BDI-13 p< 0.001 All 3 follow-up points as significantly improved with respect to baseline values p< 0.001	Interaction (Time X Group) p= 0.020

Quality Assessment

Quality Index

Item 14-26*	Total score **10**/13

* For further information look at "Attachment A – QI"

Data Collection Form

Seminowicz D A, 2020
Enhanced mindfulness based stress reduction (MBSR+) in episodic migraine: a randomized clinical trial with MRI outcomes
DOI: 10.1097/j.pain.0000000000001860

General Information

Date form completed: 04.04.2022
Name of person extracting data: Carla Difranco

Study Eligibility

Inclusion	Mindfulness as therapy for headache (migraine and/or cephalgia) ☒
Exclusion	Animals ☐; Infants ☐; Psychiatric patients ☐; Healthy subjects ☐; Abstract ☐; Review ☐; Not english ☐

Characteristics of study

Methods

Aim of study	Evaluate the efficacy of an enhanced mindfulness based stress reduction (MBSR+) versus stress management for headache (SMH)
Design	Randomized, assessor-blind, clinical trial
Unit of allocation	MBSR+ group and SMH group
Duration of participation	4 months (8 weeks + 8 weeks) + 3 follow-up visits (10, 20, 52 weeks)

Participants

Population description	Adults with episodic migraine
Inclusion criteria	- Provides a signed and dated informed consent form - Able to speak, read, and write English - To be randomized to either arm of the study (migraine patients only) - Between 18 and 65 years of age - Meets International Classification of Headache Disorders Criteria-II for migraine (migraine patients only): A. At least 5 attacks fulfilling criteria B-D B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) C. Headache has at least two of the following characteristics: 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs) D. During headache at least one of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia E. Not attributed to another disorder - Between 4 and 14 headache days over 28 days, based on a prospectively maintained daily headache diary (migraine patients only) - History of migraine for at least one year (migraine patients only) - If using non-opioid medication for pain treatment: _ Has been on the same treatment regimen for the last 30 days prior to Visit 1 _ Stay on the same treatment regimen for at least 6 months, with the addition of acute abortive or rescue medications (as needed, such as antihistamines, non-steroidal anti-inflammatory, acetaminophen, triptans, dopamine-antagonists) _ Use of acute abortive or rescue medications is restricted to use only more than 24 hours prior to QST - If of child-bearing potential, agrees to use contraception throughout the study - Is able to understand and willing to comply with all study procedures and is available for the duration of the study - Free of an acute or chronic pain condition, and does not have a history of migraines (healthy controls only)

Exclusion criteria	- Unable to undergo MRI (e.g. pacemaker), assessed on an individual basis - History of unstable major psychiatric disorder - History of migraine or chronic pain (healthy controls only) - More than 14 alcoholic drinks per week on average - Active [within 6 months] substance or alcohol abuse - Use of opioids - Severe depressive symptoms as determined by clinical assessment, triggered by score ≥ 27 on the CES-D at Visit 1. - Suicidal ideation as determined by clinical assessment, triggered by positive response to the Suicidal Ideation Item on the PHQ-9 at Visit 1. - Positive urine toxicology screening test for barbiturates, THC, alcohol, cocaine and other recreational drugs of abuse - Positive urine pregnancy test (women only) - Plan to become pregnant within next 12 months (women only) - Lactating (women only) - Anything that, in the opinion of the investigator, would place the subject at increased risk or preclude the subject's full compliance with or completion of the study - Lifetime history of formal training in mindfulness practice, MBSR, meditation - Concurrent non-pharmacological treatments with effects on mindfulness and/or stress reduction components, including but not limited to CBT, biofeedback, acupuncture, massage therapy - First migraines occurred after the age of 50 (migraine patients only)
Method of recruitment of participants	Participants were recruited from local headache clinics, primary care providers, and the community in eight cohorts (9-18 participants/cohort) from June 2014 to February 2017.
Pathology	Episodic migraine
No.	98
Age, mean (range)	36 (18–65)
Sex, males/females	9/89

Intervention Group

Group name	MBSR+ group (Enhanced Mindfulness-Based Stress Reduction)
Duration of treatment period	8 weeks + 3 follow-up visits (10, 20, 52 weeks)
No. randomised to group	50
Age mean (range)	36 (18-65)
Type of intervention	Participants were instructed to continue stable use of prescribed preventative treatments and continue use of acute abortives as needed. Separate groups for each intervention met for about 2 hours weekly for 8 weeks then bi-weekly for another 8 weeks (12 session totally). MBSR+ was administered by 2 experienced, certified instructors. The first eight sessions adapted the MBSR program developed by Jon Kabat-Zinn to include trauma-informed methods of teaching and emphasized loving kindness to distress. Study participants were provided with audio CDs and handouts and a personal copy of Full Catastrophe Living by Jon Kabat-Zinn for home use. Each session included a longer arriving practice, and a loving kindness meditation was included at week 2 and at the retreat, held between weeks 6 and 8. The week 8 class was adapted to focus on applying learning to migraines before, during and after an attack and engaging participants in deciding which MBSR practices they wished to increase practice of during the second eight weeks of the MBSR+ program. The additional four bi-weekly sessions enhanced typical MBSR training by encouraging continued mindfulness practice and self-compassion and emphasizing sympathetic joy, equanimity, and gratitude. The format of these bi-weekly sessions was similar to the original program and included both didactic content and mindfulness practice, including body scan, yoga, sitting and walking meditations.

Control Group

Group name	SMH group (Stress Management for Headache)
Duration of treatment period	8 weeks + 3 follow-up visits (10, 20, 52 week)
No. randomised to group	48
Age, mean (range)	36 (21-63)
Type of intervention	Participants were instructed to continue stable use of prescribed preventative treatments and continue use of acute abortives as needed. Separate groups for each intervention met for about 2 hours weekly for 8 weeks then bi-weekly for another 8 weeks (12 session totally). SMH was delivered by a nurse practitioner. Sessions were focused on didactic content about the role of stress and other triggers in headaches and followed a smiliar format and timing to the MBSR+ sessions, minus the retreat. Topics included stress at work and home; coping with stress mental health and personality, sleep hygiene, pain education and medications for migraine. Information, group discussion, and social support among group members was emphasized. Each session included a 10-minute period of standardized muscle stretching exercises. In addition to educational handouts, participants were provided with a personal copy of The Migraine Brain by Carolyn Bernstein.

Outcomes

Primary	**Clinical Outcomes:** Change from baseline to week 20. Headache frequency was measured using an electronic daily diary for 28 days
	Imaging Outcomes: Brain function was measured as activation during cognitive task performance in left DLPFC and cognitive task network (EMN), and resting state connectivity of right dorsal anterior insula to left DLPFC and cognitive task network (EMN). Brain structure was measured as gray matter volume in DLPFC, cingulate, and anterior insula (ROI selection was based on hypothesized areas that are involved in both pain and cognition)
Secondary	**Clinical Outcomes:** Secondary outcomes were assessed at weeks 10, 20, and 52. - HIT-6 - Headache intensity was computed as the average of all headache intensity ratings from the electronic daily diary - Response to treatment as ≥50% reduction in number of headache days from baseline to week 20
	Imaging Outcomes: Whole brain analyses of gray matter volume, activation to pain, activation to cognitive challenge, and resting state connectivity of the insula cortex were measured using Sandwich estimator toolbox

Results

Primary outcome	- Headache days (per 28 days calendar), 10 week: p= 0.04; 20 week: p= 0.04 (Both groups showed decreased anterior mid cingulate volume, p= 0.04 and decreased connectivity of right dorsal anterior insula to cognitive task network (EMN) p= 0.02 at week 20)
Secondary outcome	- At week 20, HIT-6: p= 0.04 - At week 20, 52% of the MBSR+ group were classified as treatment responders: p= 0.004 - MBSR+ group reported fewer migraine days at week 10: p= 0.0008, and week 20: p= 0.004 - MBSR+ group showed decreased activation in the bilateral cuneus and right parietal operculum at week 20 compared to the SMH group. Whole brain analyses also revealed a significant interaction of left dorsal anterior insula connectivity to the right posterior parietal cortex and right cuneus

Quality Assessment

Quality Index

Item 14-26*	Total score **12**/13

* For further information look at "Attachment A – QI"

Data Collection Form

Simshäuser K, 2021
Mindfulness-Based Cognitive Therapy as Migraine Intervention: a Randomized Waitlist Controlled Trial
DOI: doi.org/10.1007/s12529-021-10044-8

General Information

Date form completed: 04.04.2022
Name of person extracting data: Carla Difranco

Study Eligibility

Inclusion	Mindfulness as therapy for headache (migraine and/or cephalgia) ☒
Exclusion	Animals ☐; Infants ☐; Psychiatric patients ☐; Healthy subjects ☐; Abstract ☐; Review ☐; Not english ☐

Characteristics of study

Methods

Aim of study	Evaluate the feasibility and effectiveness of a migraine-adapted, group- based MBCT program
Design	RCT
Unit of allocation	MBCT group and Control group
Duration of participation	8 weeks + 7 month follow-up only for MBCT group

Participants

Population description	Adults with migraine
Inclusion criteria	- Aged 18–65 years - Diagnosis of migraine with or without aura by the trial physician in accordance with the diagnostic criteria of the International Headache Society - At least two migraine attacks per month on average - In case of a medical prophylaxis maintaining a stable dose for at least 3 months prior to inclusion until the end of the trial
Exclusion criteria	- Chronic migraine with more than 15 migraine days per month - Taking headache analgesics on more than 15 days or migraine-specific triptans on more than 10 days per month - Regular practice of meditation (>1 × per week) or yoga (>2 × per week) - Plans to start psychotherapy or any other migraine treatments during the course of the trial - Prior participation in a mindfulness training - Participation in other clinical studies throughout the study duration - Presence of a life-threatening disease or a mental disorder that might severely hinder inter- personal contacts
Method of recruitment of participants	Participants were recruited via local advertisements, local neurologists and the Pain Unit of the Medical Center of the University of Freiburg, between Nov 2014 and Feb 2015.
Pathology	Migraine
No.	54
Age, mean (SD)	44.4 (8.86) MBCT group, 46.1 (12.11) Control group
Sex, females %	92.6 MBCT group, 85.2 Control group

Intervention Group

Group name	MBCT group (Mindfulness-Based Cognitive Therapy)
Duration of treatment period	8 weeks + 7 month follow-up
No. randomised to group	27
Age mean (range)	44.4 (8.86)
Type of intervention	Participants received a headache diary with detailed instructions to be filled in daily. The intervention consisted of 8 weekly 2.5h sessions. At the start an individual intake interview was held with the MBCT teacher in order to assess personal goals and motivations. Finally, a booster session for refreshment was held after 6 months. Two courses for the invention group were conducted with an average group size of 12 participants. The courses were held by three experienced and certified MBSR/ MBCT teachers from the local mindfulness network. Regarding program content, the depression-related cognitive-behavioral elements of the original MBCT were transformed to headache-specific adaptations. This encompassed: educational elements about the condition of migraine, fostering self-monitoring of the cascades of thoughts, feelings, and bodily reactions, identifying cognitive errors, regulating the level of activity and stress in everyday life, and fostering early recognition and regulation of specific signs of stress and overload. The participants were encouraged to practice at home for 30–45 min a day.

Control Group

Group name	Control group (waitlist)
Duration of treatment period	8 weeks
No. randomised to group	27
Age, mean (range)	46.1 (12.11)
Type of intervention	Participants received a headache diary with detailed instructions to be filled in daily. The waitlist group did not receive any treatment within that period.

Outcomes

Primary	Group difference at *t*1 of the variable "headache-related impairment" assessed via three items asking for impairment in everyday life, at work and during leisure with an 11-point numeric rating scale (0-10). They were assessed on a daily basis in a headache diary.
Secondary	**Migraine related outcome:** eight columns of headache diary assessing headache intensity, headache-related impairment, headache characteristics (duration, pain character, aggravation by exercising, presence of the three attendant symptoms aura, sensitivity to light and noise, nausea and sickness), and medication use. **Psychological Outcomes** - Hospital Anxiety and Depression Scale (HADS-D) - Perceived Stress Questionnaire (PSQ) - Perceived Stress Reactivity Scale (PSRS) - The scale "dysfunctional self-attention" of the Questionnaire of Dysfunctional and Functional Self-Consciousness (DFS) - The scale "catastrophizing" of the Pain-Related Self Statements Scale (PRSS) - Self-Compassion Scale (SCS) - Short-version of the Freiburg Mindfulness Inventory (FMI) - Treatment satisfaction and homework adherence via questionnaires including Likert scales at the follow-up-assessment

Results

Primary outcome	Non-significant effect with a non-substantial effect size.
Secondary outcome	**Migraine related outcome** - Time×group interaction for the number of headache days: p= 0.041 - Time interaction for the number of headache days: p= 0.004 Follow-up: no significant effect **Psychological Outcomes** - HADS-D-anxiety: p< 0.05 - PSQ: p < 0.05 - DFS-rumination: p< 0.01 - PRSS-catastrophizing: p< 0.05 Follow-up: - Headache days p= 0.00002 - Medication days p= 0.002 - DFS-rumination: p= 0.02 - PRSS-catastrophizing: p= 0.0005 - SCS: p= 0.01

Quality Assessment

Quality Index

Item 14-26*	Total score **9**/13

* For further information look at "Attachment A – QI"

Data Collection Form

Tavallaei V, 2018
Mindfulness for female outpatients with chronic primary headaches: an internet-based bibliotherapy
DOI: 10.4081/ejtm.2018.7380

General Information

Date form completed: 04.04.2022
Name of person extracting data: Carla Difranco

Study Eligibility

Inclusion	Mindfulness as therapy for headache (migraine and/or cephalgia) ☒
Exclusion	Animals ☐; Infants ☐; Psychiatric patients ☐; Healthy subjects ☐; Abstract ☐; Review ☐; Not english ☐

Characteristics of study

Methods

Aim of study	Investigate effectiveness of mindfulness by bibliotherapy on disability, distress, perceived pain and mindfulness in women with tension headaches and migraines.
Design	Quasi-experimental randomized design with pre-test, post-test, and control group.
Unit of allocation	Mindfulness-Based Stress Reduction (MBSR group) and Medical Treatment As Usual (MTAU group)
Duration of participation	8-week

Participants

Population description	Women with migraine headache referring to headache clinic of Baqiyatallah Hospital in Tehran
Inclusion criteria	- Diagnosis of tension headache and migraine by expert physician based on criteria of the International Association for Headache - Age 18-50 years - Least education degree of diploma - Access to Internet and social network of Telegram
Exclusion criteria	- Severe psychiatric disorders - Addiction - Regular meditation or yoga exercises - Pregnancy and breastfeeding - Starting a new medical treatment to prevent headaches within the next 45 days
Method of recruitment of participants	Patients from to headache clinic of Baqiyatallah Hospital in Tehran
Pathology	Migraine headache
No.	30
Age, mean (SD)	34.87 (9.12) MBSR group, 32.47 (9.11) MTAU group
Sex, males/females	All women

Intervention Group

Group name	MBSR group (Mindfulness-Based Stress Reduction)
Duration of treatment period	8 weeks
No. randomised to group	15
Age mean (SD)	34.87 (9.12)
Type of intervention	In addition to the MTAU, the MBSR treatment was performed as bibliotherapy based on an 8-week treatment protocol. The book was given to two psychologists with experience in the field of mindfulness, to be examined in terms of the adaptation of the text to the underlying assumptions of the mindfulness. Participants were followed up weekly in a specific day and time by the support therapist and were questioned about their weekly exercise, and their ambiguities were clarified (30 minutes per week). - Week 1: Reasons for choosing the course, stress and anxiety and their role in life, list of stressors, raisins eating practice, "Mindful Check-in" practice, planning and reviewing practices - Week 2: Triangle of cognition, emotion and body senses, Stress reaction and stress response, mindful breathing practice, mindfulness for everyday stress, planning and reviewing practices - Week 3: Stages of mindfulness, bringing the stages of mindfulness into life, the effects of mindfulness on headache, mental traps and negative self-talk, wandering mind, "mindful breathing" practice, "mindful walking" practice, planning and reviewing practices - Week 4: Benefits of mindfulness for body health, "body scan" practice, dealing with physical pain, Identifying Emotions in the Body, barriers to awareness of emotions, planning and reviewing practices - Week 5: "mindful sitting" practice, regular patterns, being mindful of habits, mindful physical exercises, planning and reviewing practices - Week 6: Mindful self-inquiry, reconciliation with hard feelings, discovery of internal rules, mindful physical exercises, planning and reviewing practices - Week 7: "loving-kindness meditation" Practice, mindfulness in interpersonal relationships, six qualities of mindful relationship, "mindful listening" practice, planning and reviewing practices - Week 8: "Mindful eating" practice, "mindful exercising" practice, "mindful resting" practice, "mindful communications" practice, communication barriers, reviewing the stressors list, planning and reviewing practices, planning for the future and continuing, finish

Control Group

Group name	MTAU group (Medical Treatment As Usual)
Duration of treatment period	8 weeks
No. randomised to group	15
Age, mean (SD)	32.47 (9.11)
Type of intervention	Only the medical treatment as usual. After completing the relevant questionnaires in the post-test, subjects who wanted to receive psychological treatment were treated with MBSR

Outcomes

Primary	- Depression, Anxiety, Stress Scale - Short Form (DASS-21) - Migraine Disability Assessment Test (MIDAS) - McGill's Short Form Questionnaire (MPQ-SF) - Mindfulness Inventory (MAAS)

Results

Primary outcome	- Distress p< 0.0001 - Disability p< 0.0001 - Pain intensity index p< 0.035 - Mindfulness p< 0.0001 Sub-scale of MAAS: - Emotional dimension of pain p< 0.0001

Quality Assessment

Quality Index

Item 14-26*	Total score **10**/13

* For further information look at "Attachment A – QI"

Data Collection Form

Wells R E, 2020

Effectiveness of Mindfulness Meditation vs Headache Education for Adults With Migraine: A Randomized Controlled Trial

DOI: 10.1001/jamainternmed.2020.7090

General Information

Date form completed: 04.04.2022

Name of person extracting data: Carla Difranco

Study Eligibility

Inclusion	Mindfulness as therapy for headache (migraine and/or cephalgia) ☒
Exclusion	Animals ☐; Infants ☐; Psychiatric patients ☐; Healthy subjects ☐; Abstract ☐; Review ☐; Not english ☐

Characteristics of study

Methods

Aim of study	Determine if MBSR improves migraine outcomes and affective/cognitive processes compared with headache education
Design	Double-blinded, randomized clinical trial
Unit of allocation	MBSR group and Headache education group
Duration of participation	8-week + 3 periods follow-up (12, 24, 36 weeks)

Participants

Population description	Adults with migraine
Inclusion criteria	- Diagnosis of migraine (International Classification of Headache Disorders-2, ICHD-2) - Between 4 and 20 migraine days per month - History of migraine for at least 1 year - At least 18 years old - Availability for 8 weekly classes
Exclusion criteria	- Regular mind-body practice - Unstable medical or psychiatric illness - Severe clinical depression (Patient Health Questionnaire,PHQ-9, >20) - Nonmigraine chronic pain - Medication overuse headache (MOH by ICHD-2) - Current or planned pregnancy - Use of new migraine medication within 4 weeks - Inability to maintain stable medications for study duration - Incomplete baseline headache log - Absence of pain ratings to noxious (49 °C) stimuli - For each cohort, 1 day/ time class option was available; if the participant was not available on that day/time, they were not eligible for that cohort but could be notified for future cohort eligibility
Method of recruitment of participants	Participants were recruited by targeting patients and health care professionals from widespread community advertising and a large tertiary care academic medical center in Winston-Salem, North Carolina
Pathology	Migraine headache
No.	89
Age, mean (SD)	44 (12) MBSR group, 44 (14) Headache education group
Sex, males/females	7/82

Intervention Group

Group name	MBSR group (Mindfulness-Based Stress Reduction)
Duration of treatment period	8 weeks + 3 periods follow-up (12, 24, 36 weeks)
No. randomised to group	45
Age mean (SD)	44 (12)
Type of intervention	Participants could continue current acute and preventive migraine medications and were requested to maintain stable medications for study duration. 2 hours/week for 8 weeks (with optional retreat day), the MBSR instructor followed the standardized curriculum to teach mindfulness meditation/yoga without migraine modifications. The MBSR participants received electronic audio files for home practice and were encouraged to practice at home 30 minutes per day.

Control Group

Group name	Headache education group
Duration of treatment period	8 weeks + 3 periods follow-up (12, 24, 36 weeks)
No. randomised to group	44
Age, mean (SD)	44 (14)
Type of intervention	Participants could continue current acute and preventive migraine medications and were requested to maintain stable medications for study duration. The headache education group received instruction on headaches, pathophysiology, triggers, stress, and treatment approaches 2 hours/week for 8 weeks (with optional retreat day).

Outcomes

Primary	Change in monthly migraine day frequency from baseline to 12 weeks
Secondary	- Migraine Disability Assessment (MIDAS)-1 month - Headache Impact Test-6 (HIT-6) - Migraine-Specific quality of Life Questionnaire, version 2.1 (MSQv2.1) - Patient Health Questionnaire-9 (PHQ-9) - Generalized Anxiety Disorder-7 (GAD-7) - Pain Catastrophizing Scale (PCS) - Headache Management Self-Efficacy Scale (HMSE) - Five-Facet Mindfulness Questionnaire (Each outcome assessed changes from baseline to 12, 24, and 36 weeks)

Results

Primary outcome	Statistically significant improvemnets from baseline at all follow-up time points: - MIDAS $p< 0.001$ - MSQv2.1 $p< 0.01$ - PHQ-9 $p< 0.008$ - PCS $p< 0.001$ - HMSE $p< 0.04$

Quality Assessment

Quality Index

Item 14-26*	Total score **13**/13

* For further information look at “Attachment A – QI”