Pediatric Neurology 165 (2025) 22–30

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Review Paper

Acupuncture for Prevention of Primary Headaches in Children and Adolescents: A Literature Overview for the Pediatric Neurologist

Alessia Raffagnato, MD [a, 1], Maria Paola Rossaro, MD [a, 1], Elena Piretti, MD [b], Laura Galdiolo, MD [a], Maria Federica Pelizza, MD [c], Stefano Sartori, MD, PhD [c, d], Margherita Nosadini, MD, PhD [c], Irene Toldo, MD, PhD [c, *]

[a] Child and Adolescent Neuropsychiatric Unit, Department of Women's and Children's Health, University of Padua, Padua, Italy
[b] IRCCS, Institute of Neurological Sciences of Bologna, Bologna, Italy
[c] Pediatric Neurology and Neurophysiology Unit, Department of Woman's and Child Health, University of Padua, Padua, Italy
[d] Neuroscience Department, University of Padua, Padua, Italy

ARTICLE INFO

Article history:
Received 11 April 2023
Accepted 26 December 2024
Available online 30 December 2024

Keywords:
Acupuncture
Prevention
Children and adolescents
Migraine
Headache

ABSTRACT

Background: To deepen the role of acupuncture as preventive treatment for pediatric primary headaches in children and adolescents and to understand if acupuncture is more effective than sham acupuncture or pharmacologic preventive treatment, acupuncture tolerability, and beneficial effect on psychiatric comorbidities.

Methods: A critical literature review was performed. Following PRISMA guidelines, all reports published (PubMed, 1982-2023) were considered. PICOS method was applied for paper selection. Efficacy measures were reduction of headache frequency, duration, and intensity compared with baseline, and, if available, with a control group. We also aimed to describe treatment protocols, the reason for choosing this treatment, patients' perception of acupuncture experience, and acupuncture's impact on headache comorbidity and general functioning.

Results: Five of 90 papers were selected, corresponding to a population of 229 children/adolescents (zero to 21 years). Among these, two controlled studies evaluated reduction of headache frequency, intensity, and duration.

True acupuncture versus placebo significantly reduced headache frequency (reduction of seven to eight headache days/month versus zero to one headache days/month, respectively), intensity on a visual analog scale (5.4 points compared with 1.6 points in placebo group), and headache duration. Tolerability data on acupuncture were favorable. Acupuncture experience was positively perceived by most patients, improved pain-related total interference in functioning, and reduced anxiety levels.

Conclusions: The few studies dealing with acupuncture as preventive treatment of pediatric primary headaches, despite their methodologic limitations, highlighted its efficacy. Further detailed studies are needed.

Introduction

Headache is the most common neurological symptom and the most frequent cause of pain in children; its prevalence increases from childhood to adolescence.[1,2] Especially when characterized by intense and frequent attacks, it can be a disabling disorder at any age.[3] Moreover, symptomatic medication overuse, poor treatment of migraine attacks,[4] and other complex multifactorial elements may turn headache into a chronic condition. Therefore, about one third of children with headache need preventive treatments to

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
* Communications should be addressed to: Dr. Toldo; Pediatric Neurology and Neurophysiology Unit; Department of Woman's and Child's Health; University of Padua; Via Giustiniani, 3; Padua 35128, Italy.
E-mail address: irene.toldo@unipd.it (I. Toldo).
[1] Alessia Raffagnato and Maria Paola Rossaro are co-first Authors and are equally responsible for the work described in this paper.

https://doi.org/10.1016/j.pediatrneurol.2024.12.013

reduce the frequency, intensity, and duration of attacks; to avoid acute medication overuse; and to improve quality of life by reducing disability due to recurrent headache.[5]

Recent migraine prevention guidelines support the use of pharmacologic and nonpharmacologic therapies (Petasites, feverfew, magnesium, and riboflavin)[6] as preventive treatments. However, the CHAMP (Childhood and Adolescent Migraine Prevention) study[7] demonstrated the absence of significant differences in the reduction of headache frequency or headache-related disability in children and adolescents with migraine, treated with amitriptyline, topiramate, or placebo.

In the last decades, among nonpharmacologic therapies, a growing interest in the use of complementary and alternative medicine (CAM) in pediatric pain management has been recorded[8]; a recent paper reported a high prevalence of CAM use in young patients (aged 10 to 17 years) with recurrent headaches associated with multiple chronic conditions and difficulties in daily functioning.[9]

Acupuncture is one of the most used CAM techniques and has been the focus of systematic meta-analysis,[10-15] showing encouraging results in adults. In a recent Cochrane review, acupuncture was deemed effective for frequent episodic or chronic tension-type headaches in adults.[13] A companion review on migraine reported consistent evidence of effectiveness of acupuncture in addition to symptomatic treatment of migraine attacks, being at least similarly effective to prophylactic medications.[14] Another recent review reported on acupuncture effectiveness and safety in migraine prevention in adults.[15]

Nevertheless, data in pediatric age are very limited.[16-21] In some of these studies, acupuncture has been compared with sham acupuncture. Sham acupuncture consisted in a different type of acupuncture (needles inserted more superficially, insertion into nontraditional site, or next to the acupoint) and has been arbitrarily considered like a placebo, but it is not excluded that it may have its own therapeutic effect.

The only review available in children and adolescents did not clearly state the methodology used; it included works with heterogeneous study designs and reports regarding acute treatment of headache or using other treatment methods different from acupuncture.[15]

The neurobiological mechanisms of acupuncture in headache treatment are not fully understood. Acupuncture seems to modulate pain perception both peripherally and centrally, with release of neurotransmitters such as endorphins, enkephalins, monoamines, norepinephrine, and serotonin.[15] Acupuncture could also have a role in modulating cerebral blood flow, but the physiological effect of using various classical acupoints may vary significantly.[15] Finally, acupuncture might also play a role in decreasing the activity of matrix metalloproteinases, the activation of which causes tissue injury and inflammation, which are reported in migraineurs.[15]

Taking these data into account, we conducted a critical analysis of the literature to better understand available data on the use of acupuncture as preventive treatment for primary headaches in children and adolescents useful to the pediatric neurologist.

In particular, it could be interesting to understand if acupuncture is more effective on headache prevention than sham acupuncture or pharmacologic preventive treatment (regardless of the use of symptomatic drugs for the attack). It is also interesting to know how acupuncture is tolerated and if it has a beneficial effect on psychiatric comorbidities (anxiety and depression), general functioning, and/or quality of life; also, reasons for choosing acupuncture and patients' positive or negative perception of acupuncture are interesting information to consider in practical management.

This article aims to add more detailed and focused information about the literature available focusing on the effect of acupuncture in the prevention of pediatric primary headaches.

Materials and Methods

To critically review the literature and extrapolate the information with a solid methodologic approach, the Population, Intervention, Comparison, Outcomes and Study (PICOS) method was applied.

Eligibility criteria according to PICOS[22] are the following:

(1) Types of studies: we included any study design investigating the prophylactic effect of acupuncture for pediatric headache;
(2) Types of participants: trials in which all participants were aged under 21 years and have been diagnosed with primary headache (episodic or chronic) were included;
(3) Experimental interventions: methods of stimulating acupuncture points, such as acupuncture, electrical acupuncture, or laser acupuncture were included; other methods of stimulating acupuncture points (like massage) or methods of stimulating pain points or trigger points were excluded;
(4) Control interventions (for controlled trials and randomized controlled trials):
   - sham acupuncture: interventions simulating true acupuncture/treatment, but different in at least one aspect such as correct point location or skin penetration;
   - pharmacologic prevention for primary headache (e.g., calcium channel antagonists, antiepileptics) or herbal medications;
(5) Outcomes measures: we included studies if they measured at least one of the following outcome measures:
   - efficacy measures: any headache parameters (frequency, duration, intensity of headache, consumption of analgesics) or measure of quality of life or disability;
   - tolerability measures: number of participants reporting any adverse event.

Study selection and data extraction

The literature research was carried out in PubMed (from 1982 to 2023), complying with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

The search terms used were (acupuncture) and ((treatment) or (management)) and ((primary headache) or (migraine) or (tension-type headache)) and (children and adolescents). Language restrictions were applied: papers written in English, French, Spanish, or German were included.

The available articles were searched manually for relevant articles. Two authors (E.P. and I.T.) screened all abstracts and full texts available and excluded the nonpertinent reports from the title and abstract. The authors checked all articles for eligibility according to the mentioned selection criteria and then extracted the following data in a form designed *ad hoc*: type of study; number of patients available for analysis; age; diagnosis; diagnostic criteria; intervention and comparison; outcomes; results; duration of follow-up post-treatment; results during follow-up; traditional Chinese medicine (TCM) diagnosis (according to meridian e/or syndrome); chosen acupoints (specified or not); type of treatment chosen between individualized treatment (acupoints specific for each patient), standardized treatment (the same acupoints for all patients), and semistandardized treatment (a pool of equal acupoints for all

patients together with individual acupoints for each patient); type of sham acupuncture; type of needle or other techniques; number of needles for a treatment session; duration of a treatment session; number of treatment sessions; frequency of treatment sessions; total duration of therapy; duration of follow-up post-therapy; and details for each outcome measure (pre- and post-treatment values and *P* values).

TCM consists of a holistic approach to diagnosis, pathophysiology, and therapy and includes herbal medications, acupuncture, and other physical therapy. TCM practice is generally regarded as a complementary or "alternative" form of medicine.

Assessment of risk of bias in included studies

For the assessment of study quality, the risk of bias assessment according to the Jadad scale was applied.[23]

Results

A total of 90 studies were identified through the database search. The different phases of the review are reported in Fig.

Among these 90 studies, 85 were excluded because they were nonpertinent for the study purposes. As the present study focuses on preventive headache treatment, including frequency, duration, and intensity outcomes, articles regarding the use of acupuncture as an acute treatment in pediatric primary headaches were excluded.[24-26]

Five full-text articles were assessed for eligibility and were included in the critical review.[16-18,20,27] Two articles focused on prevention of primary headaches with acupunture,[16,17] whereas the others dealt with the effect of acupuncture and of other CAM in patients with chronic pain (including primary headaches).[18,20,27]

The main results of these five studies[16-18,20,27] have been summarized in Table 1.

The first two selected clinical studies included a controlled trial with alternating allocation (not truly randomized) conducted by Pintov et al.[16] and a randomized, double-blind, placebo-controlled study conducted by Gottschling et al.[17] The main features of both studies are summarized in Table 2. The study population included patients with migraine (with or without aura; 22 patients), diagnosed according to Prensky criteria,[16] or tension-type headache (21 patients), diagnosed according to the International Classification of Headache Disorders-III criteria.[17,28]

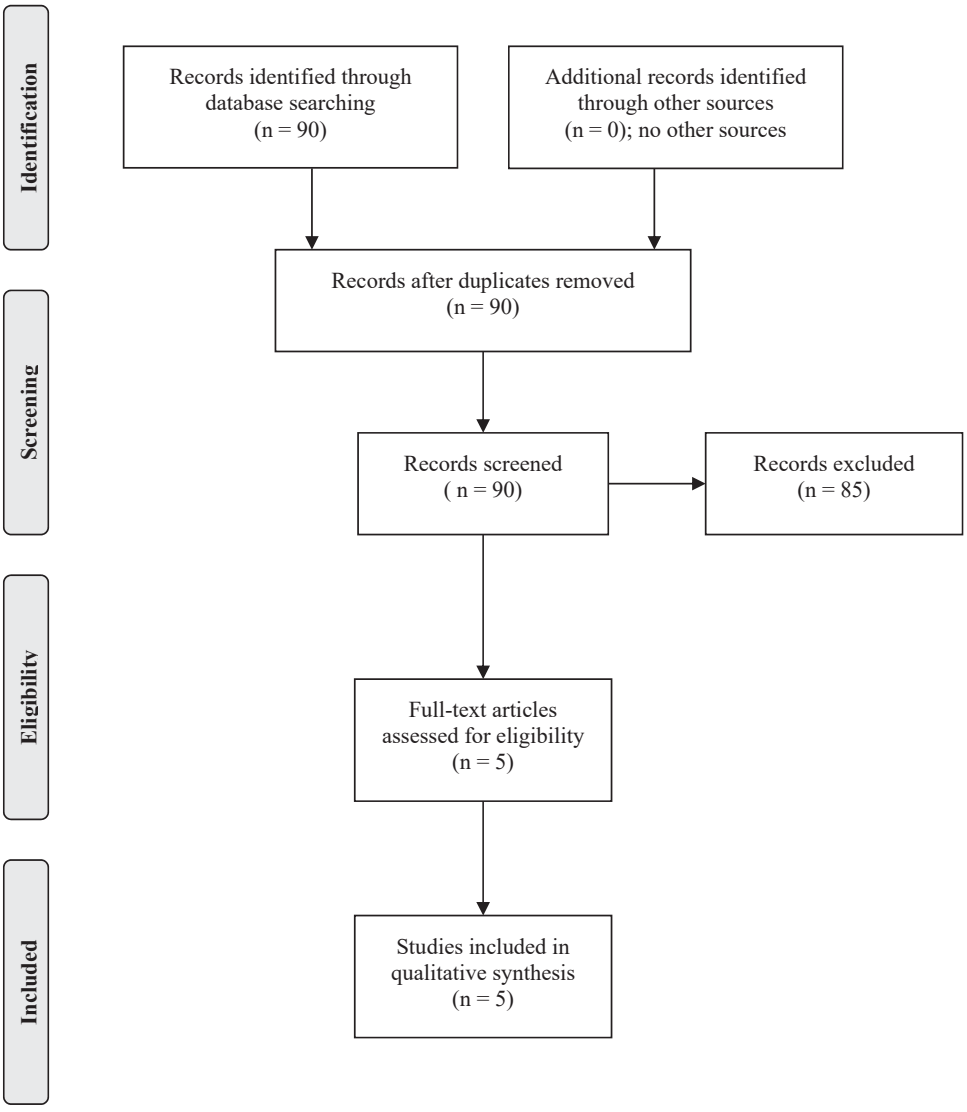

FIGURE. Flow diagram through the different phases of the review (PRISMA flowchart).

TABLE 1.
Review of Papers Focused on Acupuncture for Prevention of Primary Headaches in Children and Adolescents

Authors (Year)	No. of Patients Receiving True Acupuncture for Headache	Sex	Age (years)	Headache Type	Intervention	Comparison	Outcomes	Study Type
Pintov[16], 1997	12	7 f, 5 m	9.8 ± 1.2	MwoA, MwA (respective number unclear)	A. A B. Valuation of panopioid activity (with an opiate radioreceptor assay) and beta-endorphin-like immunoreactivity (by radioimmunoassay) in patients and in control subjects	A) A vs PA; B) A vs PA vs control subjects	1. Frequency 2. Intensity (VAS 0-10) 3. Panopioid activity (determination with an opiate radioreceptor assay) 4. Beta-endorphin-like immunoreactivity (determination by radioimmunoassay)	Alternate allocation, controlled
Kemper[18], 2000	7	37 f, 10 m*	16 (5-20)*	M	A	None	1. Answers of a qualitative interview with questions like "What was acupuncture like? Did the treatment help or hurt? Were there things that your child didn't like?" 2. Demographics and diagnostic information extracted from the medical record	Retrospective case series
Zeltzer[20], 2002	14	19 f 12 m*	13 ± 2.9*	Myofascial and M headaches	A and hypnosis	Baseline	1. Current pain and pain-related total interference in functioning 2. Depression symptoms 3. Anxiety 4. In-session pain (pre- and postsession of treatment) and anticipatory anxiety (only presession of treatment) ratings 5. Adverse events	Phase I clinical trial
Gottschling[17], 2008	22	14 f, 8 m	12.5 ± 2.8	M (MwoA, MwA) (11), TTH (11)	A (laser acupuncture)	A (laser acupuncture) vs PA (placebo laser acupuncture)	1. Frequency (headache days/month) 2. Duration (hours/month) 3. Intensity (VAS 0-10) 4. Dropouts 5. Adverse reactions	Double-blind, randomized, bicenter, placebo-controlled trial
McDonald[27], 2015	174	124 f 50 m	13.9 (0-21)	Headache or M	A) A B) Electroacupuncture C) Laser therapy D) Auricular acupuncture E) Moxibustion	None	1. Average pain score evaluation 2. Adverse events	Retrospective cohort

Abbreviations:
A = Acupuncture
f = Female
m = Male
M = Migraine
MwA = Migraine with aura
MwoA = Migraine without aura
PA = Placebo acupuncture
TTH = Tension-type headache
* On total population, not only patient receiving true (nonsham) acupuncture for headache.

The comparison was conducted between acupuncture and sham acupuncture (needles inserted more superficially)[16] and between laser acupuncture and placebo laser acupuncture.[17]

Pintov's study included 22 children (aged seven to 15 years) with migraine.

The true acupuncture group included 12 patients treated according to the principles of TCM, with subdermal insertion of the needle; in the placebo acupuncture group, which included 10 patients, a needle of the same size reached only the stratum corneum.[16] The treatment consisted of inserting three acupuncture needles in the upper and lower extremities for 15 minutes for 10 weekly sessions. None of the children received other prophylactic treatments for migraine. Patients of both arms were divided into two groups and completed the same weekly questionnaire (including number, duration, intensity, and treatment of migraine headache) for the 10-week prestudy period, the 10-week study period, and the next 10 weeks. Opioid activity in blood plasma was also assessed. *P* values were not mentioned; however, true acupuncture induced a reduction of headache frequency from 9.3 ± 1.6 to 1.4 ± 0.6 per month and of headache intensity from 8.7 ± 0.4 to 3.3 ± 1.0. By contrast, no significant changes were apparent in the frequency and intensity in the placebo group (9.4 ± 1.5 and 7.8 ± 0.6 before treatment vs 9.3 ± 1.4 and 6.2 ± 0.4 after treatment, respectively).

The true acupuncture group showed a gradual increase in the panopioid activity in plasma, which correlated with the clinical improvement.[16]

TABLE 2.
Summary of the Two Controlled Trials on Acupuncture for Prevention of Primary Headaches in Children and Adolescents

Main Features of the Studies	Pintov, 1997	Gottschling, 2008
Type of study	Controlled trial with alternating allocation (not truly randomized)	Randomized, double-blind, placebo-controlled trial
No. of patients available for analysis	22	43
Age	7-15 years. (median, mean, S.D. for total population unclear)	≤17 years (12.3 ± 2.6 years, mean and S.D.)
Diagnosis	MwoA MwA (respective number unclear)	22 MwoA, MwA 21 TTH
Diagnostic criteria	Prensky criteria	ICHD-II, 2004
Intervention and comparison	12 A vs 10 sham/ PA	22 Laser A vs 21 Laser PA
Outcomes	1. Frequency 2. Intensity (VAS 0-10) 3. Panopioid activity (determination with an opiate radioreceptor assay) 4. Beta-endorphin-like immunoreactivity (determination by radioimmunoassay)	1. Frequency (headache days/month) 2. Duration (hours/month) 3. Intensity (VAS 0-10) 4. Dropouts 5. Adverse reactions
Results A vs PA	1. A led to reduction of frequency; PA no (no *P* values) 2. A led to reduction of intensity; PA only slightly (no *P* values) 3. Greater in control subjects than in migraineurs before treatment; after A increased and became similar to control subjects, not after PA ($P < 0.01$) 4. Increased by 50% when compared with both control and PA ($P < 0.001$)	1. $P < 0.001$ 2. $P < 0.001$ 3. $P < 0.001$ 4. 5 Patients (not because headache or treatment) 5. 0 Patients
Results A and PA vs baseline	+ For A− For PA (not *P* values)	+ For A and PA but A ($P < 0.001$) > PA (only 2 $P < 0.05$ corresponding to intensity at weeks 1-4 and 13-16)
Duration of follow-up post-therapy	10 weeks	12 weeks
Does efficacy continue during follow-up?	Unclear	+ A ($P < 0.001$) > PA (only 2 $P < 0.05$ corresponding to intensity at weeks 1-4 and 13-16)
Therapeutics details of the studies		
Is TCM diagnosis made according to meridian e/or syndrome?	No	Partial, only according to meridian
Type of treatment: is treatment individualized, standardized, or semistandardized?	Unclear	Semistandardized
Are chosen acupoints specified?	No	Yes, fixed acupoints are listed
Type of PA	Minimal acupuncture	Laser placebo
Type of needle or other techniques	Unclear	True laser and laser placebo
No. of needles for a session of treatment	3	No limitations; 8.4 ± 4.7
Duration of a treatment session	15 minutes	Unclear
No. of treatment sessions	10	4
Frequency of sessions of treatment	1/week	1/week

Abbreviations:
A = Acupuncture
ICHD = International Classification of Headache Disorders
MwA = Migraine with aura
MwoA = Migraine without aura
PA = Placebo acupuncture
TCM = Traditional Chinese medicine
TTH = Tension-type headache
VAS = Visual analog scale

Gottschling[17] included 48 patients (aged zero to 17 years) with unilateral or bilateral headache, either migraine or tension-type headache, excluding patients with secondary headache.

Patients were treated with a class 3B laser (schwa-medico Modulas-Handy 2/99, 30 mW, 830 nm, continuous wave, power density 3.8 W/cm2, 1 mm laser beam diameter, REF 205237, schwa-medico, Ehringshausen, Germany) or with placebo laser. Laser radiation was in continuous wave mode, with vertical contact with the skin, 30 seconds duration, and ~0.9 J/point intensity.

Patients received a headache diary and started with a four-week-prerandomization phase, focusing mainly on days per month with headache, duration of headache per day, severity of pain on a 10-cm visual analog scale (VAS), and type and amount of rescue medications; the above-mentioned variables were then documented in the headache diary until 16 weeks from baseline.

Patients were randomized into true laser or placebo laser and received once-a-week a laser acupuncture treatment by one experienced acupuncturist. For both the acupuncturist and the patient, it was impossible to differentiate between active and placebo laser. Treatment was based on TCM criteria, in some patients combined with a computer-based measurement of skin resistance differences at defined points to narrow down the range of applicable points. A combination of TCM body acupuncture and auriculotherapy was applied. Basic points for patients with frontal headache were the large intestine and stomach; for patients with lateral headache, San Jiao and gallbladder; for patients with occipital pain, small intestine and bladder, and for patients with holocephalic pain, Du Mai. Additional body or ear acupuncture points could have been chosen on a patient basis. During all stages of the study, patients were allowed to treat acute headaches.

In Gottschling's study,[17] laser acupuncture significantly reduced the frequency (−7.0 days in the active group compared with −1.2 days in the placebo group), intensity, and duration of headache compared with the placebo treatment ($P < 0.001$).[17] No adverse effect was reported.

TABLE 3.
Risk of Bias Summary: Authors' Judgments About Each Risk of Bias Item for Each Included Study, According to the Jadad Score

Risk of Bias	Pintov, 1997	Gottschling, 2008
Was the study described as randomized (this includes words such as randomly, random, and randomization)? 0/1	1	1
Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc.)? 0/1	0	1
Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately or according to date of birth, hospital number, etc.) 0/−1	0	0
Was the study described as double blind? 0/1	0	1
Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc.)? 0/1	0	1
Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet vs injection with no double dummy)	0	0
Was there a description of withdrawals and dropouts? 0/1	1	1
Total Jadad score	2	5
Guidelines for Assessment		
Randomization A method to generate the sequence of randomization will be regarded as appropriate if it allowed each study participant to have the same chance of receiving each intervention and the investigators could not predict which treatment was next. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation should not be regarded as appropriate.		
Double blinding A study must be regarded as double blind if the word "double blind" is used. The method will be regarded as appropriate if it is stated that neither the person doing the assessments nor the study participant could identify the intervention being assessed, or if in the absence of such a statement the use of active placebos, identical placebos, or dummies is mentioned.		
Withdrawals and dropouts Participants who were included in the study but did not complete the observation period or who were not included in the analysis must be described. The number and the reasons for withdrawal in each group must be stated. If there were no withdrawals, it should be stated in the article. If there is no statement on withdrawals, this item must be given no points.		

The results of risk of bias assessment of the two above-mentioned studies have been summarized in Table 3.

Three studies[18,20,27] dealt with acupuncture as treatment for pediatric chronic pain (including primary headaches).

These series included heterogeneous study populations, and the number of patients with primary headaches is limited (seven of 47 migraine,[18] 14 of 31 migraine and myofascial pain,[20] and 27 of 174 headache not otherwise specified[27]).

Kemper et al.[18] conducted, by a qualitative telephone interview, a retrospective study on 47 patients with chronic pain, seven of them with migraine, treated with a median number of 8 acupuncture sessions, by a pediatric acupuncturist. The number and duration of sessions were variable and those data were referred to the overall study population not allowing data extraction on patients with headache. All but one patient were treated with regular acupuncture needles. Forty-five percent of patients also received intradermal needles, whereas non-needle methods of point stimulation were moxibustion or heat (85%), cupping (26%), and magnets (26%).[18]

In Kemper's study, patients and parents were asked to describe acupuncture experience as positive, negative, or neutral and to state the helpfulness of the treatment. The experience with acupuncture was rated positive by 67% of patients and 60% of parents and negative by 13% of patients and 7% of parents.[18] Among 30 patients with headache and their parents, 70% of patients and 59% of parents felt that acupuncture had definitely helped pain, 27% of patients and 34% of parents reported no change in pain perception, and no patient and only one parent reported pain seeming worse after the treatment. No information about acupuncture perception was available in the other studies.[16,17,20]

Acupuncture definitely improved pain-related total interference in functioning after treatment.[20] Moreover, after treatment, anxiety levels, anticipatory anxiety, and in-session pain ratings reduced[20]; nevertheless, depression symptoms were unchanged.[20]

Zeltzer et al.[20] conducted a clinical prospective study assessing the feasibility and the acceptability of a combined acupuncture/hypnosis treatment in 31 patients, 14 of them with migraine and myofascial pain. All participants maintained their existing treatment regimens during the study period.

Four to six needles were inserted in relevant locations. Acupuncture points were individually selected according to TCM, and performed for six treatment sessions, once every week. Serin acupuncture needles, #00, 1, or 2 gauge × 30 mm, were used. After the first session, all children became comfortable with a full treatment (six to 15 needles). After the needle's insertion, a clinical psychologist conducted the hypnosis sessions.[20]

Just before and following each treatment, children were administered an in-session rating form to evaluate their present pain. Anticipatory anxiety ratings were also obtained immediately before needle insertion. After the final (sixth) session, participants and their caregivers completed a post-treatment questionnaire. All items were rated on a 0 to 6 scale.

Current pain significantly decreased from 3.46 (S.D. 1.50) to 1.93 (S.D. 1.63) ($P < 0.001$; child rate) and from 3.19 (S.D. 1.30) to 1.81 (S.D. 1.63) ($P < 0.01$; parents' rate), although there was no change in average pain ratings.

In the post-treatment period, both parents and children endorsed a significantly reduced interference in general physical activity from 4.32 (S.D. 1.70) to 3.14 (S.D. 2.29) ($P = 0.01$) in child's reports and from 4.41 (S.D. 1.76) to 3.18 (S.D. 2.36) ($P < 0.01$) in parents' reports and a reduced interference in activities with friends from 3.97 (S.D. 2.08) to 2.57 (S.D. 2.15) ($P = 0.015$) in child's reports and from 4.97 (S.D. 2.18) to 3.19 (S.D. 2.70) ($P < 0.01$) in parents' reports.

Only parents indicated decreased interference in child's ability to concentrate on schoolwork from 4.24 (S.D. 1.86) to 2.89 (S.D. 2.06) ($P < 0.01$) and activities at home from 4.10 (S.D. 1.84) to 2.79 (S.D. 2.23) ($P < 0.01$), whereas only children endorsed a reduction in interference with eating/appetite from 3.00 (S.D. 2.27) to 2.04 (S.D. 2.36) ($P < 0.01$).

There was a significant reduction in the child's ratings of total pain-related interference in functioning from pre- to post-treatment from 30.48 (S.D. 11.50) to 23.13 (S.D. 17.11) ($P = 0.014$). Parents' ratings also indicated a significant decrease in overall pain-

related interference following treatment from 33.34 (S.D. 13.34) to 23.89 (S.D. 17.35) ($P < 0.01$).

Child-reported depression symptoms remained unchanged from pre- (z score range 1.42 to 2.38) to post-treatment (z score range 1.15 to 2.05). However, the sample was not significantly depressed at baseline. For child anxiety levels, there was a reduction from pretreatment (mean scores clinical: 34.03, S.D. 6.39) to post-treatment (mean scores in normal range: 30.39, S.D. 7.48) ($P = 0.019$).

McDonald[27] included 174 patients (124 female, 50 males), with an average age of 13.9 years with different pain syndromes (headache/migraine, back pain, abdominal pain, abdominal migraine, neuralgia, etc.). The authors used acupuncture and acupuncture-related therapies, also performing multiple treatments for the same patient: acupuncture body needling (96%), electroacupuncture (90%), auricular acupuncture (32%), laser acupuncture (49%), electron transfer facilitated by ionic cords (17%), and moxibustion (27%). VAS score was obtained before any intervention and at the end of each treatment session. Acupuncture with needles used three needle applications per visit (10 to 20 minutes for each application) and was performed with DBC Spring Ten needles (15 to 50 mm needle length); electroacupuncture was performed with a HAN E600 electroacupuncture unit with combination of low- and high-frequency stimulation (2 to 100 Hz every three seconds); auricular acupuncture was performed with Aiguille D'Acupuncture Semi-Permanente, Sedatelec gold needles in efficacious ear points; moxibustion was done with Ultra-Pure "Gold Mountain" Moxa in hand-rolled cones (heat stimulation eight times at each point); electron transfer was done with Manaka ion pumping cords; and laser therapy was performed with an HY05-A Aini therapeutic laser (large laser at 28 J/cm^2 energy, in continuous mode for 20 minutes per application, and a small laser at 85 J/cm^2 energy, in continuous mode, for stimulation of individual points for 30 seconds on each point).[27]

Overall, 91.8% of patients had decreased global pain scores (from 5.5 to 2.2 VAS scale) and 40% of patients achieved complete pain resolution. Considering the subgroups (inpatients and outpatients), pain scores in patients with headache decreased from 4.8 to 1.9 VAS scale ($P < 0.001$) and in migraineurs treated in hospital they decreased from 7.0 to 1.7 VAS scale ($P < 0.001$). No adverse events were recorded.[27]

In Table 4 we summarized the outcomes evaluated in the papers included.

Discussion

Among the five selected articles, there are only two placebo case-control studies documenting a significantly superior effect of true acupuncture versus placebo in the reduction of headache frequency and intensity, documented in both studies,[16,17] and duration, evaluated only in Gottschling study.[17] However, we should consider that Gottschling's work[17] is a true laser acupuncture treatment versus placebo laser, whereas in Pintov's work[16] the "placebo" arm consists of needle insertion in the stratum corneum; consequently, a therapeutic effect of this procedure cannot be ruled out beyond the placebo effect. It is therefore difficult to draw conclusive information with respect to the effectiveness of acupuncture versus placebo.

Regarding the analysis of the methodology of the above-mentioned two studies, a Jadad score of 5 confirms good trial quality for the randomized clinical trial conducted by Gottschling et al.[17] whereas the other study,[16] with a Jadad score of 2, has many methodologic limitations.

A strength of Pintov's study is the longitudinal evaluation of an objective variable (determination of total opioid activity and of beta-endorphin-like immunoreactivity by radioimmunoassay) with respect to headache evolution during treatment, to establish its efficacy; this work demonstrated a correlation between the gradual increase of the plasmatic panopioid activity and clinical improvement.[16] Several studies have suggested the role of the opioid system in the pathogenesis of migraine, with conflicting results. In fact, in one study,[16] plasma beta-endorphin levels were found to be reduced during migraine attacks (when compared with migraine-free periods and with healthy control subjects[16]), whereas in other studies, plasma values were similar in patients with migraine attacks compared with headache-free periods.[29,30] More studies are needed to better investigate the possible use of endogenous opioids as markers of analgesia and the possible correlation of their plasma level with clinical improvements in patients with migraine.

In the two above-mentioned studies, outcome evaluation was based on reduction of frequency, intensity, and duration of headache compared with baseline, without reporting response rates, which instead is a parameter commonly used when evaluating the effect of pharmacologic prophylaxis (i.e., CHAMP study[31]).

Moreover, other outcomes could be relevant, such as analgesic consumption[32] and the impact of treatment on general functioning/quality of life, on emotional-behavioral attitude,[13] and on psychiatric comorbidities, but this information is lacking in both studies.

To obtain more information about acupuncture in children, we also analyzed articles considering chronic or recurrent pain treatment or treatment of different medical conditions in pediatric patients, which, despite the lack of specific data about the use of acupuncture in patients with primary headaches,[18,20] might, nevertheless, allow the deduction of indirect information.

It is also interesting to know acupuncture's tolerability, reasons for choosing acupuncture, and patients' positive or negative perception of acupuncture, which are useful information to consider in practical management.

The impact of treatment on quality of life and on emotional-behavioral attitude and anxiety was evaluated only in one

TABLE 4.
Summary of the Outcomes Evaluated in the Papers Included in the Review

	Headache Frequency	Headache Intensity	Headache Duration	Associated Symptoms	Consumption of Analgesics	Quality of Life	Tolerability	Effect on Comorbidity	Acupuncture Perception
Pintov, 1997	X	X							
Gottschling, 2008	X	X	X				X		
Kemper, 2000									X
Zeltzer, 2002						X	X	X	
McDonald, 2015		X					X		

study,[20] which considered a heterogeneous population of pediatric patients with chronic pain (only 46% with headache) who underwent acupuncture combined with hypnosis. However, results are encouraging, showing an improvement in general functioning and physical and social activities and a reduction of anxiety.[20] Assessment of treatment tolerability was not reported in most of the articles,[16,18] whereas in the Gottschling's, Zeltzer's, and McDonald's studies no adverse events were recorded.[17,20,27]

Acupuncture perception was positive for the majority of patients when it was evaluated.[18]

There are no specific data in the literature on the reasons for choosing acupuncture, as the data concern the choice of CAM in general.[21]

A comparison between acupuncture and pharmacologic preventive treatments has not been performed so far.

Limitations

The small number of studies included and the heterogeneity of the samples represent a potential limitation of our study; however, in the literature data regarding this topic are scarce.

As regard the age range, it was not possible to extract data referring exclusively to patients aged less than 18 years, and this represents another limitation.

The duration of longitudinal follow-up was quite short in two studies,[16,17] making it difficult to evaluate the persistence of treatment effects in the medium-long term.

Conclusions

This study used a practical and clinically oriented approach to provide the pediatric neurologist with overall literature information for the utilization of acupuncture in the prevention of pediatric primary headaches and to implement the therapeutic strategies for these conditions, particularly in cases not responsive or not candidable to preventive drugs.

Even if available studies focusing on this topic are limited and have some methodologic limitations, their results on efficacy and tolerability in pediatric age are really encouraging.

A better knowledge of acupuncture as a therapeutic option for pediatric primary headaches is desirable to give proper individualized counseling to children and their parents on this treatment. A better alliance between parents and clinician can assure higher therapeutic compliance and higher likelihood of a positive outcome for patients.[33] Further randomized controlled trials are required to investigate efficacy and tolerability of acupuncture in the management of pediatric primary headaches to finally establish the role of this treatment.

CRediT authorship contribution statement

Alessia Raffagnato: Writing – review & editing, Methodology, Data curation, Conceptualization. **Maria Paola Rossaro:** Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Elena Piretti:** Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Laura Galdiolo:** Methodology, Data curation. **Maria Federica Pelizza:** Visualization, Data curation, Conceptualization. **Stefano Sartori:** Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Margherita Nosadini:** Project administration, Methodology, Investigation, Data curation, Conceptualization. **Irene Toldo:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

All authors are responsible for reported research and have no conflicts to disclose.

References

1. Wöber-Bingöl Ç. Epidemiology of migraine and headache in children and adolescents. Curr Pain Headache Rep. 2013;17:341.
2. Abu-Arafeh I, Razak S, Sivaraman B, et al. Prevalence of headache and migraine in children and adolescents: a systematic review of population-based studies. Dev Med Child Neurol. 2010;52:1088–1097.
3. Stovner LJ, Hagen K, Jensen R, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia. 2007;27:193–210.
4. Wakerley BR. Medication-overuse headache. Pract Neurol. 2019;19:399–403.
5. Toldo I, De Carlo D, Bolzonella B, et al. The pharmacological treatment of migraine in children and adolescents: an overview. Expert Rev Neurother. 2012;12:1133–1142.
6. Loder E, Burch R, Rizzoli P. The 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. Headache. 2012;52:930–945.
7. Powers SW, Coffey CS, Chamberlin LA, et al. Trial of amitriptyline, topiramate, and placebo for pediatric migraine. N Engl J Med. 2017;376:115–124.
8. Lin YC, Lee ACC, Kemper KJ, et al. Use of complementary and alternative medicine in pediatric pain management service: a survey. Pain Med. 2005;6:452–458.
9. Bethell C, Kemper KJ, Gombojav N, et al. Complementary and conventional medicine use among youth with recurrent headaches. Pediatrics. 2013;132:e1173–e1183.
10. Linde K, Allais G, Brinkhaus B, et al. Acupuncture for tension-type headache. Cochrane Database Syst Rev. 2009:CD007587.
11. Dach F. Acupuncture for migraine prophylaxis. Sao Paulo Med J. 2015;133:540.
12. Vickers AJ, Cronin AM, Maschino AC, et al. Acupuncture for chronic pain: individual patient data meta-analysis. Arch Intern Med. 2012;172:1444–1453.
13. Linde K, Allais G, Brinkhaus B, et al. Acupuncture for the prevention of tension-type headache. Cochrane Database Syst Rev. 2016;2016:CD007587.
14. Linde K, Allais G, Brinkhaus B, et al. Acupuncture for the prevention of episodic migraine. Cochrane Database Syst Rev. 2016;2016:CD001218.
15. Doll E, Threlkeld B, Graff D, et al. Acupuncture in adult and pediatric headache: a narrative review. Neuropediatrics. 2019;50:346–352.
16. Pintov S, Lahat E, Alstein M, et al. Acupuncture and the opioid system: implications in management of migraine. Pediatr Neurol. 1997;17:129–133.
17. Gottschling S, Meyer S, Gribova I, et al. Laser acupuncture in children with headache: a double-blind, randomized, bicenter, placebo-controlled trial. Dtsch Zeitschrift fur Akupunkt. 2009;137:405–412.
18. Kemper KJ, Sarah R, Silver-Highfield E, et al. On pins and needles? Pediatric pain patients' experience with acupuncture. Pediatrics. 2000;105:941–947.
19. Young L, Kemper KJ. Integrative care for pediatric patients with pain. J Altern Complement Med. 2013;19:627–632.
20. Zeltzer LK, Tsao JCI, Stelling C, et al. A phase I study on the feasibility and acceptability of an acupuncture/hypnosis intervention for chronic pediatric pain. J Pain Symptom Manage. 2002;24:437–446.
21. Dalla Libera D, Colombo B, Pavan G, et al. Prescription of complementary and alternative medicine (CAM) in an Italian cohort of pediatric headache patients. Neurology. 2014;35:145–148.
22. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6:e123–e130.
23. Berger V, Alperson S. A general framework for the evaluation of clinical trial quality. Rev Recent Clin Trials. 2009;4:79–88.
24. Esparham A, Boorigie M, Ablatt S, et al. Improving acute treatment of pediatric primary headache disorders with a novel headache treatment center: retrospective review of preliminary outcomes. J Child Neurol. 2021;36:54–59.
25. Graff DM, McDonald MJ. Auricular acupuncture for the treatment of pediatric migraines in the emergency department. Pediatr Emer Care. 2016;34:258–262.
26. Tsai SL, Reynoso E, Shin DW, et al. Acupuncture as a nonpharmacologic treatment for pain in a pediatric emergency department. Pediatr Emerg Care. 2021;37:e360–e366.
27. McDonald MJ. Acupuncture and acupuncture-related therapies are well-tolerated and can effectively provide pain relief in the pediatric population. Med Acupunct. 2015;27:481–486.

28. The international classification of headache disorders, 3rd edition (beta version). Cephalalgia. 2013;33:629–808.
29. Baldi E, Salmon S, Anselmi B, et al. Intermittent hypoendorphinaemia in migraine attack. Cephalalgia. 1982;2:77–81.
30. Bach FW, Jensen K, Olesen J, et al. β-endorphin and acth in plasma during attacks of common and classic migraine. Cephalalgia. 1985;5:1468–2982.
31. Hershey AD, Powers SW, Coffey CS, et al. Childhood and Adolescent Migraine Prevention (CHAMP) study: a double-blinded, placebo-controlled, comparative effectiveness study of amitriptyline, topiramate, and placebo in the prevention of childhood and adolescent migraine. Headache. 2013;53:799–816.
32. Tfelt-Hansen P, Block G, Dahlöf C, et al. Guidelines for controlled trials of drugs in migraine: second edition. Cephalalgia. 2000;20:765–786.
33. Gatta M, Ramaglioni E, Lai J, et al. Psychological and behavioral disease during developmental age: the importance of the alliance with parents. Neuropsychiatr Dis Treat. 2009;5:541–546.