

Homeopathic Treatment of Patients with Migraine: A Prospective Observational Study with a 2-Year Follow-Up Period

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Abstract

Objectives and background: The objective of this study was to evaluate treatment details and possible effects of an individualized homeopathic treatment in patients with migraine in usual care.

Design: This was a prospective multicenter observational study. Consecutive patients beginning homeopathic treatment in primary care practices were evaluated over 2 years using standardized questionnaires. The data recorded included diagnoses (International Classification of Diseases, Ninth Revision) and current complaints, including their severity (numeric rating scale = 0–10), health-related quality of life (QoL, 36-item Short-Form Health Survey), medical history, consultations, homeopathic and conventional treatments, as well as other health service use.

Results: Two hundred and twelve (212) adults (89.2% women), mean age 39.4 ± 10.7 years were treated by 67 physicians. Patients had suffered from migraine for a period of 15.2 ± 10.9 years. Most patients (90.0%) were conventionally pretreated. The physician workload included taking the initial patient history (120 ± 45 minutes), case analysis (40 ± 47 minutes), and follow-ups (7.3 ± 7.0 , totaling 165.6 ± 118.8 minutes). Patients received 6.2 ± 4.6 homeopathic prescriptions. Migraine severity showed marked improvement with a large effect size (Cohen's $d = 1.48$ after 3 months and 2.28 after 24 months. QoL improved accordingly (Mental Component Score and Physical Component Score after 24 months: 0.42 and 0.45). The use of conventional treatment and health services decreased markedly.

Conclusions: In this observational study, patients seeking homeopathic treatment for migraine showed relevant improvements that persisted for the observed 24 month period. Due to the design of this study, however, it does not answer the question as to whether the effects are treatment specific or not.

Introduction

MIGRAINE IS A COMMON ILLNESS, with a life-time prevalence of about 14% worldwide (9% in men, 20% in women), and is more commonly observed in Europe (15%) and North America (13%).¹ It typically manifests itself with disabling attacks, accompanied with a unilateral headache, often of a pulsating quality, that are often associated with nausea, phonophobia, or photophobia, and can be preceded by a peculiar aura.² The quality of life is reduced even in pain-free intervals.³ Migraine is probably caused by neuronal hyperexcitability and an alteration of pain perception.⁴ Pharmacological treatment for migraine includes nonsteroidal anti-inflammatory drugs (NSAIDs), antiemetics, triptans, and ergot alkaloids. Estrogen can also be administered for

menstrual migraine.^{2,5} Prevention can be attempted with β -blockers, antiepileptics, NSAIDs, antidepressants (tricyclics, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors), calcium channel blockers, as well as serotonin antagonists, magnesium, or vitamin B₂.^{2,5} (for a rating of the clinical effect and the quality of evidence for the individual substances see Silberstein⁵). A World Health Organization rating placed migraine among the most disabling diseases, together with active psychosis, dementia, and quadriplegia.² Patient suffering as well as recommendations to start migraine medication early have resulted in headaches from medication overuse, which is a major health problem (not in the least from the side-effects) with a prevalence of about 1%.⁶ Most nonpharmacological options (cognitive behavioral therapy, relaxation training, Indian head massage,

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hypnosis, transcutaneous nerve stimulation, cervical manipulation, and others) have not produced sufficient evidence to be recommended as the main therapy, but they may be helpful for prevention (e.g., trigger awareness and avoidance training), or as adjuvants.⁵ This status has changed since the advent of biofeedback⁷; however, this is not generally available in Europe. The evidence for acupuncture has long been inconclusive^{8–13} but is now considered “at least as effective as, or possibly more effective than, prophylactic drug treatment”¹⁴ and “has fewer adverse effects.”¹⁴

Homeopaths are often consulted for headache and migraine,^{15,16} and homeopathy is practiced in many regions of the world,¹⁷ especially in high-income countries where it ranks as the most popular among the traditional, complementary, or alternative medicines.^{17–19} In homeopathy, a diagnosis can be treated with different remedies in different patients (“individualization”), depending on varying concomitant symptoms. Homeopathic drugs (“remedies”) are produced by alternating steps of diluting and agitating a starting substance; the resulting “potencies” quickly reach dilutions beyond Avogadro’s number where the probability that one molecule of the starting substance is still present approaches zero. Such “high potencies” are often used; however, their effects constitute a subject of scientific controversy.²⁰ Meta-analyses of placebo-controlled trials (pooling a great variety of diseases and ailments) have shown inconsistent results.^{21–23} In our study, we evaluated the use and effects of a wide range of homeopathy treatments under the conditions of usual care in Germany. For this we followed 3981 patients over a 2-year period in a prospective observational study.^{16,24,25} This article presents the subgroup of 212 adults consulting homeopathic physicians because of migraine.

Methods

In this prospective multicenter observational study, patients were included consecutively upon their first consultation with a participating physician and followed up over 24 months using standardized questionnaires. This article analyses the degree of patient suffering from migraine (International Classification of Diseases, Ninth Revision (ICD-9): 346.9, ICD-10: G43.9).²⁶ Study physicians were required to have passed certified training in classical homeopathy and have 3 or more years of experience in its practice (details of recruitment:²⁴). Written informed consent and approval by ethics review boards were obtained.

Before treatment (at baseline) patients, independent of their physicians, recorded the complaints that instigated homeopathic treatment, and rated their severity on a Numeric Rating Scale (NRS, 0 = no complaints, 10 = maximum severity).²⁷ The health-related quality of life (QoL) was recorded with the Medical Outcomes Trust 36-Item Short Form Survey Instrument (MOS SF-36)²⁸ questionnaire. The first questionnaires were handed out by study physicians and were completed before treatment. Patients sent them in sealed envelopes directly to the study office, from where they received follow-up questionnaires at 3, 12, and 24 months, with every complaint being transferred to the follow-up questionnaires to ensure continuous assessment. At the same intervals (0, 3, 12, and 24 months), the participating physicians recorded up to 4 diagnoses per patient and assessed their severity on identical NRS. On a continuous basis, they

recorded the homeopathic treatment, use of any conventional therapy, and all referrals.

As outcome measures, we defined: mean migraine severity, mean severity of all baseline diagnoses (pooled physician assessment), mean severity of all complaints (pooled patient assessment), and QoL scores. Statistical analysis (using SAS/STAT[®] v8.2 software) followed the intention-to-treat approach: every included patient entered the final analyses. We replaced missing values as follows: Cured complaints: severity = 0 in subsequent records; deceased patients: severity = 10. The remaining missing values were multiply imputed according to Rubin.²⁹ Each was given five distinct, but plausible values, based on correlations with nonmissing values and reflecting the overall variability of data. This generated a total of five distinct complete data tables, each without any missing values. These were analyzed separately (see below), and the results were pooled to calculate treatment effects and *p*-values.

For each imputed data set, treatment effects were estimated on the basis of a generalized multiple linear regression model: According to the recommendations by Diggle et al.,³⁰ we assumed the treatment course to be a mix of a piecewise linear part (0–3 months and 3–24 months) and a quadratic term (starting at 3 months). The serial correlation was assumed to be exponential with time. Effect sizes (*d*) were calculated by dividing treatment effects as estimated above by baseline standard deviations. They were classified: as $|d| > 0.8$, large; $|d| > 0.5$, medium; $|d| > 0.2$, small.

Usually, patients seek treatment when their health is under par (such as severe pain, low QoL, etc.). A natural alleviation of their illnesses (regression to the mean) can be mistaken for an effect from the initiation of treatment.³¹ Separating regression to the mean from treatment effects requires the mean of the target population to be known or plausibly assumed. For the QoL, we applied Mee and Chua’s test³² under the assumption that the patients had the same QoL as in the general German population.²⁸

Results

In the present analysis 212 patients, treated by 67 physicians, were included (Table 1). All patients suffered from migraine that had lasted on average 15.2 ± 10.9 years. Patients diagnosed with additional forms of headache were excluded. Almost all accompanying diagnoses assessed at baseline were chronic diseases. These had usually been previously treated, in the majority of cases, with conventional therapy (Tables 1 and 2), and the most frequent diagnoses had lasted for at least 3.6 ± 4.9 years (Table 2).

The consultations consisted of an extensive initial case history (Table 3), followed by the analysis of the case. All but 1 of the patients received the first homeopathic medication on the same day as the first consultation. The subsequent consultations, about half of which were telephone calls, were much shorter (Table 3). The last homeopathic medication was recorded after an average of 12.9 ± 9.8 months. Half of the patients (55%) were continuing to use homeopathic care at the end of the study (Table 3) or had suspended it only temporarily. Over the course of the study, patients received 6.2 ± 4.6 homeopathic prescriptions. More than half of all prescriptions were covered by 10 homeopathic remedies (Fig. 1), but in total, 138 remedies were applied. The most

TABLE 1. DEMOGRAPHICS AND BASELINE STATUS

Population	
Patients	212
Female	89.2% (189)
Age (years) ± SD	39.4 ± 10.7
≥10 years school	57.5% (122)
Patient expected: homeopathy (% , N)	
Will help	63.7% (135)
Will maybe help	35.4% (75)
Will not help	0.5% (1)
Baseline diagnoses	
Total, number, ±SD	3.1 ± 0.9
Severity (NRS)	6.2 ± 1.5
Chronic, number, ±SD	3.0 ± 0.9
Any baseline diagnosis pretreated (% , N)	
Any treatment	90.0% (190)
Medication ^a	77.3% (163)
Surgery	16.6% (35)
Other	67.8% (143)

^aExcluding homeopathy.

NRS, numerical rating scale: 10 = maximum, 0 = cured; SD, standard deviation.

frequently used potencies were: C200, 32.5%; C1000, 24.4%; C30, 10.6%; C10000, 8.4%; Q3, 3.7%; Q1, 3.3%.

The greatest improvement in the severity of diagnoses and medical complaints was seen in the first 3 months, and it generally continued during the full observation period (Tables 4 and 5). Physicians' severity assessments tended to be more positive than patients' assessments; however, all changes from baseline were of a large effect size (1.90–2.85). All improvements in health-related QoL showed a smaller effect size (SF-36 physical component score 0.45, mental component score 0.42) and happened mostly within the first 3 months. Mee-Chua tests for the SF-36 confirmed a treatment effect after 3, 12, and 24 months for the physical component score ($p = 0.0002, 0.0001, \text{ and } 0.0001$ respectively), but not for the mental component score ($p = 0.4309, 0.2501, \text{ and } 0.1238$).

After 24 months, the severity of the migraine as well as the other baseline diagnoses were considerably relieved (Table 6), while large reductions in the use of conventional medicines and health care services were also observed (Table 7).

TABLE 2. BASELINE DIAGNOSES

	ICD-10 code	Patients (% , N)	Severity (NRS)	Duration (years)
Migraine	G43.9	100.0% (212)	6.4 ± 1.9	15.2 ± 10.9
Sleep disturbance	G47.9	8.5% (18)	6.4 ± 2.3	4.3 ± 3.0
Allergic rhinitis	J30.4	6.1% (13)	5.8 ± 2.2	16.1 ± 10.1
Atopic eczema	L20.9	5.7% (12)	5.1 ± 2.3	13.4 ± 12.9
Chronic sinusitis	J32.9	5.2% (11)	5.2 ± 2.1	7.5 ± 9.3
Dermatitis	L30.9	5.2% (11)	6.1 ± 1.9	3.6 ± 4.9
Premenstrual tension syndrome	N94.3	5.2% (11)	6.4 ± 1.7	10.8 ± 6.5

NRS, numerical rating scale: 10 = maximum, 0 = cured. Only diagnoses seen in ≥5% of the patients.

ICD-10, International Classification of Diseases, Tenth Revision.

TABLE 3. CONSULTATIONS AND CONTINUANCE OF HOMEOPATHIC TREATMENT AT STUDY END

Consultations (mean ± SD)	
1st consultation (min)	120 ± 45
Case analysis (min)	40 ± 47
Follow-ups: N, all	7.3 ± 7.0
Telephone	3.3 ± 5.4
Practice	3.2 ± 3.5
FUs duration (min), all	20.7 ± 12.5
Telephone	7.7 ± 4.1
Practice	30.3 ± 17.1
FUs cumulated (min), all	165.6 ± 118.8
Telephone	48.6 ± 54.8
Practice	132.8 ± 89.5
Last consultation (month)	15.4 ± 9.7
Homeopathy at study end	
Treatment ongoing	33.0% (70)
Changed homeopath	0.5% (1)
Currently not treated	22.2% (47)
Treatment ended because of ...	
Cure or amelioration	4.2% (9)
Reason outcome-unrelated	5.7% (12)
No effect or aggravation	19.8% (42)
No stated reason	0.5% (1)
No answer to treatment status	14.2% (30)

SD, standard deviation; FUs, follow-ups.

Discussion

This prospective multicenter observational study aimed to give an unbiased representation of contemporary homeopathic health care, including its outcomes in 212 patients with migraine. Assessments of illness severity and health-related QoL consistently showed substantial improvements, although the illness was long-standing, chronic, and conventionally pretreated. Similarly, all accompanying diseases (almost all of which were chronic) were markedly ameliorated. The major improvements were seen within the first 3 months of homeopathic treatment. Accordingly, QoL increased, and the use of health care services or conventional medication decreased markedly.

The methodological strengths of our study include the consecutive patient enrollment and use of standardized outcome instruments. For the purposes of quality assurance, we decided against a random sample of homeopathic

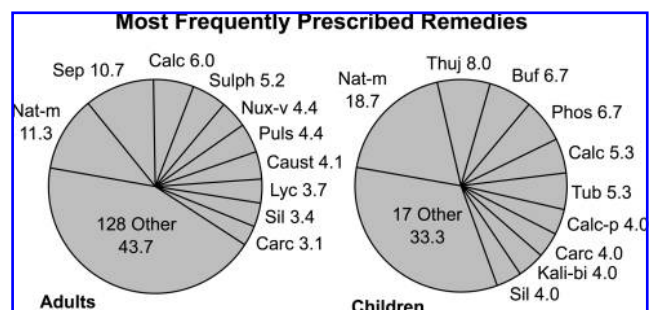


FIG. 1. Most frequently prescribed homeopathic remedies in adults and children. Percentage of prescriptions during the study period is shown next to each remedy. Remedies are identified with traditional abbreviations.

TABLE 4. DIAGNOSES, COMPLAINTS, QUALITY OF LIFE (ESTIMATED MEANS AND 95% CONFIDENCE INTERVALS [CIs] FROM THE STATISTICAL MODEL)

	Status (95% CI)					Change (95% CI)			
	Month 0	Month 3	Month 12	Month 24	Months 0–3	Months 0–12	Months 0–24	Months 0–12	Months 0–24
Severity									
Migraine, NRS ^a	6.42 (6.13; 6.70)	3.53 (3.25; 3.82)	2.47 (2.19; 2.76)	1.98 (1.70; 2.27)	-2.88 (-3.15; -2.62)	-3.94 (-4.27; -3.61)	-4.43 (-4.79; -4.07)		
All diagnoses (mean), NRS ^a	6.17 (5.95; 6.40)	3.76 (3.54; 3.99)	2.65 (2.43; 2.88)	1.98 (1.75; 2.20)	-2.41 (-2.60; -2.22)	-3.52 (-3.76; -3.28)	-4.19 (-4.46; -3.92)		
All complaints (mean), NRS ^b	6.42 (6.13; 6.71)	3.85 (3.54; 4.16)	3.45 (3.20; 3.70)	3.25 (2.99; 3.51)	-2.58 (-2.86; -2.29)	-2.98 (-3.32; -2.64)	-3.17 (-3.57; -2.78)		
Quality of life ^b									
SF-36 physical component score	44.46 (42.77; 46.15)	48.59 (46.85; 50.32)	49.31 (47.70; 50.93)	49.79 (48.17; 51.41)	4.12 (3.15; 5.10)	4.85 (3.35; 6.35)	5.33 (3.40; 7.25)		
Mental component score	40.20 (38.39; 42.00)	45.46 (43.57; 47.36)	45.15 (43.50; 46.79)	45.65 (43.98; 47.32)	5.26 (3.82; 6.70)	4.95 (3.01; 6.89)	5.45 (3.10; 7.81)		

All changes $p < 0.001$.

^aPhysicians' answers.

^bPatients' answers.

NRS, numerical rating scale; 10 = maximum, 0 = cured. Quality of life: higher values = better; SF-36, 36-Item Short Form Survey Instrument.

physicians, but recruited only physicians trained and certified in "classical" homeopathy. Our results are, therefore, representative only for classical homeopathy. However, this is the type of homeopathy that is accepted and certified by the German Medical Association. The subgroup presented in this article is a representative sample of contemporary homeopathic practice, as about 14% of participants of the main study were members of an association for physicians practicing "classical" homeopathy (the Hahnemann Association). In contrast to randomized trials, our study describes patients from everyday practice with multiple morbidities and a large variety of lifestyles. This ensures a high degree of external validity that allows extrapolation to usual medical care. Our study was designed to evaluate homeopathic treatment in patients suffering from various diagnoses. This disallowed the use of more complex disease-specific measurement instruments. We used a Numeric Rating Scale that is validated, commonly used,²⁷ and broadly accepted to measure pain. In addition, we used generic QoL questionnaires.

As a general observation, especially for industrialized countries, homeopathic patients tend to be younger, better educated, of higher socioeconomic status than conventional patients, and are more often female.³³ These factors could be indicative of a health-awareness above average and an inclination to self-treatment for lesser ailments.³⁴ As a result, accompanying chronic diseases were strongly predominant in our study, as was seen in other observations.^{15,34–37} Additionally, waiting lists of up to several months would exclude the shorter periods of acute illnesses. The reputation of homeopathy as a "medicine for the whole person" (reflected in the extensive initial case history) may cause a self-selection of patients seeking more than a quick fix for a single issue. In addition to migraine, many of the patients also suffered from sleep disturbance, allergic rhinitis, and atopic dermatitis/eczema. The latter two were also among the most frequent in other homeopathic observational studies.^{15,38} The long duration of the diseases was also typical,^{35,38,39} along with the high number of pretreated patients, indicating that patients turn to homeopathy after finding conventional care unsatisfactory for their conditions. In comparison to (hypothetical) conventional practices, the patients in our study are likely to suffer from more severe, long-standing diseases and to seek help from a homeopath at an advanced stage of the disease, possibly they have a more critical or demanding attitude toward health care providers, due to previous disillusionment.

The cost-effectiveness of an early-referral strategy has not been thoroughly investigated to date.^{40,41} Medication costs are negligible, while the duration of homeopathic consultations is clearly longer than the average 7.6 ± 4.3 minutes of a German General Practitioner consultation.⁴² This might be compensated by their low frequency. On average, conventional consultations take place about 24 times per patient in 24 months, with a resulting doctor workload of about 190 minutes in 2 years.⁴³

Our study focused on the widespread individualizing ("classical") homeopathy and did not evaluate other types of homeopathy. In a broader interpretation of the rule of similes (like treating like), remedies were selected for symptoms both typical of the diagnoses and those accompanying the predominating pathologies ("constitutional"). The broad variety of chosen remedies, the frequent use of high potencies,

TABLE 5. EFFECT SIZE OF CHANGES IN DIAGNOSES, COMPLAINTS, AND QUALITY OF LIFE

	Effect size (95% CI)		
	Months 0–3	Months 0–12	Months 0–24
Severity			
Migraine, NRS ^a	1.48 (1.62; 1.35)	2.03 (2.20; 1.86)	2.28 (2.47; 2.09)
All diagnoses (mean), NRS ^a	1.64 (1.76; 1.51)	2.39 (2.55; 2.23)	2.85 (3.03; 2.66)
All complaints (mean), NRS ^b	1.54 (1.71; 1.37)	1.78 (1.98; 1.58)	1.90 (2.13; 1.66)
Quality of life ^b			
SF-36 physical component score	0.35 (0.26; 0.43)	0.41 (0.28; 0.54)	0.45 (0.29; 0.61)
Mental component score	0.41 (0.30; 0.52)	0.38 (0.23; 0.54)	0.42 (0.24; 0.61)

All effects $p < 0.001$.

^aPhysicians' answers.

^bPatients' answers.

NRS, numerical rating scale, negative change = improvement. Quality of life: positive change = improvement. Absolute effect size > 0.8 large, > 0.5 medium, > 0.2 small. 95% CI, 95% confidence interval.

and the similar frequencies of the leading remedies in migraine treatment (Fig. 1), are typical for this type of homeopathy and were also observed in the main study.¹⁶

The effect size of the severity ratings after 12 and 24 months was large. This may be partly explained by placebo effects and/or regression to the mean, which our study was not designed to control (effect sizes in between-group comparisons are usually smaller). In addition, we cannot rule out an overestimation of the treatment effect. The QoL improvements, on the other hand, may have been greater than recorded: The SF-36 is unlikely to overestimate changes; the mental scales have even been found to be less sensitive than the mental and social scales of other instruments such as the Duke Health Profile.³⁵ We assume that a diagnosis-specific tool to measure the psychosocial component in migraine suffering might report greater effects.

It would be almost impossible to ascribe all of the observed QoL improvements to a regression toward the mean phenomenon. These improvements were significantly greater than could be expected, when defining chronically ill patients with several, often severe, diseases as having the same QoL as the general German population. This was itself an extremely conservative approach. Moreover, patients received homeopathic treatment after years of other treatment and a waiting period. It would be expected that regression toward the mean would long have faded out by then.

Our results are consistent with another prospective observational study by Muscari-Tomaioli et al.⁴⁴ (44 patients,

chronic migraine or tension-type headache, assessed after 4–6 months). This study found marked improvements in all SF-36 scores. However, neither study should simply be interpreted as supporting conclusions regarding the efficacy of homeopathic remedies in migraine treatment. Our study was designed to observe real-life conditions and did not aim to determine the specific effect of a homeopathic remedy. Therefore, the extent to which the observed effects are due to the homeopathic remedies remains unclear.

Only one of four randomized clinical trials (RCTs) saw a difference between the homeopathic remedies and the placebo controls in the primary outcomes.⁴⁵ However, there has been some discussion on how to interpret the results. The early RCT published in 1991 by Brigo and Serpelloni⁴⁶ (60 patients, chronic migraine, last assessment after 4 months) found dramatic superiority in the verum group (frequency, intensity, duration, spontaneous resolution), whereas the RCT by Walach et al.⁴⁷ (98 patients, any chronic headache except post-traumatic, treated for 12 weeks) found no superiority of homeopathy, and its continuation as open-label prospective observation⁴⁸ made no substantial difference. Patients in this trial were older than the patients in our study (median verum group = 51 years, median placebo group = 46 years; our study: median = 37.5 years), they had suffered from migraine/headache for much longer (mean = 29 years, median = 23 years; our study: median = 14.5 years) and probably at a greater intensity (median headache duration of 8 hours/day). Study physicians observed that they were "much more difficult to treat than the patients that they usually see."⁴⁸ This study⁴⁷ excluded patients taking hormonal contraception, which certainly shifted the patient selection toward atypical cases (women in their reproductive years constitute the largest group of migraine sufferers⁴⁹). Also, the recruitment through advertisements may have attracted patients who otherwise would not have considered homeopathy. Whether the highly unusual prescribing by consensus (where group dynamics may override the intuition of the experienced homeopath) contributed to the result can only be speculated.⁵⁰

Patients in the Whitmarsh RCT⁵¹ (64 patients, migraine by International Headache Society (HIS) criteria, treated for 3 months) had baseline differences: The placebo group had more frequent but less severe headaches. The trial found no differences between the groups despite improvements in both.

TABLE 6. RESPONSE RATES AT STUDY END

Responders, migraine (patients, %, N)	
Fully cured	19.8% (42)
Better by $\geq 50\%$ baseline	28.3% (60)
Better by $\geq 10\%$... <50%	4.7% (10)
Change within $\pm 10\%$	0.0% (0)
Worse >10%	0.9% (2)
Responders, all diagnoses (diagnoses, %, N)	
Total number	452
Fully cured	34.3% (155)
Better by $\geq 50\%$ baseline	28.3% (128)
Better by $\geq 10\%$... <50%	6.6% (30)
Change within $\pm 10\%$	4.6% (21)
Worse >10%	0.9% (4)

TABLE 7. USE OF OTHER TREATMENT AND HEALTH CARE SERVICES

	Baseline % (N)	3 Months % (N)	12 Months % (N)	24 Months % (N)
Patients using conventional drugs ^a				
Any drug ^b	104.7% (222)	71.2% (151)	75.0% (159)	82.5% (175)
ATC class Z—central nervous system	28.3% (60)	21.2% (45)	20.8% (44)	22.2% (47)
Not ATC classified	13.7% (29)	8.5% (18)	7.1% (15)	15.1% (32)
Analgetics	15.1% (32)	9.4% (20)	7.1% (15)	11.8% (25)
	Baseline	>0–3 Months	>3–12 Months	>12–24 Months
Patients using nonpharmaceutical treatments ^a				
Any therapy ^b	70.8% (150)	20.8% (44)	36.8% (78)	45.3% (96)
Nonsurgical therapies	67.0% (142)	19.3% (41)	33.0% (70)	40.1% (85)
Acupuncture	33.5% (71)	2.8% (6)	8.0% (17)	13.7% (29)
Patients consulting other health care ^a				
Any physician ^b	96.2% (204)	39.6% (84)	64.2% (136)	75.9% (161)
Total number of consultations ^b	(857)	(341)	(356)	(561)
General practitioner	70.8% (150)	12.3% (26)	27.4% (58)	42.0% (89)
Hospital	17.5% (37)	1.4% (3)	4.7% (10)	10.4% (22)
Neurologist	35.8% (76)	3.3% (7)	9.0% (19)	12.7% (27)
Any CAM treatment	24.1% (51)	2.4% (5)	6.6% (14)	10.4% (22)
Other homeopath	19.8% (42)	0.0% (0)	2.4% (5)	5.2% (11)
Osteopath	1.9% (4)	0.9% (2)	1.4% (3)	1.4% (3)
Nonmedical CAM practitioner	4.2% (9)	1.4% (3)	2.8% (6)	4.7% (10)
Referrals by homeopath ^c				
Any physician ^b	-/-	1.4% (3)	3.3% (7)	4.2% (9)
Neurologist	-/-	0.0% (0)	0.5% (1)	0.5% (1)

Data are related to migraine only.

^aPatients' answers.

^bIncluding all diagnoses and routine checks (e.g., dentist, gynecologist). Multiple answers possible.

^cPhysicians' answers. Table lines holding only 0 values were omitted.

CAM, complementary and alternative medicine; ATC, Anatomical Therapeutic Chemical Classification System.

The verum group stopped having moderate to severe headaches, while the mild headaches improved in the placebo group. The placebo group improved early in the study but worsened again toward the end, whereas the verum group improved more slowly but continued to improve at the end of the study. Whitmarsh argues that a longer study duration would have shown a clear difference.⁵⁰ The RCT by Straumshiem et al.⁵² (64 patients, migraine by IHS criteria, treated for 4 months) found a similar 30% decrease in the frequency of diary-recorded attacks for both verum and placebo groups and thus no significant group difference for the primary outcome. Four (4) months after the treatment was started, an assessment of the treatment outcome by patients and a (blinded) neurologist showed a significant difference in the frequency of attacks per month in favor of homeopathy. This discrepancy is puzzling, but might be understood from a homeopathic point of view. The self-assessment of treatment outcome could be based on a general feeling of well-being that would have preceded a clinical improvement – such is often observed in homeopathic practice. As far as the available data allows a conclusion, the populations in the above RCTs differed from the patients in our study. Whitmarsh commented on the three abovementioned RCTs^{47,51,52} that “none of the studies are really studying ‘typical patients’ and all are looking at groups hard to treat by any standards.”⁵³ Yet interestingly, none of the above studies found severe side-effects of the homeopathic treatment.

The observed reduction in conventional or alternative medication and treatments is to a certain extent due to the

homeopathic doctrine of reducing interventions to a minimum (making classical homeopaths effective “gatekeepers”). The resulting cut-down in (self-)medication for acute relief, the overuse of which can cause refractory headaches that may require strict withdrawal regimens and auxiliary medication,^{2,6} could have contributed to our results. Indeed, other increasingly recognized aggravating psychologic and behavioral factors may be involved,^{2,6} which can potentially cause a transformation or chronification of headache.⁶ The homeopathic approach not only restricts medication but also regulates or often prohibits stimulating agents such as coffee, other drugs, remedy-specific “antidotes,” or behaviors that cause known individual aggravations.^{2,54}

Finally, contextual effects strongly affect migraine treatment outcomes, which have been established for pharmaceutical placebos⁵⁵ and sham-acupuncture,^{13,56} with stronger effects for the latter: After 8 weeks of treatment, the number of headache days was reduced by $\geq 50\%$ in 51% of the acupuncture patients and 53% of the sham-acupuncture patients (waiting list: 15%), despite some degree of unblinding.¹³ Another study saw 52% verum and 49% sham responders (50% responder rates) after 6 weeks of treatment.⁵⁶ Here needling pain, violation of the body boundary, and direct biological effects might explain the strong effects and why sham-acupuncture appears to be superior to pharmaceutical placebos in migraine treatment.^{13,55,56} Other effects from the treatment context might be more influential than currently acknowledged. In general, every distinct treatment, such as homeopathy, will attract a population that reacts to it.⁵⁷

Patients' expectations and physicians' convictions are in concordance with the respective medical worldviews (for homeopathy see Astin and Bell et al.^{58,59}), and both are powerful triggers for placebo responses.^{60,61} This fact makes patients' self-selection into treatment courses a factor that cannot be neglected in its contribution toward healing. Besides the (debated) effect of homeopathic remedies, the patients in our study could thus have profited from the way homeopathy is perceived socially and psychologically. Additionally, theory and practice of homeopathy have throughout its history undergone several modifications that have, unintentionally, increased the active-healing context (e.g., longer and more detailed consultations, increased attention to psychosocial issues, conceptual bridges to worldviews of local culture and *zeitgeist*).⁶² The true extent of placebo/contextual effects in homeopathic treatment has not yet been investigated, and disentangling the above factors will be a difficult but promising task for future research. A detailed exploration of a complete classical homeopathic health care regimen under everyday conditions should provide insights into the active mechanisms that will, with no doubt, be of great use, for the optimization of care both for patients and health economic perspectives as well as for a better understanding of curative means that can be augmented in other areas of medicine.^{63–66}

Conclusions

In our observational study, patients with migraine showed marked and long-standing improvements under homeopathic treatment. Whether the observed effects can be attributed to the setting and contextual effects or to the homeopathic drug remains unknown. The evidence from previous RCTs was not in favor of a specific effect from homeopathic remedies. These studies, however, included only a very select group of patients and they have a low external validity. Future research under everyday conditions should help resolve these unanswered questions.

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