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Complementary and alternative medicine in epilepsy: A global survey of physicians' opinions

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ABSTRACT

Purpose: To investigate the opinions of physicians on the use of complementary and alternative medicine (CAM) in patients with epilepsy (PWE) worldwide.
Methods: Online survey addressed to neurologists and psychiatrists from different countries.
Results: Totally, 1112 physicians from 25 countries (different world region: Europe, North America, South America, Middle-East, Africa, Former Soviet Union Republics) participated; 804 (72.3%) believed that CAM might be helpful in PWE. The most commonly endorsed CAM included meditation (41%) and yoga (39%).

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Female sex, psychiatry specialization, and working in North and South America were associated with the belief that CAM is helpful in PWE. Two-hundred and forty five out of 1098 participants (22.3%) used/prescribed CAM to PWE; among them, 174 (71%) people perceived CAM to be less effective and 114 (46.5%) people found CAM to be safer than conventional antiseizure medications (ASMs). The most common reasons to prescribe CAM for PWE were: to satisfy the patient (49.9%), dissatisfaction with the efficacy (35.6%), and dissatisfaction with the adverse effects (31.2%) of conventional therapies.

Conclusion: Although the evidence supporting the use of CAM for the treatment of epilepsy is extremely sparse, most physicians worldwide believe that it could be integrated with the use of conventional ASMs, at least in some patients. High-quality controlled trials are warranted to provide robust evidence on the usefulness of CAM options in PWE.

1. Introduction

Epilepsy is a common chronic neurological disorder affecting about seventy million people worldwide [1]. Antiseizure medications (ASMs) represent the cornerstone of epilepsy treatment [2]. Despite the use of appropriate ASMs, about one-third of patients with epilepsy (PWE) have persistent epileptic seizures [3]. Epilepsy surgery is a valuable option for a limited proportion of patients with drug-resistant epilepsy [3]. On the other hand, ongoing drug-resistant epileptic seizures are associated with increased morbidity and mortality [4,5], and consequently may lead patients to seek unconventional treatment options for their problem.

Complementary and alternative medicine (CAM) is defined as healthcare and medical practices that are not an integral part of conventional medicine [6]. Complementary and alternative medicine is widely used worldwide, including in high-, middle-, and low-income countries [7,8].

The purpose of this international survey was to inquire about the opinions of physicians (neurologists and psychiatrists) on the use of CAM in the treatment of epilepsy. This information may provide useful guidance for public authorities involved both in education and healthcare to regulate the use of CAM in PWE.

2. Materials and methods

Practicing neurologists and psychiatrists from around the world were invited to participate in an online survey. On August 12th, 2020 we (AAP and FB) emailed an invitation including a questionnaire (using Google-forms) to lead neurologists and psychiatrists from 50 countries around the world. Only one person per nation was contacted primarily. We asked them to share the survey with as many of their colleagues as possible in their corresponding nations (the number is unknown). A reminder was sent every week. The study was closed on October 8th, 2020. The survey anonymously collected data about demographics, years in practice, discipline (neurology, psychiatry), country, work setting (university, hospital, or private clinic), and work location (urban, rural), and answers to questions about perception and usage of CAM [Do you think that any of the following might be helpful to treat seizures in people with epilepsy?; Have you ever used (recommended) anything other than conventional ASMs to treat your patients with seizures?; If yes, how did its effectiveness compare with the effectiveness of the conventional antiseizure medicines you prescribed?; If yes, how did its safety compare with the safety of conventional antiseizure medicines?; If you have used anything other than conventional antiseizure medicines to treat your patients, which were the reasons?] (Appendix 1). Fellows and residents were not included. There was no compensation for participation. The survey was conducted purely in the English language. This study was conducted with the approval of the Shiraz University of Medical Sciences Institutional Review Board.

We descriptively summarized the demographic variables and responses from the whole cohort. Univariate comparisons were made through the Mann–Whitney *U* test or Chi-squared test, as appropriate. The associations between baseline characteristics of the survey participants and responses to selected questions were determined by logistic regression entering all variables with $p < 0.05$ from the comparison of baseline characteristics into a multivariate model. Odds ratios (OR) and 95% confidence intervals (CI) were estimated. Results were considered significant for *p* values <0.05 (two-sided). Data analysis was performed using STATA/IC 13.1 (StataCorp LP, College Station, TX, USA).

Availability of data and material: The data will be shared upon request.

3. Results

Overall, 1112 physicians participated in this study. Appendix 2 shows the baseline characteristics of the participants. The physicians taking part in the survey came from the following regions across the world (only nations with more than 15 participants were singled out): North America (81) [USA (81)], South America (246) [Ecuador (45), Venezuela (44), Brazil (43), Argentina (42), Colombia (35), Chile (34)], Europe (211) [Italy (79), Austria (51), Sweden (37), Spain (30)], Middle-East (256) [Iran (64), Iraq (41), Kuwait (38), United Arab Emirates (36), Qatar (35), Oman (32)], Africa (155) [Egypt (48), South Africa (46), Nigeria (27), Morocco (27)], former Soviet Union Republics (134) [Kazakhstan (41), Armenia (40), Russia (36), Kyrgyzstan (17)], and others (29). The following nations were contacted, but did not participate in this study or had less than 15 participants: Europe: Belgium, Denmark, France, Germany, Ireland, Portugal, Switzerland, Turkey, UK, Ukraine; America: Canada and Mexico; Asia: China, India, Indonesia, Japan, Pakistan, Saudi Arabia, South Korea; Africa: Algeria, Kenya, Sudan, Tunisia; Oceania: Australia and New Zealand.

Among all the participants in the survey, 804 (72.3%) believed that CAM (one or more options) might be helpful to treat seizures in PWE. Detailed responses of the participants to the question: "Do you think that any of the following might be helpful to treat seizures in people with epilepsy?" are shown in Table 1. The most commonly endorsed CAM options included meditation (41%) and yoga (39%). Table 2 shows the characteristics of the participants according to their belief in CAM. Participants who reported to believe in CAM were more commonly women, had their specialization in psychiatry, and were in practice for fewer years. Across the world, the European physicians were those who less frequently believed in CAM (65.4%) and physicians working in North and South America were those who most frequently did so (81.5% and 82.9%, respectively). Female sex, specialization in psychiatry, and working in North and South America were independently associated with the likelihood of believing that CAM is beneficial to treat seizures (Table 3).

Table 1
Do you think that any of the following might be helpful to treat seizures in people with epilepsy?

Complementary and Alternative Medicine Modality	Helpful	Not helpful	I do not know
Herbal drugs	209 (18.8)	630 (56.7)	273 (24.6)
Exercise	428 (38.5)	478 (43.0)	206 (18.5)
Yoga	439 (39.5)	431 (38.8)	242 (21.8)
Meditation	455 (40.9)	422 (37.9)	235 (21.1)
Hypnosis	141 (12.7)	640 (57.6)	331 (29.8)
Acupuncture	134 (12.1)	677 (60.9)	301 (27.1)
Chiropractic care	52 (4.7)	796 (71.6)	264 (23.7)
Massage therapy	120 (10.8)	783 (70.4)	209 (18.8)
Reflexology	108 (9.7)	709 (63.8)	295 (26.5)
Aromatherapy	93 (8.4)	741 (66.6)	278 (25.0)
Homeopathy	89 (8.0)	726 (65.3)	297 (26.7)
Biofeedback	261 (23.5)	531 (47.8)	320 (28.8)
Psych readers	70 (6.3)	841 (75.6)	201 (18.1)
Exorcism	17 (1.5)	915 (82.3)	180 (16.2)
Prayers	174 (15.6)	712 (64.0)	226 (20.3)
*Traditional medicine	438 (39.4)	453 (40.7)	221 (19.9)

Data are number (%).
* This option was included to compensate and cover for any possible CAM option in different cultures that we might have missed in specific entities.

There were significant inter-region variabilities on beliefs in different items of CAM. The US participants most often believed in traditional medicine (TM) and meditation. The South American participants most often believed in TM and exercise. The European participants most often believed in TM and meditation. The Middle-Eastern participants most often believed in meditation and yoga. The African participants most often believed in yoga and meditation. The former Soviet Union participants most often believed in TM and yoga.

In response to the question "Have you ever recommended anything other than conventional ASMs to treat your patients with seizures?" Two-hundred and forty five out of 1098 participants (22.3%) answered "Yes". The most commonly recommended CAM therapies were exercise, yoga, and meditation (Table 4). The characteristics of the participants who recommended and did not recommend the use of CAM are shown in Table 5. Participants who recommended CAM were about five years younger and in clinical practice for a shorter time (about two years); the highest rate of CAM recommendation was observed among participants working in South America (32.1%). In the logistic regression analysis, residence in South America was the only independent predictor to recommend CAM to PWE ($_{adj}$OR 1.98, 95% CI 1.27–3.09; $p = 0.002$).

Among physicians who responded to have prescribed CAM to patients with seizures, 23 (9.4%) perceived CAM option to be more effective, 174 (71.0%) less effective, and 43 (17.6%) equally effective compared with conventional ASMs; five participants did not give any answer. Among practitioners who have prescribed CAM, 114 (46.5%) considered CAM option to be safer, 52 (21.2%) less safe, and 70 (28.6%) equally safe compared with ASMs; nine participants did not give any answer.

Table 3
Associations between baseline characteristics of the survey participants and belief in a beneficial role of complementary and alternative medicine to treat seizures in regression analysis.

Independent variables	‡Adjusted Odds Ratio (95% Confidence Interval)	*p* value
Female sex	1.37 (1.02–1.84)	0.034
*Discipline	1.58 (1.04–2.40)	0.031
Years in practice	1.00 (0.98–1.01)	0.471
**World region		
North America	2.51 (1.31–4.81)	0.006
South America	2.87 (1.81–4.56)	<0.001
Middle-East	1.19 (0.79–1.79)	0.401
Africa	1.13 (0.70–1.84)	0.614
Former Soviet Union	0.91 (0.56–1.48)	0.703
Other	1.43 (0.56–3.62)	0.457

‡ Adjustment for sex, discipline, years in practice, and world region.
* Discipline categorized as neurology versus psychiatry.
** The reference is Europe.

The most common reasons to prescribe CAM to treat PWE were: to satisfy the patient (49.9%), dissatisfaction with the efficacy (35.6%), dissatisfaction with the adverse effects (31.2%), and dissatisfaction with the cost (9.3%) of conventional therapy. Complementary and alternative medicine was more frequently prescribed in adult patients with drug-resistant epilepsy, in patients who used conventional ASMs, and those who explicitly asked for alternative/complementary treatments (Table 6). Since the participants could choose more than one answer, for the statistical analysis we compared those who exclusively mentioned "to satisfy the

Table 2
Baseline characteristics of the survey participants according to their belief in a positive role of complementary and alternative medicine to treat seizures in univariate analyses.

	Belief in CAM (*N* = 804)	No belief in CAM (*N* = 308)	*p* value
Sex (Male:Female)	367:431	165:142	0.021
Age (median [interquartile range]), years	42 [35–52]	43 [37–54]	0.089
Discipline (Neurology:Psychiatry)	662:138	265:37	0.043
Years in practice (mean ± standard deviation)	13 [6–24]	15 [8–25]	0.032
World region (Europe:North America:South America: Middle-East:Africa:Former Soviet Union:Others)	138:66:204:176:110:88:22	73:15:42:80:45:46:7	<0.001
Work setting (University:Hospital/Private Clinic)*	259:531	94:203	0.722
Work location (Urban:Rural)	763:36	290:18	0.354

Abbreviation: CAM = complementary and alternative medicine.
* Since participants could select "all that apply", we categorized this as University (Academia) (with or without others) *vs.* Not (Hospital/Private Clinic).

Table 4
Have you ever recommended any complementary and alternative medicine to your patients?

Complementary and Alternative Medicine Modality	Recommended to patients
Herbal drugs	77 (31.4)
Exercise	138 (56.3)
Yoga	108 (44.1)
Meditation	107 (43.7)
Hypnosis	19 (7.7)
Acupuncture	31 (12.6)
Chiropractic care	10 (4)
Massage therapy	18 (7.3)
Reflexology	19 (7.7)
Aromatherapy	19 (7.7)
Homeopathy	27 (11)
Biofeedback	48 (19.6)
Psych readers	19 (7.7)
Exorcism	9 (3.6)
Prayers	30 (12.2)
*Traditional medicine	68 (27.7)

* This option was included to compensate and cover for any possible CAM option in different cultures that we might have missed in specific entities. Data are number (%); percentages refer to the survey participants who answered "Yes" to the question (n = 245).

patient" (N = 99) with those who provided other reasons (N = 122); their recommendations were more or less similar (the most common recommendations were exercise, yoga, and meditation in the former and exercise, meditation, and yoga in the latter group).

4. Discussion

In this global survey, we observed that most physicians worldwide believe that CAM might overall be helpful to treat seizures in PWE. Previous studies have shown similar high rates of belief in CAM's antiseizure efficacy [9–11]. However, so far no large well-designed double-blind randomized placebo-controlled trial has evaluated the efficacy of any specific CAM option in the treatment of epilepsy [7].

While most of the neurologists and psychiatrists taking part in this survey believed in the helpfulness of CAM in treating PWE, only a minority reported having prescribed CAM to treat seizures and less than 10% have found CAM to be more efficacious than ASMs. In randomized, placebo-controlled, clinical trials of ASMs (add-on treatment in patients with drug-resistant epilepsy), the proportion of patients with ≥50% improvement in seizure frequency compared to their baseline ranged from 9.9% to 15.2% among the participants allocated to placebo groups [12]. Therefore, the rate of the perceived efficacy of CAM in controlling seizures that emerged in this survey (i.e., 9.4%) overlaps with the placebo response rates found in clinical trials.

The perception of the efficacy of CAM in treating epileptic seizures is most probably influenced by cultural backgrounds [11]. In our study, the world region was significantly associated with that: European physicians were those who less frequently believed in CAM, and physicians working in North and South America were those who most frequently did so. However, it is not clear whether the idea of using CAM in these countries have come from the patients or the physicians. In a previous study from Iran [8], 70% of the PWE, and 55% of the neurologists believed that CAM would help in treating epileptic seizures [8].

Other factors such as the gender of the treating physicians (women more commonly than men) and their discipline (psychiatry more commonly than neurology) might also influence this belief (Table 3). To the best of our knowledge, there is no previous study comparing neurologists with psychiatrists with regard to their belief in CAM for other disorders. However, previous studies have shown that generally speaking, women are more often keen to use CAM for various disorders [13,14]. The reasons behind this sex difference should be studied in the future.

Various other reasons may underlie the belief in CAM to treat epilepsies, including failure of conventional ASMs in controlling seizures, the comorbidities associated with epilepsy for which ASMs are of little help, the perception that CAM therapies are more natural and safer than ASMs, and the cost of ASMs [7,8,15]. In the current study, the most common reasons provided by the physicians for prescribing CAM were to satisfy the patient and also their dissatisfaction with the efficacy or tolerability of the current ASMs.

In the following sections, we discuss different CAM therapies used in PWE according to the current availability of data in the literature.

4.1. Herbal drugs

In our survey, approximately one-fifth of the physicians believed that herbal drugs might be helpful to treat seizures in people with epilepsy. Although herbal medicine is a centuries-old medical practice for the treatment of epilepsy in many nations and cultures, including the Middle-East, Africa, Europe, Asia, and America, there is no robust evidence on the efficacy and safety of most herbal drugs in humans [16]. Furthermore, differences exist in the use of herbal medicine across countries. In developed countries, herbal drugs are mainly used to control seizures, reduce the adverse-effects of ASMs, and maintain general health. In developing countries, herbal drugs are generally used as a substitute for conventional Western medicines [17].

While herbal drugs may provide a base for target-oriented ASM discovery and development, some herbal drugs may increase the risk of seizures because of their intrinsic proconvulsant properties or contamination by heavy metals, or through their effects on the cytochrome P450 enzymes and P-glycoproteins, altering ASMs pharmacokinetics [18].

Table 5
Baseline characteristics of the survey participants who recommended complementary and alternative medicine to treat seizures.

	CAM not recommended (N = 853)	CAM recommended (N = 245)	p value
Sex (Male:Female)	408:440	118:125	0.902
Age (median [interquartile range]), years	42 [35–51]	47 [37–55]	0.002
Discipline (Neurology:Psychiatry)	703:143	210:32	0.169
Years in practice (mean ± standard deviation)	13 [6–22]	15 [8–25]	0.021
World region (Europe:North America:South America: Middle-East:Africa:Former Soviet Union:Others)	165:65:167:208:117:109:22	46:16:79:41:37:19:7	0.001
Work setting (University:Hospital/Private Clinic)	271:561	78:163	0.952
Work location (Urban:Rural)	809:41	230:13	0.739

Abbreviation: CAM = complementary and alternative medicine.

Table 6
In which patients with epilepsy have you used (recommended) anything other than conventional antiseizure medications?

Only in patients with drug-resistant epilepsy	98 (40)
Only in seizure-free patients or those with a good seizure control	29 (11.8)
In patients with epilepsy, irrespective of seizure control with medications	66 (26.9)
Only in children	18 (7.3)
Only in adults	66 (26.9)
In patients of any age	41 (16.7)
Only in patients who explicitly asked for alternative/complementary treatments	87 (35.5)
Also in patients who did not ask for alternative/complementary treatments	35 (14.2)
Only in patients who refused conventional antiseizure medications	23 (9.4)
Also in patients who used conventional antiseizure medications	94 (38.4)

Data are number (%); percentages refer to the survey participants ($n = 245$) who answered "Yes" to the question "Have you ever recommended any complementary and alternative medicine to your patients?"

4.2. Exercise

In the present study, around two-fifths of the physicians believed that exercise might be helpful to treat seizures, and it was one of the most commonly recommended CAM therapies for PWE. The effects of exercise on mental health, cognition, and brain function have been extensively studied [19]. While the beneficial effects of exercise on PWE have been demonstrated in human and animal studies, the underlying mechanisms are still poorly understood [19].

Most experts believe that there should be no restrictions on the practice of exercise in patients with controlled epilepsy, except for scuba diving, skydiving, and other sports at heights. Broader restrictions may apply for people with uncontrolled seizures within the frame of an individual risk assessment taking into account the seizure types, frequency, and triggers [20].

4.3. Yoga

In the current study, near two-fifths of the physicians believed that yoga might be helpful to treat seizures, and it represents one of the most widely recommended CAM therapies to PWE. The possible beneficial effect of yoga in controlling epileptic seizures has been shown in 50 PWE from two trials [21]. Yoga induces relaxation and stress reduction and may influence the nervous system, thereby controlling seizures [21]. In a study of 300 people with epilepsy from India, the use of CAM by the respondents included yoga in 25.6% [22].

4.4. Meditation

In the current study, more than two-fifths of the physicians believed that meditation might be helpful to treat seizures. A systematic review of 20 randomized controlled trials including 958 subjects (397 experimentally treated and 561 controls) demonstrated no serious adverse events associated with meditation techniques [23]. The strongest evidence for the efficacy of meditation was found for epilepsy, mood, and anxiety disorders [23].

Transcendental (spiritual) Meditation (TM) has some physiological effects. Clinical studies using these techniques suggested that meditation may have potential antiseizure effects [24].

4.5. Hypnosis

Only a minority of the physicians believed in hypnosis as a good CAM option in epilepsy and recommended it. Hypnosis may help differentiate functional (psychogenic nonepileptic) seizures from epilepsy, as a suggestion (provocation) technique. However, there is no convincing evidence in the literature that supports the potential antiseizure efficacy of hypnosis [25].

4.6. Acupuncture

Few participants in the survey believed in acupuncture as a good CAM option in epilepsy. Acupuncture is a simple and safe traditional healing modality applied in a wide range of diseases [26]. However, available clinical trials on the efficacy of acupuncture are small, heterogeneous, have a high risk of bias, and do not support it as a therapeutic option in PWE [27].

4.7. Biofeedback

In the current study, approximately a quarter of the physicians believed that biofeedback might be helpful to treat seizures. Biofeedback is a noninvasive and seemingly adverse-effect free therapeutic option [28,29]. In a systematic review of biofeedback techniques in epilepsy, four studies were identified, involving 99 patients with drug-resistant epilepsy. The difference in seizure frequency percentage (Biofeedback-Control) was between −54.4 and −74.0%, with an overall weighted mean difference of −64.3%. The response rates varied from 45% to 66% across the studies [28].

4.8. Prayers

Around 12% of the physicians believed that prayers might be helpful to treat seizures. To the best of our knowledge, there is no evidence in the literature on antiseizure effects of prayers, spirituality, or religiosity. However, prayer and spirituality was the most commonly used form of CAM in a study of 228 PWE in the Midwestern United States [9]. Another study from Iran provided similar results to the previous study [8].

The practice of spirituality and religiosity may provide a positive coping strategy [30] and beneficial effects on mental health and quality of life [30,31]. Healthcare professionals could make use of spirituality by respecting individual beliefs [30].

4.9. Chiropractic care

According to this survey, less than 5% of the physicians believed that chiropractic care might be helpful to treat seizures and this practice was rarely recommended. However, in a study on the use of CAM in the Midwestern United States, chiropractic care was used by 24% of the 228 PWE [9]. There are some anecdotal reports on the usefulness of chiropractic care [32]. In a review of 17 reports of pediatric PWE who received chiropractic care, upper cervical care to correct vertebral subluxation was administered in 15 cases, and all reported favorable outcomes [32].

4.10. Reflexology

In the current study, approximately 10% of the physicians believed that reflexology might be helpful to treat seizures. In a clinical trial, 77 patients with drug-resistant epilepsy were randomly assigned to ASMs (control group) or ASMs combined with reflexology therapy [33]. The authors hypothesized that hand reflexology therapy could produce results similar to those of vagus nerve stimulation (VNS), and foot reflexology therapy could maintain homeostasis in the functional status of individual body parts. In the reflexology group, the median seizure frequency decreased from 9.5 to 2 ($p < 0.001$). In the control arm, the decrease was less than 25% [33]. Four patients in the reflexology group reported

adverse effects [nausea/vomiting ($n = 1$), change in voice ($n = 2$), and hoarseness ($n = 1$)] [33].

4.11. Aromatherapy

In the present study, only a minority of the physicians believed in aromatherapy to treat epilepsy. In a single low-quality study (uncontrolled trial, without clear inclusion and exclusion criteria) over a third of the patients using aromatherapy with or without hypnosis became seizurefree for at least one year [34].

4.12. Homeopathy

Only 8% of the participants in the survey answered to believe in homeopathy as a treatment option in epilepsy. In a study of 164 parents of children with epilepsy from Germany, 14 (9%) people reported using homeopathy as CAM for their children [13]. In a study of 300 PWE from India, the use of CAM included homeopathy in 16.3% of the respondents [22].

A polyherbal formulation was developed following the classical texts of homeopathy and further evaluated for its anticonvulsant activity in rats. The findings suggested that such polyherbal formulation might have possible efficacy in the treatment of epilepsy [35]. However, there are also reports of seizures associated with polyherbal formulations [36].

4.13. Exorcism

Less than 2% of the physicians believed in exorcism as a CAM option in epilepsy. In a face-to-face interview of 365 individuals without epilepsy in Nigeria, traditional medicine was the first preferred treatment option in 81% of the participants, and treatment approaches included herbal preparations (68%), spiritual exorcism (34%), and special cultural diets (29%) [37]. No evidence in the literature supports exorcism as an effective option in the treatment of epilepsy.

4.14. Others

Psych reading and massage therapy were considered valuable options for the treatment of epilepsy only by a few practitioners taking part in this survey. Currently, no study has evaluated these therapeutic options in PWE.

Of note, we included the option of "Traditional medicine" to compensate and cover for any possible CAM option in different cultures that we might have missed in specific entities; this was made to have the best picture possible on the response of the participants to the question "Do you think that any of the following might be helpful to treat seizures in people with epilepsy?". As traditional medicine is a very generic and not specific description, we decided to not explore this issue any further. Finally, there are some other CAM options (e.g., music therapy) that have been suggested to be applied in the treatment plan of PWE [38]; we did not include these in our study.

5. Limitations and Conclusion

This study has some limitations. The actual representativeness of the participants for each nation is not known (the ratio of the participants to the total number of the physicians in each nation) and also it is possible that physicians with a positive attitude/experience of CAM were more likely to participate in such a survey. Furthermore, the structure and language of the survey might have influenced the results. Finally, almost all participants (>95%) were from urban rather than rural work settings and this may have affected the results.

However, we can conclude that while the evidence supporting the use of CAM for the treatment of epilepsy is extremely scarce and of low quality, most participants worldwide believed that CAM could represent a possible therapeutic option for PWE. Remarkably, the rate of antiseizure efficacy of CAM options in PWE reported by the participants in this survey was consistent with the placebo response rates observed in randomized clinical trials of ASMs. Nonetheless, based on the available evidence, it seems that, at least in some cases, harmless CAM options (e.g., exercise, yoga, and biofeedback) could be integrated with conventional therapies to help patients with seizures. However, well-designed large randomized clinical trials are required to investigate the precise efficacy and safety profile of various CAM options in PWE before any recommendations could be made.

Alongside the ethical principles of respecting the patient's autonomy and avoidance of unnecessary costs for ineffective treatments, the principle of non-maleficence ("do no harm") should inform the appropriate use of CAM in clinical practice. Consequently, more efforts should be made to increase the knowledge of CAM among physicians practicing in the field of epilepsy, particularly with regard to its safety, efficacy, and costs, cultivating an evidence-based culture.

Conflict of interest

Ali A. Asadi-Pooya: Honoraria from Cobel Daruo, Tekaje, Sanofi, Actoverco, and RaymandRad; Royalty: Oxford University Press (Book publication); Grant from the National Institute for Medical Research Development. Others: no conflict of interest.

Simona Lattanzi has received speaker's or consultancy fees from Eisai, UCB Pharma, and GW Pharmaceuticals and has served on the advisory board for GW Pharmaceuticals.

Vicente Villanueva has participated in advisory boards or pharmaceutical industry-sponsored symposia by Arvelle, BIAL, EISAI, GW pharma, Newbridge, Novartis, UCB.

Torbjörn Tomson has received speaker's honoraria to his institution from Eisai, Sanofi, Sun Pharma, and UCB, and received research support from Stockholm County Council, EU, CURE, GSK, UCB, Eisai, and Bial.

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Authors' contributions

Ali A. Asadi-Pooya, Francesco Brigo, and Simona Lattanzi: study design, data collection, statistical analyses, and manuscript preparation.

Others: data collection and manuscript preparation.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2021.107835.

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