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Use of dietary and herbal supplements in adult patients with epilepsy

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ABSTRACT

Purpose: To study the extent and characteristics of dietary and herbal supplements use in a large cohort of adult patients with epilepsy.

Methods: This prospective study included 490 patients receiving care at a university epilepsy clinic. A number of variables, including demographics, characteristics of epilepsy and its treatment, comedication as well as data related to supplements intake were collected from medical records and a dedicated questionnaire.

Results: Overall 247 patients (50.4%) took at least one dietary supplement; nearly half (111, 44.9%) of this group took > 1 products. Multivitamins and magnesium were the most prevalent supplements. Most of the patients used supplements for general health rather than their epilepsy condition. The average number of supplements and prescription medications used per person was 5.4. Ten percent (25 of 247) of subjects used dietary supplements which could have proconvulsive effect or potential for interaction with prescription medications. Multivariate analysis revealed two independent variables associated with supplements intake, younger age and female sex.

Conclusion: Dietary and herbal supplements use is common in patients with epilepsy, adding to the burden of overmedication. Concurrent use of supplements may potentially lead to interactions with prescription medications or loss of seizure control. Health care providers should routinely check for dietary supplements use to limit potential harm related to their intake.

1. Introduction

Epilepsy is one of the most common neurological disorders. For the majority of patients with epilepsy (PWE), antiepileptic drugs (AEDs) are the mainstay of treatment. A substantial percentage of patients require polytherapy to suppress their seizures; this poses a risk of pharmacokinetic interactions. Moreover, PWE are at an increased risk of comorbidities, which often require long-term co-medication with additional potential for interactions (Gaitatzis et al., 2004; Bosak et al., 2019). The use of dietary supplements may add to the burden of overmedication in PWE. Supplements are generally considered by patients to be safe and natural. Although many supplements seem to be harmless, various dietary products may have proconvulsive effect or have the potential for interaction with AEDs. Herbal products may increase the frequency of seizures through intrinsic proconvulsive effect, contamination by heavy metals, undisclosed AEDs content, or pharmacokinetic interactions (Haller et al., 2005; Samuels et al., 2008). Furthermore, contrary to prescription medications, supplements are not subject to premarket safety and efficacy trials (Gurley et al., 2018). The use of supplements as a part of complementary and alternative medicine has been studied extensively in PWE. Supplements may be used for other reasons, e.g. overall health, filling nutrient gaps, treatment of comorbidities. The patterns of supplements use may vary across countries and cultures (Samuels et al., 2008). Therefore, more data are needed on the use of dietary supplements in the different populations of PWE.

This study aimed to analyze the extent and characteristics of use of dietary and herbal supplements (DHS) in a large cohort of adult PWE.

2. Material and methods

The study involved consecutive patients diagnosed with epilepsy (Fisher et al., 2014) who visited the epilepsy clinic, at the Department of Neurology within University Hospital in Krakow (Poland) at least twice between June 2017 and December 2018. All patients agreed to participate. Patients with concomitant psychogenic seizures were excluded.

The study protocol followed the principles of Declaration of Helsinki and was approved by the bioethical committee. All patients (or their legal representatives) provided their informed consent to participate.

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Data were collected by a structured interview and a dedicated questionnaire. The following information was collected: age, sex, age at the onset of epilepsy, duration of epilepsy, type(s) of epilepsy/seizures, and currently used AED(s) and non-AEDs. The types of epilepsy were defined in accordance with the ILAE classification (Scheffer et al., 2017). During the initial visit, patients/caregivers were asked to fill the questionnaire, which listed the following supplements: vitamins/multivitamins, minerals, herbs or other botanicals, fatty acids, coenzyme Q10, amino acids, glucosamine, chondroitin, carnitine, and others (Suppl.Mat.). Patients were also requested to bring all containers with supplements currently used. In addition, we asked the patients who recommended them supplements and what is the purpose of taking supplements. All data were collected by the senior author (MB).

2.1. Statistical analysis

Data were analyzed with Student's t-test, Mann–Whitney U or with χ^2 test. For testing the causal inferences between the dependent and independent variables, we built the multiple logistic regression model with selected, potential factors affecting the patients' state, after adjusting for sex and age. Calculations were performed using the Statistica 13.1 package.

3. Results

An initial cohort comprised 506 patients. Sixteen patients who did not attend the second visit within the study period were excluded from the analysis. The final cohort consisted of 490 adult patients with the mean age of 36.1 years, (SD ± 12.7; range 18–84). Of these patients, 300 (61.2%) were females; 364 (74.3%) patients had focal epilepsy and 228 (46.5%) were in remission. A total of 268 (54.7%) patients were on monotherapy, and the most commonly prescribed AEDs (in mono- or polytherapy) were levetiracetam, valproate, and lamotrigine. The mean number of currently used AEDs was 1.6 [range 1–5].

Overall, 247 patients (50.4%) took at least one DHS; nearly half of this group (111, 44.9%) took > 1 product. The average number of supplements per person was 1.7. Multivitamins and magnesium were the most prevalent supplements. Cannabis-based oil or liquid extracts were used by 10 patients for medical purposes and were not recommended by a physician. DHS intake is summarized in Table 1.

The most common reason for the use of supplements was "to improve general health," followed by "to protect myself against infections." Other common reasons were "to improve my diet," "to counteract AEDs side effects," "to prepare for pregnancy," and "to treat comorbid conditions." The majority of patients listed ≥ 2 reasons. Only 7% of patients took supplements "to improve seizure control."

In one third of patients, supplements were recommended by a health care professional (6.5% physician, 21.9% pharmacist). The majority of patients were prompted to take supplements by advertising (42.5%) or by family/friends recommendations (29.1%). A total of 27% of patients using DHS took medications other than AEDs for the treatment of comorbid conditions, and the average number of non-AEDs drugs per person was 2.1.

Twenty patients took supplements that could have proconvulsive effect or potential for interaction with AEDs (Gingko biloba, evening primrose oil, Hypericum perforatum). In further 5 subjects, supplements (ginseng) had potential for interaction with psychiatric comedication (antidepressants).

We compared supplement users and nonusers with regard to sex, age, age at onset of epilepsy, epilepsy type, seizure frequency, and epilepsy therapy (Table 2).

Univariate and multivariate analyses results are presented in Table 3. PWE using supplements were younger and had younger age at the onset of epilepsy; they were more often females and were more likely to suffer from generalized epilepsy. Multivariate analysis revealed two independent variables associated with supplement intake; younger age and female sex.

Table 1
Supplement use in prior 30 days among adult patients with epilepsy.

Dietary supplement used	N (%)
Groups of supplements	
Vitamins/multivitamins	116 (23.7) 98 (20)
Minerals	67(13.9) 34 (6,9)
Herbs or other botanicals	34 (6.9) 84 (17.1)
Carnitine	
Fatty acids	
Others	
The most commonly used specific supplements	
Magnesium	82 (16.7)
Multivitamins	50 (10.2)
vitamin D	35 (7.1)
Carnitine	34 (6.9)
Omega-3 fatty acids	25 (5.1)
Folic acid	25 (5.1)
Number of supplements used per patient	N (% of patients using supplements)
1	136 (55.1)
2	73 (29.5)
3	22 (8.9)
4	13 (5.2)
5	2 (0.8)
6	1 (0.4)

Table 2
Comparison of suplement users and nonusers.

	Users	Nonusers
Age	33.9 (SD ± 11.8); range 18-74	38.3 (SD ± 13.2); range 18-84
Sex (female)	168 (68.0%)	132 (53.3%)
Age at the onset of epilepsy	17.7 (SD ± 11.9); range 1-62	20.2 (SD ± 14.2); range 1-72
Epilepsy type (generalized)	73 (29.5%)	53 (21.8%)
Epilepsy therapy (monotherapy)	145 (58.7%)	123 (50.6%)
Seizure frequency (remission)	118 (48.6%)	110 (45.3%)

Abbreviation: SD-standard deviation.

4. Discussion

Our results demonstrated that the use of DHS is a widespread practice among PWE; 50.4% of subjects took at least one dietary supplement. Our findings are in agreement with studies from tertiary epilepsy centers (Kaiboriboon et al., 2009; Kelly and Chung, 2012; Eyal et al., 2014) and general population-based studies (Kantor et al., 2016). No studies on supplement intake in Polish PWE have been published, but their use in general population is common across different age groups (Gajda et al., 2016; Sadowska and Bruszkowska, 2016).

Similar to the findings of Kaiboriboon et al. (2009) and Kelly and Chung (2012), the most commonly used supplements were vitamins/multivitamins. The intake of folic acid is warranted in women of childbearing age with epilepsy (Harden et al., 2009). Vitamin D deficiency is highly prevalent in Poland, and its supplementation is recommended according to the recent guidelines (Rusińska et al., 2018). Furthermore, vitamin D intake may be beneficial in patients taking AEDs (Fernandez et al., 2018). However, results from observational or randomized controlled studies have often not supported the health benefits of other supplements or multivitamins in general population, and no such studies have been conducted in PWE (Sesso et al., 2008; Neuhouser et al., 2009).

Hypocarnitinemia has been linked to valproate therapy, and carnitine supplementation is sometimes recommended along with valproate treatment (Hamed and Abdella, 2009). However, only 14 carnitine

Table 3
Analysis of variables associated with supplement intake.

	Univariate analysis					Multivariate analysis*				
	Beta°	SE	Wald statistics	OR (95% CI)	P-value	Beta°	SE	Wald statistics	OR (95% CI)	P-value
Age	**−0,03**	**0,01**	**13,83**	**0,97 (0,96-099)**	**< 0,001**	**−0,03**	**0,01**	**8,05**	**0,97 (0,96-099)**	**0,005**
Sex (female)	**0,58**	**0,19**	**9,60**	**1,79 (1,24-2,58)**	**0,002**	**0,49**	**0,19**	**6,26**	**1,63 (111-2,38)**	**0,012**
Age at the onset of epilepsy	**−0,01**	**0,01**	**4,27**	099 **(0,97-100)**	0039	< 0,01	0,01	0,08	100 (099-1,02)	0,777
Epilepsy type (generalized)	**0,41**	**0,21**	**3,82**	**1,50 (100-2,26)**	**0,051**	0,19	0,22	0,77	1,21 (0,79-1,86)	0,380
Epilepsy therapy (monotherapy)	0,31	0,18	2,91	1,36(0,96-1,95)	0088	–	–	–	–	–
Seizure frequency (remission)	0,10	0,18	0,21	111 (0,78-1,58)	0578	–	–	–	–	–

Abbreviations: SE- standard error; OR- odds ratio.
°standardized (regression) coefficient.
*Only the variables showing significance in the univariate test were selected.
The Hosmer-Lemeshow goodness of fit test = 12.49, p = 0.130, Nagelkerke R2 = 0.060.

users in our cohort were on valproate treatment. Furthermore, carnitine was recommended by neurologists in only 5 patients.

A major concern noted is that 10% (25 of 247) subjects used dietary supplements (herbal products) that could have proconvulsive effect or potential for interaction (Samuels et al., 2008; Woroń and Siwek, 2018). The average number of prescription medications and supplements taken by supplement users was 5.4. The pattern of pharmacokinetic interactions in such patients may be unpredictable. However, frequent use of levetiracetam in the studied group reduced the probability of interactions. Furthermore, only one third of the patients followed recommendations of pharmacists or physicians with regard to DHS use.

Our findings suggest that most patients used dietary supplements for overall health and wellness rather than for their epilepsy. Women and younger patients were more likely to use DHS, but similarly to Kaiboriboon et al. (2009) we found no correlation between the use of DHS and epilepsy severity measures such as pharmacoresistance or polytherapy. However, some DHS, such as cannabis or carnitine could have been used for reasons related to epilepsy. Results of this study could have been affected by higher percentage of women in the cohort

The major strength of our study is a large cohort of PWE studied and the reliable method of data collection. Limitations include the use of population of the university clinic, which may differ substantially from the general population of PWE with regard to seizure frequency or use of polytherapy.

5. Conclusion

The results from the survey of PWE seen in the university center emphasize the importance of obtaining comprehensive data on the intake of dietary and herbal supplements. Their use is common in PWE, which adds to the burden of overmedication. Concurrent use of DHS may potentially lead to interactions with prescribed medications or loss of seizure control. Epileptologists and other health care providers should routinely check for DHS use to limit potential harm related to their intake.

Declaration of Competing Interest

MB received honoraria for publications, lectures, travel expenses, and conference fees from Sanofi, Adamed, Teva, Neuraxpharm, UCB.

AS received honoraria for lectures from Bayer, Novartis, Polpharma, Bristol-Myers, Biogen, Teva, Medtronic and honoraria for the participation in advisory meetings from Bayer, Novartis.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.eplepsyres.2019.106168.

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