Dietary and Lifestyle Behavior in Adults With Epilepsy Needs Improvement: A Case-control Study From North-eastern Poland

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Research

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Abstract

Background: Several factors predispose people with epilepsy to cardiovascular diseases. Among them nutrition and lifestyle have not been sufficiently studied.

Methods. The study involved 60 epileptic male and female volunteers and 70 healthy controls, corresponding to age and gender. Medical information was collected during the study and a detailed questionnaire survey concerning eating and lifestyle habits was conducted. Physical activity was evaluated using International Physical Activity Questionnaire (IPAQ). Nutritional status was assessed by bioelectric impedance. Venous blood samples were taken for lipid and 25-hydroxyvitamin D3 (25(OH)D3) analyses.

Results. A tendency to an increase in LDL cholesterol was found in epileptics. Significantly higher body fat and insignificantly higher visceral fat was found in epileptic men compared to healthy men. In epileptic women a tendency to lower lean body mass was found. Patients with epilepsy were more sedentary, had lower consumption of cottage cheese, fruit, pulses, nuts and seeds, vitamin C and potassium, and higher intake of sugar-sweetened soda, energy from fat and sodium compared to healthy people. As a positive point, epileptics consumed less coffee and alcoholic beverages. More than 80% of diets of epilepsy people were low in folic acid, vitamin D and calcium, but similar tendency was observed in the healthy people. The diets of patients with epilepsy were in a higher percentage poor in niacin, vitamin C and potassium compared to the control group, 25% to 7%, 50% to 31% and 73 to 56% respectively. A significantly lower serum concentration of 25(OH)D3 was observed in epileptic individuals, which in this group was found to be positively modulated by physical activity.

Conclusions. The study indicates that several behavior-related habits, which may predispose epileptic people to cardiovascular disease, need to be improved. For this reason, patients with epilepsy should be provided with more comprehensive medical care, including advice on nutrition and physical activity.

Background

Epilepsy is a chronic disease of the nervous system that affects people of all ages. It is caused by structural, genetic, metabolic, infectious, or immunological factors [1]. In many cases, the cause of the disease is unknown. Sixty percent of epilepsy cases are idiopathic and have no clear cause, but genetic burden is possible [2].

In epilepsy, deficiencies of such nutrients as B vitamins, vitamin D, zinc, and selenium have been observed [3-6]. The most common consequence of vitamin D deficiency is the loss of bone mass, which can occur in epilepsy as a result of pharmacotherapy, including the direct effect of drugs on bone tissue [7,8]. An important problem in epilepsy is co-occurrence of diet-related disorders. The epileptic population is characterized by a higher risk of cardiovascular disease (CVD) and dyslipidemia, which may be a consequence of behavioral risk factors, medication, or seizure-related cardiac arrythmias [9,10,11]. In addition to this, epileptic patients tend to have excessive body weight and abdominal obesity, which is
risk factor of metabolic diseases [12]. Despite some controversy, it is believed that vitamin D may be important for the CVD prevention [13,14].

The role of physical activity in epilepsy has been discussed by medical specialists, caregivers, and patients themselves over time. Recommendations and guidelines issued by medical organizations are few and general, although in recent years they have been aimed at encouraging rather than reducing physical activity in this group of patients [15,16]. Although the possibility of practicing particular types of exercises and their intensity should always be considered individually with regard to factors such as the frequency of seizures or the type of epilepsy, there are studies showing that physical activity can have a positive effect on the course of the disease [16]. Patients with epilepsy often limit their physical activity mainly due to the fear of seizures and show less physical fitness than healthy individuals [17,18].

Some irregularities in the dietary habits, nutritional status, and lifestyle of the adult epileptic population have been identified over time, but limited knowledge in this area encourages further research. The aim of the study was an assessment of epileptic patients in terms of diet, body composition, and the level of physical activity.

**Methods**

**Design and study group**

The study was conducted in 2016-2019 at the Kendron neurological clinic in Białystok. Eligibility criteria were: adult patients who had been suffering from epilepsy for at least one year. Recruitment process was conducted through the Kendron neurological clinic, media advertisements (press, television and internet), and health center advertisements aimed at epileptic patients from the city of Białystok. During the study, mentally ill patients were supported by caregivers. Of the 70 patients who volunteered to participate in the study, 10 had incomplete records due to inability to take part in the body composition analysis (problems with maintaining a standing position). Eventually, the study group involved 60 epileptic patients aged 18-73 years (mean age 37.22 ± 12.88). The flow-chart of the epileptic participants is given in Figure 1.

The control group consisted of 70 healthy subjects, selected according to age and gender. The detailed characteristics of the study and control group are presented in Table 1. Medical information about the cause of the disease, its onset, duration, symptoms, treatment, and mental comorbidities was taken from the patient’s medical records. The medication used in the form of monotherapy included carbamazepine, valproic acid, lamotrigine, levetiracetam, and pregabaline. In the case of polytherapy, patients took the above-mentioned medication in different configurations with less frequently used drugs, including topiramate and gabapentin. The diseases and mental disorders associated with epilepsy included depression, anxiety, and schizophrenia.

The study collected data on the age, employment, body measurements and vitamin D supplementation.
Body measurements such as height and body mass were taken by personnel trained in standard procedures. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Table 1. Characteristics of the study group vs. a healthy control.
|                                | Study Group | Healthy Control | p   |
|--------------------------------|-------------|-----------------|-----|
|                                | N = 60      | N = 70          |     |
| **General Characteristics**    |             |                 |     |
| Gender (%)                     | 58.3        | 67.1            | 0.299 |
| Women                          | 41.7        | 32.9            |     |
| Men                            |             |                 |     |
| Age (years) mean ± SD          | 37.22 ± 12.88 | 37.13 ± 11.65 | 0.885 |
| Occupation (%)                 | 36.7        | 2.9             | <0.001 |
| Retirement/pension             | 0           | 2.9             |     |
| Parental leave                 | 10          | 1.4             |     |
| Unemployed                     | 8.3         | 7.1             |     |
| Part-time job                  | 36.7        | 82.9            | 0.29 |
| Permanent employment           | 8.3         | 2.9             |     |
| Student                        |             |                 |     |
| BMI [kg/m2] (%)                | 1.7         | 1.4             | 0.935 |
| Underweight (BMI <18.5)        | 45          | 45.7            |     |
| Normal weight (BMI 18.5-24.99) | 36.7        | 37.1            |     |
| Overweight (BMI 25-29.99)      | 16.7        | 15.7            |     |
| Obesity (BMI > 30)             |             |                 |     |
| Vitamin D supplementation (%)  | 11.7        | 7.1             | 0.378 |
| **Characteristics of the Study Group** |          |                 |     |
| Age at disease onset (years) mean ± SD | 18.25±13.38 | -               | -   |
| Duration of the disease (years) mean ± SD | 18.98±15.63 | -               | -   |
| Number of medications taken mean ± SD | 1.4±0.7    | -               | -   |
| Type of epilepsy (%)           | 73.3        | -               | -   |
| Idiopathic                     | 6.7         |                 |     |
| Post-neonatal                  | 13.3        |                 |     |
| Post-traumatic                 | 6.7         |                 |     |
| Post-operative                 |             |                 |     |
| Seizures (%)                   | 43.4        | -               | -   |
| Yes | 56.6 |
|-----|------|
| No  |      |

| Anti-epileptic medication | 53.3 | 46.7 | - | - |
|---------------------------|------|------|---|---|
| Monotherapy               |      |      |   |   |
| Polytherapy               |      |      |   |   |

| Mental illnesses and disorders (%) | 23.3 | - | - | - |

SD - standard deviation

**Blood sample collection and biochemical analyses**

Twelve milliliters of venous blood from the antecubital vein were collected from the fasting participants. The samples were left for clotting for 30 min. Blood samples were centrifuged at 1500 x g for 10 min, and serum was separated immediately after centrifugation. The obtained serum was frozen to -80 °C and stored until determination. The lipid profile (total cholesterol, LDL and HDL cholesterol, and triglycerides) was determined using standard laboratory procedures in the university clinical hospital, in the Department of Biochemical Diagnostics of the Medical University of Bialystok, which is accredited for performing laboratory tests.

**Body composition assessment**

Body composition was assessed using the bioelectric impedance method using the InBody 270 analyzer, InBody Co. Ltd., Seoul, Korea. The electrical resistance was measured, which depends on resistance and reactance. The resistance is related to the resistance of individual tissues, while the reactance results from the electrical capacity of cell membranes that act as capacitors [19]. Body mass (BM), lean body mass (LBM), percentage body fat (PBF), skeletal muscle mass (SMM), and percentage water content (PWC) were determined in epileptic and control subjects.

**Dietary assessment**

After consenting to participate in the survey, a detailed questionnaire survey concerning eating and lifestyle habits was conducted among epileptic participants and a control group. In the case of mentally disabled epileptic participants, the questionnaire was filled in by the patient’s caregiver. Food consumption frequency and 24-hour dietary records from three consecutive days preceding the study were recorded. The questionnaire of habitual frequency of food consumption included 6 types of frequencies ranked from lowest to highest: 1: usual consumption once a month or less often; 2: consumption 2-4 times a month; 3: consumption 3 times a week; 4: consumption 4-6 times a week; 5: consumption daily; 6: consumption several times a day. The data obtained from 3-day 24-hour dietary recalls were compiled using the computer program Diet 5.0 (Food and Nutrition Institute, Warsaw), and...
energy and nutrients were calculated. The results were compared with the current nutrition recommendations for the Polish population [20].

Determination of 25-hydroxyvitamin D3

The serum concentration of 25-hydroxyvitamin D3 (25-(OH)D3) was determined by high performance liquid chromatography (HPLC) using a Prominence system (Shimadzu, Kyoto, Japan) consisting of an LC-20AD solvent delivery system, a DGU-20A5 degasser, a ThermaSphere TS-130 column heater (Phenomenex, Torrance, CA, USA), and an SPD-M20A diode-array detector (DAD). Chromatographic separations were performed on a Synergi Hydro-RP 80Å (250x4.6 mm) 4 μm column.

To 0.5 mL of serum, a 0.35 mL mixture of methanol-2-propanol (80:20 v/v) was added. The samples were vortexed for 30 s and subsequently extracted three times with 2 mL of hexane. The extraction procedure consisted of mixing with n-hexane containing 0.01% butylated hydroxytoluene (BHT) for 60 s on a vortex mixer and transferring the supernatant to glass test tubes. Phases were separated by 10 min centrifugation at RCF 2100 x g, and the upper phases were collected and dried under nitrogen at room temperature. The residue was dissolved in 100 μL of mobile phase of acetonitrile and methanol (75:25 v/v), and 50 μL were injected. An isocratic separation was performed in a 30-min run with a flow rate 1.5 mL/min with the column heater temperature set at 25°C. 25(OH)D3 was determined at 265 nm. A calibration curve was prepared using four concentrations of 25(OH)D3 (Sigma Aldrich, Saint Louis, MN, USA) in the range 37.5-300 nmol/l. The recovery was 83%. The interpretation of the results included the season of the year in which the blood samples were taken.

Due to differences in sunlight at different times of the year, the results were adjusted for the spring-summer and autumn-winter period.

Physical activity assessment

The International Physical Activity Questionnaire (IPAQ) short form, the Polish language validated version, was used to assess the level of physical activity in epileptic and control participants [21]. The level of physical activity was calculated taking into account the intensity of physical activity during 7 days prior to the survey and time spent walking and sitting. Physical activity was expressed in metabolic equivalents of task MET-min/week, which is an equivalent of basal metabolic rate equal to energy expenditure, which corresponds to 3.5 mL O2 per kilogram of body weight per minute [22]. Taking this into account, physical activity is classified into one of three activity levels: 1) high (3 or more days of intense physical activity with at least 1500 MET-min/week or 7 or more days of any combination of physical activity exceeding 3000 MET-min/week), 2) moderate (3 or more days of intense physical activity with not less than 20 minutes per day, 5 or more days of moderate physical activity or walking of not less than 30 minutes per day, or 5 or more days of any combination of physical activity exceeding 600 MET-min/week), and 3) low (no physical activity at all or no sufficient or high level activity).

Statistical analysis
The results were analyzed using the IBM SPSS Statistics package, IBM Corp., New York, USA. In group comparisons of quantitative data, the Student's t-test was used. The independence Pearson's Chi^2 test was used to compare categorical variables between the groups. The relationships between the examined parameters were determined using the Spearman correlation coefficient. To compare the level of 25(OH)D3 in blood serum, statistical weights were used, which took into account two seasons differing in sunshine intensity in Poland, spring-summer (April-September) and autumn-winter (October-March) periods. In the calculations, the significance level p < 0.05 was assumed as statistically significant.

Results

Biochemical analyses

In this study, the concentration of cholesterol and triglyceride fractions was determined. The lipid profiles of patients with epilepsy did not differ significantly from those of healthy people. The average serum LDL cholesterol (LDL-Ch) level was significantly higher in the study group, but the difference was not statistically significant. In both groups of participants, LDL-Ch was higher compared to the current guidelines for the management of dyslipidemia in the European population [23] (Table 2).

| Table 2: Serum lipid concentration in the study group and in the healthy control. |
|---------------------------------|-----------------|-------------|
| Study Group | Healthy Control | p     |
| N = 60        | N = 70          |    |
| Mean ± SD     | Mean ± SD       |    |
| TC [mg/dL]    | 192.60 ± 42.16  | 193.43 ± 38.46 | 0.754 |
| LDL-C [mg/dL] | 128.30 ± 44.55  | 117.71 ± 35.98 | 0.270 |
| HDL-C [mg/dL] | 54.48 ± 14.09   | 56.44 ± 13.08  | 0.446 |
| TG [mg/dL]    | 109.20 ± 72.21  | 101.74 ± 53.59 | 0.939 |

3.2. Body composition

During the study, an analysis of body composition was performed using the bioelectric impedance method [24]. Generally, parameters such as protein content, minerals, water content, fat free mass (FFM), muscle mass, waist-to-hip ratio (WHR), and visceral fat did not differ significantly between the epilepsy participants and the control group; however, in epileptic men, a significantly higher percentage of body fat (PBF) was found. A similar tendency was observed with regard to visceral fat, which was 33% higher in men with epilepsy, but the difference was not statistically significant.
Table 3
Body composition parameters in the study and control groups.

| Parameter                  | Study Group | Healthy Control | p    | Study Group | Healthy Control | p    |
|----------------------------|-------------|----------------|------|-------------|----------------|------|
|                            | Women       | Men            |      |             |                |      |
|                            | Study Group | Healthy Control |      | Study Group | Healthy Control |      |
|                            | N = 35      | N = 47         |      | N = 25      | N = 23          |      |
| Protein [kg]               | 8.84 ± 1.09 | 9.29 ± 1.14    | 0.0754 | 12.44 ± 2.16 | 13.07 ± 1.61 | 0.2612 |
| Minerals [kg]              | 3.22 ± 0.46 | 3.36 ± 0.41    | 0.1505 | 4.31 ± 0.67 | 4.44 ± 0.62 | 0.4900 |
| Total Body Water [L]      | 33.03 ± 3.96 | 34.53 ± 4.12 | 0.1013 | 46.18 ± 7.96 | 48.09 ± 6   | 0.3560 |
| Fat Free Mass [kg]        | 45.1 ± 5.5  | 47.19 ± 5.65   | 0.0649 | 62.93 ± 10.78 | 65.6 ± 8.19 | 0.3422 |
| Percent Body Fat [%]      | 32.1 ± 8.98 | 30.71 ± 7.37   | 0.4440 | 27.65 ± 7.8  | 22.2 ± 6.94 | 0.0142 |
| Skeletal Muscle Mass [kg] | 24.76 ± 3.25 | 25.95 ± 3.47  | 0.1186 | 35.38 ± 6.45 | 37.38 ± 4.84 | 0.2337 |
| Waist-to- Hip Ratio       | 0.9 ± 0.06  | 0.9 ± 0.07     | 1.0000 | 0.97 ± 0.11  | 0.95 ± 0.08 | 0.3914 |
| Visceral Fat Level        | 10.06 ± 5.02 | 9.49 ± 4.42   | 0.5873 | 11.12 ± 5.79 | 8.35 ± 4.59 | 0.0743 |

3.3. Dietary assessment

Dietary habits of epileptic and healthy participants were assessed with a food frequency questionnaire and with triple 24-hour records. The food consumption questionnaire included 6 types of consumption frequency, from lowest to highest, which were assigned ranks 1–6, respectively. Compared to controls, epileptic participants significantly less often consumed cottage cheese, fruit, legumes, nuts and seeds, sugar, honey and sweets, coffee, and alcohol (Table 4). In contrast, they consumed sugar-sweetened soda more often.
Table 4
Food frequency consumption according to ranks, determined via the Chi^2 test.

| Food                                        | Study Group Mean ± SD | Healthy Control Mean ± SD | p     |
|---------------------------------------------|-----------------------|----------------------------|-------|
|                                             | rank                  | rank                       |       |
| White bread                                 | 3.62 ± 1.56           | 3.57 ± 1.6                 | 0.444 |
| Wholemeal bread                             | 3.26 ± 1.4            | 3.67 ± 1.31                | 0.096 |
| Fine grained groats, white rice             | 2.62 ± 1.1            | 2.74 ± 0.97                | 0.726 |
| Coarse grained groats, brown rice           | 2.22 ± 1.2            | 2.46 ± 1.07                | 0.300 |
| Milk, yogurt, kefir                         | 3.48 ± 1.43           | 4.11 ± 1.32                | 0.108 |
| Cottage cheese                              | 2.13 ± 1.11           | 2.98 ± 1.04                | < 0.001 |
| Cheeses and processed cheeses               | 2.81 ± 1.17           | 3.18 ± 1.19                | 0.321 |
| Poultry meat and sausages                   | 3.43 ± 1.25           | 3.67 ± 1.11                | 0.546 |
| Pork meat and sausages                      | 3.85 ± 1.21           | 3.9 ± 1.27                 | 0.688 |
| Fish                                        | 2.4 ± 1.03            | 2.44 ± 0.71                | 0.050 |
| Eggs                                        | 3.16 ± 1.12           | 3.24 ± 0.94                | 0.074 |
| Raw vegetables                              | 3.66 ± 1.53           | 4.3 ± 1.16                 | 0.083 |
| Fruit                                       | 3.7 ± 1.6             | 4.46 ± 1.0                 | 0.005 |
| Pulses                                      | 2.02 ± 1.11           | 2.6 ± 0.92                 | < 0.001 |
| Nuts, seeds                                 | 2.5 ± 1.4             | 2.98 ± 1.22                | 0.009 |
| Sugar, honey, sweets                        | 3.4 ± 1.5             | 3.76 ± 1.4                 | 0.015 |
| Fruit juices                                | 2.23 ± 1.28           | 2.41 ± 1.16                | 0.217 |
| Sugar-sweetened soda                        | 2.6 ± 1.7             | 1.87 ± 1.07                | 0.022 |
| Coffee                                      | 3.6 ± 1.97            | 4.73 ± 1.54                | 0.010 |
| Beer                                        | 1.48 ± 0.85           | 2.36 ± 1.19                | < 0.001 |
| Wine                                        | 1.3 ± 0.53            | 1.91 ± 0.88                | < 0.001 |
| Spirits                                     | 1.23 ± 0.64           | 1.59 ± 0.67                | < 0.001 |
| Fast food                                   | 1.52 ± 0.73           | 1.69 ± 0.77                | 0.551 |

Energy and macro- and micronutrients were calculated on the basis of 24-hour dietary records from the three consecutive days preceding the study. The mean energy 1777 ± 557 kcal/d in the study group did
not differ from 1723 ± 534 kcal/d in the control group. In epilepsy patients, a significantly higher percentage of energy from fat 35.08 ± 9.11% was found compared to healthy subjects 30.96 ± 7.35% (p = 0.01). The percentage of macronutrients in the energy supply for both groups is shown in Fig. 2.

Table 5. shows a comparison of selected nutrient intakes in the study group and in the control group. The patients with epilepsy provided significantly less vitamin B3 in their diet compared to the control. In both groups, however, the mean values were in line with the Estimated Average Requirement (EAR), which is set to meet requirements for 50% of a given population. In the study group, more people (as much as 25%) did not meet the EAR, while among healthy volunteers it was only 7%. The same was the case with vitamin C, although in both groups the average intake was consistent with EAR. However, in the study group the intake was significantly lower, and every second person did not provide enough vitamin C. In people with epilepsy, a significantly lower potassium intake was found in comparison with the control group, which was not within the range of sufficient consumption for the Polish population. Almost three-fourths of patients with epilepsy presented a below average intake (AI) of potassium in their diet. Moreover, in the study group, sodium intake was higher than in the control group, and in both groups more than 200% AI for this element was provided. Both the study group (83% < AI) and the control group (57% < AI) showed insufficient calcium intake. As many as 96% of the subjects from the study group and ~ 97% of the controls did not contain enough vitamin D in their diet. The intake of saturated, monounsaturated, and polyunsaturated fatty acids, and cholesterol was higher in the study group compared to healthy individuals, but the differences were not statistically significant.
Table 5
Dietary intake of selected vitamins, minerals, fatty acids, and cholesterol in the study and control groups.

|                          | **Study Group** | **Healthy Control** | **p** |
|--------------------------|-----------------|---------------------|-------|
|                          | **Mean ± SD (% deficient)** | **Mean ± SD (% deficient)** |     |
| **Vitamin B1 [mg]**     | 1.19 ± 0.47 (120) | 1.24 ± 0.51 (128.7) | 0.538 |
| <EAR (%)                | 33.3            | 34.2               |      |
| **Vitamin B2 [mg]**     | 1.52 ± 0.51 (155.64) | 1.58 ± 0.62 (164.49) | 0.525 |
| <EAR (%)                | 13.3            | 10                 |      |
| **Vitamin B6 [mg]**     | 1.88 ± 1.2 (166.04) | 1.89 ± 0.88 (165.83) | 0.293 |
| <EAR (%)                | 16.7            | 17.14              |      |
| **Folic acid [µg]**     | 244.23 ± 85.18 (76.3) | 270.23 ± 87.09 (84.45) | 0.081 |
| <EAR (%)                | 80              | 77.14              |      |
| **Vitamin B12 [µg]**   | 4.28 ± 3.9 (213.83) | 3.58 ± 2.86 (179.03) | 0.304 |
| <EAR (%)                | 21.7            | 22.8               |      |
| **Vitamin A [µg]**     | 1113.5 ± 966.25 (202.55) | 995.4 ± 729.2 (183.27) | 0.772 |
| <EAR (%)                | 20              | 25.7               |      |
| **Vitamin C [mg]**     | 83.06 ± 63.29 (124.85) | 122.15 ± 92.52 (189.09) | 0.005 |
| <EAR (%)                | 50              | 31.4               |      |
| **Vitamin D [µg]**     | 3.79 ± 5.45 (25.26) | 2.85 ± 2.56 (19)   | 0.469 |
| <AI (%)                 | 96              | 98.6               |      |
| **Na [mg]**             | 3524.27 ± 1313.5 (234.95) | 3096.7 ± 1091.4 (206.45) | 0.046 |
| <AI (%)                 | 1.6             | 1.4                |      |
| **K [mg]**              | 2939.11 ± 1033.13 (83.97) | 3335.05 ± 1077.65 (95.29) | 0.022 |
| <AI (%)                 | 73.3            | 55.7               |      |
| **Ca [mg]**             | 575.2 ± 281.55 (55.65) | 623.71 ± 252.72 (70.98) | 0.211 |
| <EAR (%)                | 83.3            | 57.14              |      |
| **P [mg]**              | 1170.84 ± 410.65 (200.96) | 1225.62 ± 362.04 (211.31) | 0.338 |
| <EAR (%)                | 5               | 1.4                |      |
| **Mg [mg]**             | 282.57 ± 94.81 (95.75) | 308.66 ± 104.48 (107.96) | 0.258 |
| <EAR (%)                | 51.6            | 51.4               |      |
|                      | Study Group       | Healthy Control     | p     |
|----------------------|-------------------|---------------------|-------|
|                      | Mean ± SD (% deficient) | Mean ± SD (% deficient) |      |
| Fe [mg]              | 10.6 ± 3.41 (158.24) | 11.11 ± 3.18 (159.36) | 0.245 |
| <EAR (%)             | 16.6              | 12.85               |       |
| Zn [mg]              | 9.57 ± 3.22 (121.61) | 9.66 ± 2.87 (126.79) | 0.698 |
| <EAR (%)             | 33.3              | 24.2                |       |
| I [µg]               | 117.03 ± 50.92 (123.19) | 113.11 ± 46.88 (119.06) | 0.671 |
| <EAR (%)             | 33.3              | 40                  |       |
| SFA [g]              | 25.41 ± 10.79     | 21.97 ± 9.94        | 0.077 |
| MUFA [g]             | 30.05 ± 16.7      | 25.1 ± 10.6         | 0.116 |
| PUFA [g]             | 10.04 ± 6.09      | 8.86 ± 3.8          | 0.262 |
| Cholesterol [mg]     | 287.22 ± 118.1    | 270.97 ± 148.11     | 0.241 |

3.4. Serum 25(OH)D3 concentration

The median serum concentration of 25(OH)D3 in epilepsy patients was 77.1 (63.81–89.02) nmol/L and was significantly lower than in healthy subjects 90.228 (77.41-102.67) nmol/L. In both groups, the mean results were within the recommended range (> 75 nmol/L) [25]. Additionally, the serum concentration of 25(OH)D3 was analyzed, depending on sex and age. Women in the study group had significantly lower concentrations of 25(OH)D3 compared to healthy women, although there were no significant differences between men. Regardless of age (both < 35 and ≥ 35 years), the serum concentration of 25(OH)D3 in the study group was lower than in the healthy group (Table 6).
Table 6
Serum concentration of 25(OH)D3*.

| Study Group       | Healthy Control          | p       |
|-------------------|--------------------------|---------|
| N = 60            | N = 70                   |         |
| 25(OH)D3 [nmol/L]| Median (P25-P75)         | Median (P25-P75) |
| Median            | 77.1 (63.81–89.02)       | 90.228 (77.41-102.67) | 0.000074* |
| Women             | 79.58 (64.03–87.6)       | 89.93 (78.44-103.48)  | 0.000693* |
| Men               | 72.018 (63.59–94.03)     | 92.22 (72.60-102.04)  | 0.062509  |
| Age               | 75.794 (63.59–84.59)     | 92.088(79.207–102.36) | 0.000409* |
| < 35              | 78.426 (64.74–94.03)     | 85.623 (74.54-103.48) | 0.039658* |
| ≥ 35              |                          |         |

*Adjusted for season.

3.5. Physical activity

The International Physical Activity Questionnaire - short form (IPAQ-S) was used to assess the level of physical activity. IPAQ estimates the level of physical activity expressed in metabolic equivalents of task (METs) per week and the number of hours spent in a sitting position during the day. The questionnaire takes into account the number of days per week when physical activity of a certain intensity occurs and the duration of these activities. The interpretation of the results makes it possible to determine the level of physical activity as insufficient, sufficient, or high. The data obtained are shown in Table 7. Epileptic participants were significantly less moderately or intensively active than the healthy subjects. They also spent significantly more hours sitting during the day. Generally, the overall level of physical activity (MET-min per week) was insignificantly lower in epileptic individuals; however, according to the IPAQ's interpretation criteria, the level of physical activity was sufficient in both groups.
Table 7
Physical activity (PA) assessed with IPAQ-S.

| Parameter IPAQ                                                                 | Study Group          | Healthy Control       | p    |
|-------------------------------------------------------------------------------|----------------------|-----------------------|------|
| Vigorous physical activities (days per week)                                  | 1.12 ± 2.02          | 1.77 ± 2.02           | 0.009|
| Moderate physical activities (days per week)                                  | 1.78 ± 2.65          | 2.33 ± 2.38           | 0.010|
| Walk for at least 10 min at a time (days per week)                            | 5.4 ± 2.27           | 5.89 ± 2.03           | 0.103|
| Time spent walking (minutes per day)                                          | 104.08 ± 135.94      | 136.36 ± 145.74       | 0.025|
| Time spent sitting (hours per day)                                            | 6.88 ± 2.7           | 5.67 ± 3.03           | 0.022|
| Level of PA (MET-min/week)                                                    | 4038.058 ± 6126.738  | 5801.66 ± 7221.716    | 0.139|
| (moderate)                                                                    | (moderate)           |                       |      |

The potential relationship between serum 25(OH)D3 concentration and physical activity was studied. The results are shown in Table 8. The study group showed a significant, weak positive correlation between the time spent walking during the day and overall physical activity (expressed in MET-min/week) and vitamin D3 concentration. There was also a significant negative correlation between the number of hours spent in a day sitting and 25(OH)D3. No such correlations were found in the control group.
Table 8
Spearman rank correlations between 25(OH)D3 and physical activity according to IPAQ parameters.

| Correlation of Vitamin D3 Concentration | Study Group | Healthy Control |
|----------------------------------------|-------------|-----------------|
|                                        | Correlation R value (p) | Correlation R value (p) |
| Vigorous physical activities (days per week) | 0.114 (0.387) | 0.023 (0.847) |
| Moderate physical activities (days per week) | 0.163 (0.214) | -0.069 (0.569) |
| Walk for at least 10 min at a time (days per week) | 0.244 (0.060) | -0.071 (0.562) |
| Time spent walking (minutes per day) | 0.279 (0.031) | -0.032 (0.792) |
| Time spent sitting (hours per day) | -0.257 (0.047) | -0.156 (0.198) |
| Level of PA (MET-min/week) | 0.305 (0.018) | -0.04 (0.74) |

Discussion

Epileptic people are a difficult group to study due to frequent mental, behavioral and social problems [17, 26]. The current studies on dietary behavior and lifestyle in this group of patients are limited [9, 12, 17, 27, 28] and need to be expanded. In this study, recruitment for the research took place in 2016–2019 through various information channels. In the end, 70 epilepsy patients were enrolled in the study, which was quite a good result considering the reluctance of epileptic patients to participate in scientific research [29]. Finally, 60 people were qualified for further research. Of them, 23.3% had mental illnesses or disorders and were therefore supported by caregivers. Compared to healthy people, in this study only 36.7% of epileptics had a permanent job compared to 82.9% of healthy controls, and as much as 36.7% compared to 2.9% in the control group received a pension/retirement. The control and study group did not differ in terms of gender, age, BMI and vitamin D supplementation.

Studies show that epileptic patients have a higher risk of comorbidities including dyslipidemia [10, 30], which is a risk factor of cardiovascular disease. One of the risk factors of dyslipidemia can be antiepileptic treatment, but it cannot be clearly determined which kind of medication (drugs and drug combinations) has the greatest impact [31]. In some studies, the monotherapy with old-generation drugs, such as carbamazepine, valproic acid, and phenytoin, was associated with an increase in cardiovascular risk [32]. In contrast, a study by Vicanco-Hidalgo et al. [33] concluded that, despite a higher percentage of
dyslipidemia in epileptic patients, they do not have a greater cardiovascular risk. In the above study compared to healthy people, epileptic individuals had a lower rate of hypertension and diabetes [33], what indicates the need for a better assessment of epileptic patients prior to statin treatment. In our study, patients were treated with various antiepileptic drugs, both in mono- and polytherapy. Although we found elevated levels of LDL-cholesterol in the blood serum of epileptic patients compared to the controls, the results were not statistically significant. No significant differences were found between these groups with respect to other lipids. These and other findings suggest that the epilepsy treatment may not be the only factor behind dyslipidemia. Some other factors, such as dietary behavior and lifestyle, can contribute to disorders of lipid metabolism. Kim et al. [27] analyzed the effect of lifestyle modification and the use of statins on the reduction of vascular risk in patients with epilepsy. Pharmacotherapy was found to be more effective, but lifestyle changes also had positive effects.

There are very few studies in the literature on nutritional status and dietary habits in epilepsy. One of them, the California Health Interview Survey, concluded that the eating behavior and physical fitness in epilepsy are similar to these of healthy people [28]. In contrast, some evidence shows that epilepsy may increase overweight and obesity, as well as the risk of cardiovascular diseases [10]. The percentage of overweight and obesity measured in our study was 53.4% for epilepsy patients and 52.8% for healthy controls, which was similar to another study where this percentage was 55.2% [34]. In addition, we analyzed the body composition using electrical bioimpedance. A significantly higher percentage of body fat (PBF) was found among epileptic men compared to the healthy men, 27.65% and 22.2%, respectively. However, no significant differences were found among women. There is not much research on body composition in epilepsy. In another study, patients treated with antiepileptic drugs had a PBF similar to the controls [35]. According to the World Health Organization (WHO), abdominal obesity is a risk factor of metabolic diseases [36]. Overall, the average waist-to-hip ratio (WHR) in this study, for both women and men, regardless of the prevalence of epilepsy, was above the normal range. Due to these results and the associated risk of metabolic diseases, it is reasonable to pay attention to the dietary behavior of patients with epilepsy [37]. Some studies show high carbohydrate and protein intake in epilepsy as well as low fat intake, including polyunsaturated fatty acids [12]. In contrast to these results, our research shows a different tendency. While carbohydrate and protein intakes were at the recommended levels, more fat was consumed by the epilepsy patients compared to the controls. In turn, the intake of polyunsaturated fatty acids (PUFAs) was at a similar level in both groups of participants. Compared to another study [12], the average cholesterol intake in epilepsy patients was in the normal range, both in men and in women.

The frequency of food consumption was further analyzed. It was found that patients with epilepsy showed less favorable eating behavior compared to healthy people. They have consumed significantly less frequently vegetable products such as fruit, pulses, seeds, and nuts, which are sources of vitamins, minerals, and dietary fiber. These food products are recommended for the prevention of cardiovascular risk [38]. Compared to other studies [28], epilepsy patients in our study showed less frequent consumption of vegetables and fruits and sugar sweetened soda, while they consumed legumes more often. Some countries have formulated dietary guidelines for epilepsy patients. In the UK, the dietary recommendations emphasize a balanced diet providing all macronutrients, with particular emphasis on
vegetables and fruits [39]. Attention is also drawn to foods that provide complex carbohydrates, which raise blood glucose levels more slowly and for longer, allowing a longer sense of satiety after a meal. Similarly, the dietary recommendations for the US patients are mainly based on the elimination of monosaccharides and food products with high glycemic indexes from the diet, while promoting a balanced, varied diet and an appropriate amount and quality of fluids [40]. In our study, epileptic participants consumed less dairy products, including cottage cheese, which is a source of easily absorbable calcium, important for bone health. In addition to this, fish and eggs, which are food sources of vitamin D, were consumed less frequently, but this difference was insignificant. It is worth noting that patients with epilepsy also showed a lower serum concentration of 25(OH)D3. In this study, epilepsy patients were more likely to consume sugar-sweetened soda, which, due to the content of sugar, preservatives, and dyes, are considered less beneficial to health [41].

The intake of stimulants such as coffee and alcohol was analyzed in this study. Patients with epilepsy consumed coffee less often than healthy individuals. There are many indications that regular coffee drinking may exacerbate seizures in some patients due to the effect on the central nervous system [42, 43]. So far, the role of caffeine in the control of epilepsy is unclear. Studies on animal models suggest that, depending on the dose and length of caffeine intake, it may have both positive and negative effects on seizure control [44, 45]. Moreover, caffeine may reduce the effectiveness of some anticonvulsant drugs, mainly topiramate [46]. Some studies indicate the need to reduce caffeinated beverages due to the possibility of increasing the frequency of epileptic seizures and reducing the effectiveness of anticonvulsant drugs. It should be noted that caffeine is not currently considered a seizure inducing factor [47].

Epileptic participants in this study consumed alcohol less frequently than the control group, and this finding is consistent with Elliot et al. [28]. A study by Hinnell et al. [48] found that patients with epilepsy consumed alcohol less frequently than the general population; however, one-fourth of them declared regular use of alcoholic beverages. In another study, patients with epilepsy declared addictive drinking less frequently than healthy people [49]. The influence of alcohol consumption on the occurrence of epileptic seizures is the subject of many studies. Some of them suggest that moderate alcohol consumption does not increase the frequency of seizures, while others show the possibility of intensifying epileptic seizures due to various mechanisms of action, e.g., effects on neurotransmission and metabolic changes [50]. Hamerle et al. [51] found a negative impact of significant amounts of alcohol in epileptic patients, but concluded that moderate consumption seems safe for most patients. Scientific research has been reflected in dietary recommendations for epileptic patients. The recommendations for patients in Australia point to the negative consequences of alcohol consumption, especially of larger quantities, and the need to consult a physician in relation to the type of drugs taken [52]. It is important that alcohol may interact with anticonvulsant drugs, reduce their effectiveness, intensify side effects, and increase the risk of seizures, caused by sleep disturbances and reduced sleep quality [53].
The analysis of vitamin and mineral intake showed that most (over 80%) of the deficient nutrients were folic acid, vitamin D, and calcium. This is particularly important due to the role of B vitamins, including folic acid and vitamin D, in proper development and functioning of the nervous system [54]. Moreover, vitamin D and calcium are responsible for bone and mental health, and patients treated with antiepileptic drugs are particularly vulnerable to osteoporosis and depression [55]. Other studies have shown low calcium intake by patients with epilepsy [56]. The study also showed significantly lower vitamin C and potassium and higher sodium intakes by epileptics. In contrast to supplementation studies, meta-analyses of prospective studies found that higher dietary intakes of vitamin C and potassium were associated with reduced risk of cardiovascular disease [57, 58]. On the contrary, increased sodium intake was associated with higher mortality due to CVD [59]. The intake of minerals and vitamins in epilepsy has been rarely studied. Therefore, there is a need for more research that would allow for a formulation of dietary recommendations for this group of patients, taking into account potential deficiencies in these nutrients.

The role of vitamin D in the etiology and course of epilepsy is still not clearly understood; however, in the 1990s, a higher birth rate of children with epilepsy was observed in the winter period [60]. It has also been noted that, in patients with epilepsy, both the severity of epileptic seizures, their frequency, and the number of sudden unexpected deaths occur during the winter period when insolation is limited [61]. In animal models, vitamin D may reduce the severity of chemically induced seizures and increase the anticonvulsant effect of some antiepileptic drugs [62, 63]. However, studies assessing serum concentrations of 25(OH)D3 in epileptic patients are still scarce. In a study conducted in India, lower average serum concentrations of vitamin D were observed compared to our results [64]. It should be noted that, although the territory of India is characterized by high sunshine, clothing covers most of the body, limiting skin synthesis of vitamin D. Cultural differences and skin pigmentation are also important. In the above study, no significant differences by gender or between the study and control groups were found. A recent literature review found that the vitamin D deficiency affects the entire European population [65]. Other European studies showed significantly lower serum concentrations of vitamin D in epilepsy patients, but also lower seizure rates after vitamin D supplementation [66]. However, it should be noted that this study was conducted on a small group of 13 patients with epilepsy. A larger US study found a frequent vitamin D deficiency in patients with epilepsy [67]. The average serum concentration of 25-hydroxyvitamin D was lower than in the general population.

A significant part of research on epilepsy concerns the influence of antiepileptic drugs, which cause a decrease in blood vitamin D concentration, which in turn negatively affects the skeletal system [68]. When considering the possible influence of drugs on vitamin D, one should mention the frequent co-occurrence with epilepsy of other disorders, including mental disorders. Mental disorders occurring during the interictal period are the most common problem in epilepsy patients. Dementia syndrome, interictal psychosis, and affective disorders such as mania or depression among the interictal psychiatric disorders can be distinguished. Patients with mental disorders are particularly at risk of vitamin D deficiency, especially those treated with clozapine, as well as people with low physical activity and poor eating habits [69].
Physical activity is an element of lifestyle, which is important for maintaining health. Although participants with epilepsy as well as healthy participants in the study were moderately active, patients with epilepsy spent more time during the day sitting and less often performed intensive and moderate physical activity during the week, what is consistent with other findings [70]. Lower physical activity may be affected by low occupational activity of epileptics compared to healthy people, 36.7% compared to 82.9%, respectively. The latest meta-analysis of population studies shows that further research is needed before specific recommendations on physical activity in people with epilepsy are formulated [70]. Among patients with epilepsy, but not in the control group, a positive relationship was found between the level of physical activity and serum concentration of vitamin D3. Vitamin D is mainly synthesized by sunlight, so outdoor physical activity can increase the concentration of this vitamin in the blood serum. Some studies, however, show that any type of physical activity, including indoor activity, may increase the synthesis of vitamin D [71], which was also found in our study. Although there were no significant differences in the level of physical activity between the study group, in which the serum vitamin D concentration was significantly lower, and healthy controls, the level of physical activity in both groups was estimated to be moderate. However, participants with epilepsy spent much less time walking and more time sitting. Moreover, in epileptics, a weak positive correlation was observed between vitamin D concentration in blood and time spent walking and between vitamin D and overall physical activity. There was also a weak negative correlation between vitamin D concentration and the time spent sitting. Unfortunately, numerous studies indicate that people with epilepsy are less physically active and less willing to participate in sports activities [72]. In general, fewer people with epilepsy show physical activity at the recommended level [44]. Importantly, other studies address the potentially beneficial role of physical activity in improving the cognitive function of patients with epilepsy [73] and quality of life [74]. Scientific evidence indicates that it is reasonable to educate patients with epilepsy about their lifestyle. Despite the proven role of physical activity in epilepsy, as shown by research results, recommendations for physical activity are not uniform. In some countries, epilepsy patient associations promote recommendations for physical activity [75]; however, there are no general guidelines. When making such recommendations, factors such as the type of epilepsy, seizure control, type of treatment, and safety of various forms of physical activity should be taken into account [76].

This study has several limitations. It assessed various aspects of nutritional behavior and lifestyle, as well as biochemical and anthropometric parameters, which is a strength of this study, but can also be a burden on participants. Therefore, a smaller number of respondents volunteered to take part in the survey than initially assumed. On the other hand, the data obtained during the research was complete for each participant. Another limitation is related to data on dietary behavior and physical activity that have been self-reported and may therefore be biased.

**Conclusions**

Our study found that patients with epilepsy have several lifestyle-related risk factors predisposing them to cardiovascular diseases, thus confirming the results of other studies. They were more sedentary, had worse body composition, higher LDL, lower vitamin D and less favorable dietary behavior compared to
healthy people. In conclusion, the study indicates that several behavior-related habits, which may predispose epileptic people to cardiovascular diseases, need to be improved. For this reason, patients with epilepsy should be provided with more comprehensive medical care, involving advice on nutrition and physical activity.

**Abbreviations**

AI
average intake
BHT
butylated hydroxytoluene
BM
body mass
BMI
body mass index
CVD
cardiovascular disease
DAD
diode array detector
EAR
estimated average requirement
HDL
high density lipoprotein
HPLC
high pressure liquid chromatography
IPAQ
International Physical Activity Questionnaire
IPAQ-S
IPAQ short form
LBM
lean body mass
LDL
low density lipoprotein
LDL-Ch
LDL cholesterol
MET
metabolic equivalent of task
PA
physical activity
PBF
percentage body fat
PWC
percentage water content
SMM
skeletal muscle mass
25(OH)D3
25-hydroxyvitamin D3

Declarations

Ethical approval and consent to participate

The study protocol was approved by the Bioethics Committee of the Medical University of Białystok, approval number R-I-002/110/2016. Participants gave their informed consent before taking part in the study.

Consent for publication

Not applicable.

Availability of supporting data

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

AMW, JK and KK made a concept of the study. Methodology was developed by AMW, JK, KK and MC. Formal analysis was carried out by KK and AMW. Investigation was carried out by KK, AMW and MC. Resources provided AMW and JK. KK prepared original draft. AMW and JK reviewed and edited the manuscript. AMW supervised the study. All authors read and approved the final manuscript.

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Figures
Figure 1

Flow-chart of epileptic participants *calculation according to the register of Statistics Poland (total number of epilepsy cases minus children with epilepsy).
Figure 2

Percentage of energy from macronutrients and alcohol in the total energy supply in epileptic and healthy participants.

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