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Survey of risk factors for osteoporosis and osteoprotective behaviors among patients with epilepsy

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ABSTRACT

The prevalence of risk factors for osteoporosis in persons with epilepsy, patients' awareness of their risk, and their engagement in osteoprotective behaviors were assessed in this study. Two hundred and sixty patients with epilepsy (F = 51.5%, average age = 42) completed a survey tool. Of 106 patients with a dual energy X-ray absorptiometry (DXA) result, 52% had low bone mineral density, and 11% had osteoporosis. The results suggest that the majority of patients with epilepsy do not engage in bone-protective behaviors. Those who have undergone a DXA scan may be more likely to take calcium and vitamin D supplementation compared with those who did not undergo a DXA scan, but they do not engage in other osteoprotective behaviors. Many patients did not accurately report their DXA results, indicating that better patient education is warranted.

1. Introduction

Patients with epilepsy are two to six times more likely to fracture a bone compared with the general population [1,2]. While patients with epilepsy are predisposed to fracture due to seizure-related falls, a meta-analysis attributed seizures as a cause for only one-third of the fractures [2]. The risk of falls and subsequent fracture is exacerbated by impaired balance from adverse effects of antiepileptic drugs (AEDs) and/or comorbid neurological deficits [3–5]. Concomitantly, there is a high prevalence of osteopenia and osteoporosis found in the patient population with epilepsy, especially in groups normally considered with a low risk of developing bone disease, such as males under the age of 50 and women in the premenopausal period [1,6–10]. Therefore, bone disease, specifically osteopenia and osteoporosis, contributes to the high fracture rate in this population.

Antiepileptic medications increase patients' risk of debilitating osteoporosis. Older enzyme-inducing AEDs (phenytoin, phenobarbital, primidone, and carbamazepine) accelerate vitamin D metabolism and adversely affect bone mineral density (BMD), bone quality, and bone turnover. However, other mechanisms, such as a direct effect on bone cells, the endocrine system, and vitamin K, may also cause bone loss as low BMD is observed with AEDs that are not enzyme inducers (e.g., valproic acid) [11–15]. Most likely, multiple factors, in addition to AED exposure, may lead to poor bone health in patients with epilepsy.

Other medications prescribed to patients with epilepsy may further increase their risk of bone loss. Depot medroxyprogesterone acetate injection (Depo-Provera®), a progestin-based contraceptive, is often recommended to women of child-bearing age with epilepsy, but studies find that it reduces BMD by as much as 3% in adolescents and young women at an age when increases of BMD are a norm [16–18]. Consequently, Depo-Provera® has a black box warning indicating that women may lose significant BMD, and long-term use (greater than two years) should be limited to patients in whom other birth control methods are inadequate. The bone-reducing effects may be reversible, but studies are lacking to determine whether reaching peak bone mass is impeded by the use of the contraceptive and if it increases risk of fracture at an older age [19–21].

Behavioral risk factors for osteoporosis include low calcium intake, vitamin D insufficiency, increased alcohol intake, inadequate physical activity, smoking, and falling [22]. However, few studies have investigated the prevalence of these risk factors among patients with epilepsy. Population surveys in Ohio, Georgia, and Tennessee using the Behavioral Risk Factor Surveillance System (BRFSS) found that persons with a

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history of epilepsy report that they exercise less frequently and smoke more compared with the general population [23,24]. In contrast, the 2005 California Health Interview Survey (CHIS) found no difference in exercise patterns [25]. To date, there are no studies that determine which risk factors are most prevalent or predict low BMD in patients with epilepsy.

Patients with epilepsy may also be less likely to engage in bone-protective behaviors. Awareness among patients with epilepsy of their increased risk of bone disease may increase their likelihood of engaging in bone-protective behaviors [26]. Interestingly, studies of other populations found that patients who were told that they have low BMD results after dual energy X-ray absorptiometry (DXA) testing were more likely to increase dietary calcium, start an exercise program, and stop smoking compared with patients with normal BMD results [27]. Unfortunately, trends in adoption of osteoprotective behaviors in patients with epilepsy have not been studied.

Thus, it is important that the relationship between risk factors for osteoporosis and epilepsy be understood in order for better preventative measures to be adopted to minimize the risk of debilitating osteoporosis. This study aimed to assess the following: (1) risk factors for developing osteoporosis in patients with epilepsy and (2) patients' awareness of their risk and engagement in osteoprotective behaviors.

2. Methods

2.1. Subjects

Patients visiting the University Medical Group's Epilepsy Clinic at Robert Wood Johnson Clinical Academic Building in New Brunswick, NJ for a regular appointment with their neurologist were asked to complete a survey tool about demographics and behaviors. Patients managed by three neurologists with a specialty in epilepsy participated in the study. Surveys were completed by either the patient or the caretaker or were verbally administered by an investigator from June 2008 to January 2011. We collected survey tools from (1) adult patients $\geq$18 years of age, (2) those with a diagnosis of epilepsy determined by their neurologists, (3) both those who completed a DXA scan and those who did not complete a DXA scan, and (4) those who were fluent in English or had an available translator (phone translator service was used for one patient). Patients who had cognitive impairment and whose caretakers were not present, who experienced seizures during their appointment, or who were uncooperative were excluded. Additionally, the DXA results were retrieved from an existing database, which our research group created to track BMD changes of our patients with epilepsy or from patients' electronic chart when available. All protocols were reviewed and approved by the Institutional Review Board of the University of the Medicine and Dentistry New Jersey (UMDNJ) and Rutgers University, and informed consent was collected from all patients.

2.2. Survey tool

The survey tool included a variety of question formats. Patients were asked to fill in their age, gender, sex, height, weight, ethnicity, current AEDs, and number of seizures per month, and they were asked to select from a list of AEDs to determine self-reported lifetime exposure to AEDs. Questions regarding family history of osteoporosis, engaging in weight-bearing exercise, smoking cigarettes, drinking one alcoholic beverage in the last month, and fracture history were in a yes/no format. When asked if each patient ever underwent a DXA scan, patients could choose between yes/no/I am not sure. If a patient reported undergoing a DXA scan, they were asked to provide the approximate date of the last DXA scan and to report their result as either "low bone density" or "normal bone density". For supplement history, patients were asked to select if they currently took calcium, vitamin D, combination product, multivitamins, or other supplements. If a patient reported taking one or more of the supplements, they were asked to list the dose, brand, or ingredients and to select an intake frequency of less than three times per week or greater or equal to three times per week. To determine dietary calcium intake, we asked patients to calculate the number of servings of calcium-rich foods they ate per day (1 serving = 1 cup of milk, yogurt, or pudding; 1 1/2 slices of cheese; 2 cups of dark vegetables; or 6 oz. of salmon). For frequency of exercise and sunlight exposure, patients were asked to select between less than three times per week and greater or equal to three times per week. Finally, bone health perception was listed on a scale of poor, fair, average, good, or great. Female patients were asked to select if they were menstruating, menopausal, or postmenopausal. The survey tool was not validated, but the questions were adopted from previously published articles, the BRFSS questionnaire, and the National Health and Nutrition Examination Survey (NHANES) [23,28].

2.3. Data collection

Data from the survey tool were entered into an Excel spreadsheet. The DXA results were characterized as low if the t-score was less than or equal to −1.0 SD at either the femoral neck or the L1–L4 spine. Additionally, t-scores between −1.0 and −2.5 SD were characterized as osteopenic, and less than −2.5 SD were characterized as osteoporotic [22]. Each patient's BMI was calculated using the formula BMI = kg/m^2. Patients reporting dual ethnicity (i.e., Black and Italian) were put into the "other" category, and those reporting Indian ethnicity were put into the "Asian" category.

Each patient's risk of bone loss was defined by the AEDs they had taken and the presence/absence of osteoporosis risk factors, including engagement in osteoprotective behaviors. Patients who reported a lifetime exposure to phenytoin, phenobarbital, primidone, valproic acid, oxcarbazepine, and/or carbamazepine were identified as higher-risk patients as these drugs are reported to reduce bone density (AED reducers). Categories of AED exposure were also subdivided into low/unknown reducers (levetiracetam, lamotrigine, gabapentin, lacosamide, zonisamide, pregabalin, and topiramate), medium reducers (oxcarbazepine and valproic acid), and strong reducers (phenytoin, phenobarbital, carbamazepine, and primidone).

Patients were characterized as having poor seizure control if they met the following criteria: three or more convulsive seizures in different occasions per year, three or more complex partial seizures per year, status epilepticus within one year, and/or frequent episodes of behavioral outburst with uncontrolled psychiatric symptoms and confusion.

Patients who completed a DXA scan were compared with patients who did not complete a DXA scan. We hypothesized that patients reporting having undergone a DXA scan would have a higher rate of osteoprotective behaviors compared with those not reporting having undergone a DXA scan. Post hoc analysis included comparing patients who reported having low bone mineral density with those who reported having normal bone mineral density; comparing patients with the presence of risk factors for osteoporosis (age greater than fifty, family history of osteoporosis, postmenopausal, and BMI less than 19 kg/m^2) with those without risk factors, comparing patients with a family history of osteoporosis with those without, comparing male patients with female patients, comparing patients who had good perception of bone health with those who had poor perception of bone health, and comparing patients with good seizure control with those with poor seizure control. The patients' DXA scan results were correlated with their perception of their bone health.

2.4. Data analysis

Survey tool data were converted to categorical values. "Adequate dietary calcium" was defined as greater than or equal to 3 servings of calcium-rich food per day, "regular intake of calcium and vitamin D supplementation" as calcium and vitamin D supplementation (either a