Epilepsy & Behavior 43 (2015) 61–65

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

An evaluation of the impact of memory and mood on antiepileptic drug adherence

James W. McAuley [a,b,*], Nina Passen [a], Christine Prusa [a], Joanne Dixon [a], Sheri Cotterman-Hart [b], Bassel F. Shneker [b,a]

[a] Ohio State University College of Pharmacy, Columbus, OH 43210, USA
[b] Ohio State University College of Medicine, Columbus, OH 43210, USA

ARTICLE INFO

Article history:
Received 29 September 2014
Accepted 17 November 2014
Available online 2 January 2015

Keywords:
Memory
Adherence
Mood
Depression
Antiepileptic drug
Pharmacy
Medication possession ratio

ABSTRACT

Rationale: Antiepileptic drugs are the mainstay of treatment for patients with epilepsy. Adherence to the prescribed regimen is a major factor in achieving a reduced seizure burden, which can decrease morbidity and mortality. Patients with epilepsy oftentimes complain about difficulty with memory. Because little is known about the relationship between memory and mood and adherence, the purpose of this project was to determine the impact of the confounding factors of memory and mood on antiepileptic drug adherence in patients with epilepsy.
Methods: One hundred adult patients with epilepsy were recruited from the outpatient neurology clinic for this cross-sectional study. Patients who met the inclusion criteria completed measures of subjective memory (subset of 6 memory questions from the QOLIE-89) and objective memory (Hopkins Verbal Learning Test – Revised), subjective adherence (Morisky scale) and objective adherence (medication possession ratio), and mood (Neurological Disorders Depression Inventory for Epilepsy). Refill records from each patient's community pharmacy were used to objectively assess adherence. Medication possession ratios were calculated based on the antiepileptic drug refill records over the previous 6 months. Patients were considered adherent if their MPR was >80%.
Results: Women made up the majority of the sample (n = 59), and, on average, patients had been living with epilepsy for nearly 20 years. Approximately 40% of the sample were on antiepileptic drug monotherapy; most patients (>70%) took their antiepileptic drugs twice daily, and the mean number of total medications was 4.25 ± 2.98. Based on the objective measure of adherence, 35% of the patients were nonadherent. Patients self-reported better adherence than what was objectively measured. Only the retention metric of the objective memory measure differentiated adherent patients from nonadherent patients. Patients in the adherent group had significantly lower depression scores (indicating better mood) compared with those in the nonadherent group ($p = 0.04$).
Conclusions: Objective memory measures were not robustly correlated with adherence. However, we observed that patients with higher depressed mood scores were more likely to be nonadherent. By targeting patients with epilepsy and comorbid depression, practitioners may identify patients at greatest risk of nonadherence and subsequent harm.

1. Introduction

Epilepsy is a common neurological problem affecting 1%–2% of the population. Antiepileptic drugs (AEDs) are the mainstay of treatment for patients with epilepsy, and adherence to the prescribed drug regimen is a major step in achieving a reduced seizure burden. Faught and colleagues have shown that decreased AED adherence is associated with more than a 3-fold increase in mortality [1]. Periods of nonadherence in patients with epilepsy were also associated with significantly more emergency department visits, hospital admissions, injuries, and fractures. A comprehensive review on AED adherence has recently been published [2].

As in patients with epilepsy, medication adherence is an important determinant of reaching optimal outcomes in patients with chronic conditions. Adherence studies have been done in patients with other chronic diseases such as hypertension, heart disease, diabetes, arthritis, chronic obstructive pulmonary disease, asthma, depression, osteoporosis, and high cholesterol [3].

The medication possession ratio (MPR) is a measure of adherence frequently utilized in the literature [1]. It is calculated by dividing the number of days of medication supplied within the refill interval by the number of days in the refill interval. The resulting value is typically between 0 and 1, with an MPR value >0.8 being the widely accepted cutoff indicative of adherence.

* Corresponding author at: The Ohio State University College of Pharmacy, 500 West 12th Ave, Columbus, OH 43210, USA. Tel.: +1 614 292 9713.
E-mail address: McAuley.5@osu.edu (J.W. McAuley).

http://dx.doi.org/10.1016/j.yebeh.2014.11.017
1525-5050/

The complex interaction of disease, treatment, and comorbid conditions is especially evident in the care of patients with epilepsy in tertiary care epilepsy centers. Despite verbal reports of adherence in most patients, in a small prospective project, six (54.5%) of 11 patients had a baseline AED MPR < 0.8 (unpublished data). Based on the current literature, the full contributors to adherence are unclear. There is extensive literature on memory dysfunction in patients with epilepsy, and recent data indicate that patients with epilepsy have a higher than previously detected level of concern with their memory [4]. An additional confounding factor is the interplay of mood with subjective and objective measures in patients with epilepsy [5]. To date, no literature that explores the relationship between these confounding factors and adherence in patients with epilepsy exists. The purpose of this project was to determine the impact of the confounding factors of memory and mood on AED adherence in patients with epilepsy.

2. Materials and methods

One hundred patients were recruited from the Ohio State University Wexner Medical Center's Comprehensive Epilepsy Program for this cross-sectional study. Institutional review board approval was obtained before any patients were recruited. Adult patients with epilepsy taking at least one AED for the prior 6 months and capable of providing consent and completing the surveys by themselves were recruited. The patients were also required to get their monthly AED refills from a community pharmacy.

Demographic and seizure activity data were gathered. As an incentive, all 100 patients were entered into a random drawing for four $25 gift certificates to a local store. Patients completed a brief battery of tests to assess memory (subjective and objective), mood, and self-reported adherence during their regularly-scheduled clinic appointment.

2.1. Memory

Subjective memory was assessed by asking the six memory domain questions from the validated Quality of Life in Epilepsy-89 questionnaire (QOLIE-89) which is reported as a percentage, with a higher score equating to better memory [6]. Objective memory was measured by the Hopkins Verbal Learning Test — Revised (HVLT-R), a brief assessment of recognition and recall for individuals 16 years and older. Recommended by the Epilepsy Common Data Elements group [7], the HVLT-R has been validated within populations with brain disorders such as Alzheimer's, Parkinson's, and Huntington's diseases as a measure of verbal learning and memory [8] and has been found to be independently predictive of everyday instrumental activities of daily living, problem-solving, and psychomotor speed [9]. This test provides four measures: total recall, delayed recall, retention %, and recognition discrimination index. To determine if patients who report subjective memory complaints had a corollary deficit on an objective measure of memory, we compared each patient's QOLIE-89 subset score (subjective) with their HVLT-R score (objective). The HVLT-R total recall score (0 to 36) was converted into a percentage (HVLT-R %), and a difference score (subjective − objective) was calculated. A negative score reflects that the patient did better on the objective memory test than on the subjective memory test.

2.2. Mood

Mood was assessed by the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E). This is a patient-answered six-item questionnaire that has been shown to be sensitive and specific in patients with epilepsy [10]. Lower scores represent better mood.

2.3. Adherence

Self-reported adherence was assessed by using the 4-question Morisky scale [11] and a visual analog scale (VAS). Morisky et al. developed a brief, easily understood, and valid scale to be administered to patients in the clinical setting. Scores range from 0 to 4, with 4 depicting high and 0 depicting low medication-taking behavior. Patients were categorized into three groups: low (score of 0 or 1), medium (score of 2 or 3), and high (score of 4) scores. For the VAS, patients were asked to mark on a line anchored by “nonadherent” and “completely adherent” where they felt depicted their AED adherence. Their VAS score was calculated as a percent, with higher scores denoting better self-reported adherence. Patients were also given the opportunity to identify barriers and facilitators of their AED adherence (with the option to choose more than one response).

Each patient's community pharmacy provider was contacted to obtain their AED refill history records over the previous 6 months. This information was used to calculate each patient's AED MPR: the objective measure of adherence. For those patients on AED polytherapy, an average MPR was calculated. Based on MPRs, patients were separated into adherent (ADH) [MPR > 0.8] and nonadherent (non-ADH) [MPR < 0.8] categories. Refill histories were not gathered for non-AED medications.

2.4. Statistical analysis

Categorical data were subjected to chi-square analysis with between group comparisons of continuous data analyzed with Student's t-tests. Continuous variable correlations were measured using Pearson's correlation, and between-group comparisons of correlation were calculated using Fisher's method [12].

3. Results

3.1. Demographics

A convenience sample of 100 patients was recruited. Their demographic information is summarized in Table 1. Women made up the majority of the sample, and, on average, patients had been living with epilepsy for nearly 20 years. Approximately 40% of the sample were on AED monotherapy; most patients (>70%) took their AEDs twice daily, and the mean number of total medications was just over four. There were no demographic differences between the ADH patients and the non-ADH patients.

3.2. Adherence

Objective adherence data (individual MPR scores) are presented in Fig. 1. Sixty-five patients had an MPR greater than or equal to 0.8 and, thus, were categorized as ADH. Patients' self-assessment of medication adherence (subjective adherence) via the Morisky score and VAS demonstrated that a majority of both the ADH patients and the non-ADH patients put themselves in the “medium” or in the “high” adherence category (Table 2). When examining correlations between adherence measures, we correlated both the Morisky scores ($r = 0.25$, $p = 0.005$) and the VAS scores ($r = 0.2$, $p = 0.02$) with MPR. There was no difference in either subjective adherence score between the ADH group and the non-ADH group nor was there a significant difference between the groups in correlation of subjective adherence and Morisky ($z = 0.003$, NS) or VAS ($z = 0.17$, NS) scores.

When patients were asked to identify barriers to their adherence, a majority of each group (>70%) reported no adherence barriers (Fig. 2). Ten percent of the entire sample identified cost as a barrier, though this was slightly higher (14.3%) in the non-ADH patients, possibly due to more patients in the latter group having income < $30,000 (77%) compared with the ADH group (54%). When patients were asked to identify adherence facilitators, the most common responses were “own routine” (59% of the sample) and a pillbox (52% of the sample) (Fig. 3).