Patient characteristics and treatment patterns in patients with newly diagnosed epilepsy: A US database analysis

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ABSTRACT

Objective: The objective of this study was to determine patient characteristics and antiepileptic drug (AED) treatment patterns in patients with newly diagnosed epilepsy in a United States (US) population followed for ≥180 days.
Methods: In this retrospective cohort study, Commercial, Supplemental Medicare, and Medicaid insurance claims from US-based Truven Health MarketScan® claims database were analyzed for incident epilepsy cases (index date: January 2010–June 2013; prior baseline of 2 years [1 year for ages 1 to <2 years; none for those <1 year]). Cases met epilepsy criteria consistent with the International League Against Epilepsy diagnostic guidelines, with continuous medical and pharmacy enrollment without an epilepsy or seizure diagnosis or AED prescription during baseline. Treatment was classified as monotherapy (one AED for ≥90 continuous days), polytherapy (at least two AEDs for ≥90 days), or untreated (no AED claims but other pharmacy or healthcare claims). Treatment pattern comparisons used matched cohorts across seizure types.
Results: Of 58,757 incident cases, 50,838 had a follow-up of ≥180 days. The median (range) follow-up duration was 529 (180–1096) days. Patient characteristics were similar across seizure types (matched focal vs. generalized epilepsy, N = 9949 each). At 6 and 12 months post-index, 46.8% and 52.2% of patients, respectively, had received AED treatment. Of 29,226 patients receiving treatment, 74.7% and 1.6% received monotherapy and polytherapy for ≥90 days, respectively, as first-line treatment; remaining patients received AED for <90 days and were excluded. The probability of remaining on initial treatment after 1 year was 61.0% for monotherapy and 36.5% for polytherapy. The most common first-line AEDs were levetiracetam (44.4%), phenytoin (6.5%), valproic acid (6.4%), lamotrigine (6.3%), oxcarbazepine (5.7%), topiramate (5.5%), and gabapentin (5.3%).
Conclusion: Although the majority of treated patients received AED monotherapy consistent with guidelines, suboptimal rates of AED treatment and persistence of first-line treatment after initial epilepsy diagnosis suggest that efforts are needed to improve patient care.

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1. Introduction

Epilepsy has a significant impact on direct and indirect healthcare costs [1] as well as quality of life [2]. Epilepsy guidelines provide recommendations for treatment with antiepileptic drugs (AEDs) with the goal of preventing future seizures [3,4]. Initial treatment with AED monotherapy is recommended for new-onset epilepsy, with subsequent substitution with another AED monotherapy if results are unsatisfactory [4]. Antiepileptic drug polytherapy is typically reserved for cases where seizure control has not been obtained with AED monotherapy trials. Few studies shed light on whether treatment patterns in clinical practice align with guidelines. In studies of incident epilepsy populations, approximately 80% of treated patients were reported to receive AED monotherapy as initial treatment [5,6]. In one study, the proportion of patients receiving any AED treatment decreased from 90.3% to 74.8% between 1 to 4 years of follow-up. However, treatment patterns across the 4 years of follow-up were relatively consistent, with approximately 81% of treated patients receiving AED monotherapy and 16%, 2%, and <1% receiving two, three, or at least four AEDs in each year of follow-up [6]. Because successive lines of AED treatment have been associated with declining rates of seizure freedom [7], it is of interest to identify patterns in treatment changes. However, data on disease progression in new-

onset epilepsy are limited, and large representative, population-based studies in the United States (US) examining AED treatment choices and patterns are lacking.

We used a large sample of patients with epilepsy to discern patient characteristics and current AED treatment patterns in patients with newly diagnosed epilepsy in a US population followed for at least 6 months. We also explored whether treatment patterns differed based on type of insurance and seizure type.

2. Methods

2.1. Data source

This was a retrospective cohort study designed to identify and analyze incident epilepsy cases using Commercial Claims and Medicare Supplemental (CCMC) and Medicaid insurance claims data from the US-based Truven Health MarketScan® claims database. The claims database, representing >100 million lives, included data from US patients running the spectrum from employees and their dependents, to persons aged ≥65 years with supplemental Medicare and persons on state-paid insurance (Medicaid in 13 representative states).

2.2. Patient population and study design

Incident epilepsy cases with an index date between January 2010 and June 2013 were identified. The index date was defined as the first date the patient met the diagnosis of epilepsy (as defined below), with a preceding 2-year baseline period (1 year for those aged 1 to <2 years; none for those <1 year); for diagnoses requiring at least two International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes, the index date was the date of the first diagnosis code (below). Diagnostic criteria were consistent with guidelines published by the International League Against Epilepsy (ILAE) on defining epilepsy diagnosis in epidemiological studies [8]. Cases were required to have continuous medical and pharmacy enrollment without an epilepsy or seizure diagnosis or AED prescription during the baseline period.

Diagnosis required that any of the following criteria be met:

- At least two ICD-9-CM 345.xx (epilepsy and recurrent seizures) codes at separate encounters in any care setting
- At least one ICD-9-CM 345.xx code AND ≥1 ICD-9-CM 780.39 (other convulsions) code among separate encounters
- One ICD-9-CM 345.xx code and code(s) for AED prescription after the 345.xx code
- At least two ICD-9-CM 780.39 codes among separate medical encounters AND code(s) for AED treatment (AED treatment code occurred after the second 780.39 code irrespective of the presence/absence of an AED code after the first 780.39 code).

These algorithms have been validated with reported sensitivity ranging from 88.9–99.6% and specificity ranging from 82.5–93.2% in identifying patients with epilepsy in the claims databases [9].

Patients with ICD-9-CM code 345.3 (grand mal status) were required to have the following:

- At least two ICD-9-CM 345.3 codes separated by ≥30 days, or
- One ICD-9-CM 345.3 code and at least one ICD-9-CM code 780.39 separated by ≥30 days, or
- At least one ICD-9-CM code 345.3 and at least one ICD-9-CM code 345.xx encounters on separate days.

Seizure types were defined as focal (at least one ICD-9-CM codes 345.4x, 345.5x, or 345.7x AND no occurrences of ICD-9-CM codes 345.0x, 345.1x, or 345.2); generalized (at least one ICD-9-CM codes 345.0x, 345.1x, or 345.2x AND no occurrences of ICD-9-CM codes 345.4x, 345.5x, or 345.7x); or undefined (all other cases, including epilepsy/seizure codes that were nonspecific as to focality [ICD-9-CM codes 345.3x, 345.6x, 345.8x, 345.9x, or 780.3x] as well as inconsistent codes [some indicating focal and others indicating generalized]). Cases were followed for a minimum of 180 days from and including the index date, up to a maximum of 3 years.

2.3. Outcomes

Treatment was classified as monotherapy (prescription claims for one AED for ≥90 continuous days), polytherapy (simultaneous prescription claims for at least two AEDs for ≥90 continuous days), or undetermined (either AED claims for <90 days or AED claims started within 90 days of the end of the follow-up period).

Patients were classified as untreated if they had no AED prescription claims during the follow-up period but had other pharmacy or healthcare claims. The duration of AED treatment was defined as the number of days from first to last AED dispensing record plus the number of days of drug supply following the date of the last dispensing record. A treatment line was defined as a period of time during which the patient was treated with a constant AED regimen, and a drug persistence window of 90 days was allowed where patients with a gap less than the persistent window were considered to still be under treatment. The treatment line started (or ended) when any specific AED was started or discontinued. Therefore, first-line treatment commenced upon prescription for the first AED and ended after at least 90 continuous days of treatment, followed by either discontinuation of that AED or addition of another AED. Changes in dose were not assessed. Treatment outcomes were defined as continued (no treatment change until end of follow-up period); augmented (addition of at least one AED to the current AED regimen); switched (current treatment line contained AED not in the next line and next line contained AED not present in the current line); or discontinued (no prescription for the AED after the last prescription of >90 days).

2.4. Statistical analysis

Treatment patterns between matched cohorts (matched by age, sex, insurer, and duration of follow-up) of patients with focal and generalized epilepsy seizure types were examined based on baseline characteristics. Descriptive analyses were used, and continuous variables were presented using mean and standard deviation (SD), median and quartiles, or range. Categorical variables were presented using frequencies and percentages.

3. Results

3.1. Disposition and patient characteristics

Of the 50,838 patients who met the criteria for epilepsy diagnosis and had ≥180 days of follow-up, 38,674 (76.1%) and 12,164 (23.9%) were covered by CCMC and Medicaid, respectively. The mean (SD) and median (range) duration of follow-up was 563.7 (257.0) days and 529 (180–1096) days. Patient characteristics were similar across epilepsy seizure types (Table 1) for the overall population. Matched cohorts for comparison were available for the overall focal vs. general epilepsy (N = 9949 each) (eTable 1). The CCMC population was older than the Medicaid population (mean [SD] age, 42.3 [26.9] years vs. 16.0 [17.6] years). Nearly three-quarters (73.3%) of the Medicaid population was aged ≤19 years vs. 29.6% of the CCMC population (Fig. 1). The CCMC population had a higher prevalence of somatic comorbidities compared with the Medicaid population, and there were differences in the prevalence of psychiatric comorbidities in two study populations (eTable 2).