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Newer antiepileptic drug use and other factors decreasing hospital encounters

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ABSTRACT

A retrospective analysis was conducted in one claims database and was confirmed in a second independent database (covering both commercial and government insurance plans between 11/2009 and 9/2011) for the understanding of factors influencing antiepileptic drug (AED) use and the role of AEDs and other health-care factors in hospital encounters. In both datasets, epilepsy cases were identified by AED use and epilepsy diagnosis coding. Variables analyzed for effect on hospitalization rates were as follows: (1) use of first-generation AEDs or second-generation AEDs, (2) treatment changes, and (3) factors that may affect AED choice. Lower rates of epilepsy-related hospital encounters (encounters with an epilepsy diagnosis code) were associated with use of second-generation AEDs, deliberate treatment changes, and treatment by a neurologist. Epilepsy-related hospital encounters were more frequent for patients not receiving an AED and for those with greater comorbidities. On average, patients taking ≥1 first-generation AED experienced epilepsy-related hospitalizations every 684 days, while those taking ≥1 second-generation AED were hospitalized every 1001 days (relative risk reduction of 31%, $p < 0.01$). Prescriptions for second-generation AEDs were more common among neurologists and among physicians near an epilepsy center. Use of second-generation AEDs, access to specialty care, and deliberate efforts to change medications following epilepsy-related hospital encounters improved outcomes of epilepsy treatment based on average time between epilepsy-related hospital encounters. These factors may be enhanced by public health policies, private insurance reimbursement policies, and education of patients and physicians.

1. Introduction

Of the more than two million people with epilepsy in the United States, about 45% do not achieve complete control of seizures with antiepileptic drugs (AEDs) [1]. This high degree of AED failure imposes a substantial burden on individuals and society and has resulted in calls for patient-centric care that reflects current best evidence and access to specialists and treatments [2]. There are studies supporting better seizure control when patients are seen by epileptologists at specialty care centers, yet only about half of all patients have seen a neurologist in the previous year [3,4]. Treatment choices are largely driven by efficacy, safety, and the physician's prior experience with an AED [5]. One possible reason for inadequate seizure control may be AED choice guided by a perception that first-generation drugs – those available before 1993 – and second-generation drugs - those that became available from 1993 until September, 2011- equivalent in terms of efficacy, though the newer drugs may have advantages in terms of pharmacokinetics and side effects [6].

Evaluations of patient care and cost effectiveness depend on measurable outcome data. Claims data do not include typically evaluated clinical data on seizure freedom, seizure severity/frequency, and quality of life, as these are dependent upon patient report. Therefore, an approach commonly used in epidemiological studies is the use of surrogate measures available from claims data for these outcomes [7,8]. In fact, some surrogate metrics can better approximate success in the real world as the combination of side effects, dosing, formulary coverage, out-of-pocket costs, administration, and other characteristics of medicines beyond efficacy can be reflected in the stability of treatment and, thus, successful treatment. For this paper, the rate of epilepsy-related hospitalizations and emergency department visits for an individual may be a reasonable proxy of a negative outcome, and this rate can be measured for populations

Abbreviations: SDI, Surveillance Data Incorporated; HIPAA, Health Insurance Portability and Accountability Act; NAEC, National Association of Epilepsy Centers.

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using administrative claims data [9]. Hospital encounters are major contributors to the costs of epilepsy; between 1993 and 2008, the average hospital charge per admission for patients with epilepsy increased 138% (from $10,050 to $23,909, $p < 0.001$), despite a 33% decrease in average length of stay (from 5.9 days to 3.9 days) [10].

What are the factors influencing AED use, and how do they impact hospital encounters? Using two large patient claims datasets, we examined and confirmed negative correlations of hospital encounters associated with an epilepsy diagnosis code with use of second-generation AEDs, proximity to specialized treatment centers, frequency of visits to physicians, and physician changes to AED therapy.

2. Materials and methods

2.1. Data sources

We analyzed data captured from November 2009 through September 2011 in two medical claims databases, Surveillance Data Incorporated (SDI) and Truven Health MarketScan® Research Databases. Surveillance Data Incorporated was the primary dataset, and MarketScan was used for validation of the observations within the SDI dataset. Surveillance Data Incorporated aggregates patient information from multiple provider sources: Dx — patient and physician demographics, diagnoses, and procedures; Rx — prescriptions originating from retail, specialty, or mail order pharmacies; and Hx — data from hospital charge master systems. Surveillance Data Incorporated is an open database that links services for an individual across provider sources by a unique encrypted patient ID but may not capture all claims for individual patients if they use providers that do not submit data to SDI. Eligibility requirements applied to the data ensured continuous reporting from the sources and served as a proxy for "closing" the dataset. In contrast, data from the Truven Health MarketScan Research Commercial, Medicare Supplemental, and Medicaid databases (closed datasets) include all claims related to each beneficiary's prescriptions, physician office visits, and both inpatient and outpatient hospital activities as long as they were continuously enrolled during the analysis timeframe and used this insurance (rather than cash or alternate insurance) to pay for their health services. The SDI and MarketScan databases are composed of deidentified data in compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations, thus making the study exempt from institutional review board review.

To investigate factors influencing prescription of first-generation AEDs versus second-generation AEDs, we used data from the IMS Xponent Plan Trak database and Pinsonault formulary data. IMS Xponent Plan Trak aggregates retail pharmacy prescriptions by type and by prescriber. Pinsonault formulary data were used to investigate AED formulary coverage status for commercial Medicare Supplemental and Medicaid programs (e.g., coverage, tiering, restriction, and prior authorization).

2.2. Patient selection

For both the SDI (primary) and the MarketScan (validation) datasets, we began by defining an analysis set of patients who were 12 years of age and older and (1) had at least one encounter with an epilepsy diagnosis code (International Classification of Diseases, Ninth Revision codes: 333.2 (myoclonus), 345.xx (epilepsy), or 780.3x (convulsions, except 780.33)) or (2) lacked an epilepsy diagnosis code but had received one or more prescriptions for AEDs with epilepsy as the only FDA-approved indication — lacosamide, levetiracetam, rufinamide, vigabatrin, or phenytoin during the analysis timeframe — to allow us to include patients with rich Hx and Rx data, where the Dx data were missing. In both datasets, the individual must have received at least one AED prescription during the final year of observation to be included to ensure that the patients were actively being treated for epilepsy.

Additional eligibility requirements applied to the SDI dataset included that patients must have had continuous prescription data (once every 6 months for last 6 periods, each period consisting of 6 months) and must have been hospitalized for any cause at least once during the study period. The prescription requirement was intended to ensure that we had reasonable visibility into the patient's health-care activity, and no attempt was made to address adherence to therapy. The hospitalization requirement was used to increase confidence that a patient's hospital activity was captured in the SDI dataset. In contrast to the SDI dataset, the MarketScan validation dataset facilitated analysis of patients with and without hospital encounter claims and only required that patients had three years of continuous enrollment.

2.3. Analysis

Descriptive statistics for demographic and clinical variables are reported separately for the SDI and MarketScan populations. Operational definitions for enrollee characteristics, epilepsy-related hospital encounters, other treatment variables, and calculations are provided in Table 1. With the SDI dataset, we analyzed the effect of the use of first-generation AEDs versus second-generation AEDs on epilepsy-related hospital encounter rates (as defined in Table 1) and also whether demographic characteristics (sex, age, comorbidities [Charlson Comorbidity Index [11]], and regions of the U.S.) had an effect on observed differences. We also assessed the effect of "deliberate effort" by a prescriber – defined as switches or additions of any AED – following a hospital encounter event on the rate of subsequent epilepsy-related hospital encounters. Using Pinsonault formulary data and Xponent Plan Trak data, we calculated the ratio of prescription of second- to first-generation AEDs, based on three variables: (1) prescriber specialty (neurologist versus primary care physician), (2) prescriber's proximity to a National Association of Epilepsy Centers (NAEC) member center, and (3) formulary access to second-generation AEDs. For the analysis of the impact of formulary access, the ratio of second-generation AED prescriptions to first-generation AED prescriptions was plotted for each group of classifications to determine the correlation between formulary coverage and utilization of second-generation AEDs. Differences in rates between groups were compared by chi-square tests and t-tests; p-values <0.05 determined the significance of comparisons. In our confirmatory analysis, Cox proportional hazards models were applied to the MarketScan dataset to assess the effects of independent predictors on the rate of epilepsy-related hospital encounters, providing hazard ratios with 95% CIs. These models also accounted for the nature of time-to-event data by censoring cases in which an epilepsy-related hospitalization had not occurred by the end of the observation period. Analyses were carried out on Stata® v.13 (StataCorp LP, College Station, TX).

3. Results

The inclusion criteria allowed us to define populations who are very likely to have epilepsy and with data sufficient for analysis of epilepsy-related hospital encounter frequency and medication changes over time. Of 18 million patients with prescription claims for AEDs in the SDI dataset, 391,000 had a required epilepsy diagnosis code plus at least one prescription for an antiepileptic drug or were prescribed one of the five AEDs that had epilepsy as their only approved indication. Among those patients with epilepsy, there were 17,743 meeting the hospitalization criterion. These 17,743 patients constituted our primary analysis set. Of 1.55 million persons prescribed an AED in the MarketScan databases, 196,000 were confirmed to be patients with epilepsy and were used as the analysis set.

3.1. SDI dataset

Demographics for the SDI and MarketScan populations are shown in Table 2. The SDI dataset included approximately 6000 events of inpatient hospitalizations and 9500 outpatient emergency department visits.