The objective of this review is to compare trials of the four anti-epileptic drugs (AEDs) approved specifically for the adjunctive treatment of primary generalized tonic-clonic seizures. Not all data were reported for each trial.

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SYSTEMATIC LITERATURE REVIEW OF ADJUNCTIVE ANTI-EPILEPTIC DRUG TRIALS IN PATIENTS WITH PRIMARY GENERALIZED TONIC-CLONIC SEIZURES ILLUSTRATES CHANGES IN STANDARD OF CARE OVER 12-20 YEARS

BACKGROUND

Four anti-epileptic drugs (AEDs) have been approved for the adjunctive treatment of primary generalized tonic-clonic seizures (PGTCS) in adults (Gabapentin [Lyrica], Lamotrigine [Lamictal], Levetiracetam [Keppra], and Primidone [Mysoline]). These drugs were all approved before 2000, with the exception of Gabapentin which was approved in 1993. The advent of new AEDs has led to a shift in the baseline AED composition for patients with PGTCS. This review aimed to illustrate the changes in the standard of care (SOC) for PGTCS over time.

METHODS

Primary Data Search

A systematic literature review of published randomized controlled trials (RCTs) was conducted to identify trials that met the inclusion criteria.

Exclusion Criteria

1. Published in the years: 1989-2014
2. Any of the interventions in the PICOS statement
3. Studies with patients on monotherapy treatment
4. Studies not including at least one of the interventions of interest listed in the inclusion criteria
5. Studies with less than 10 patients per arm
6. Abstracts without full papers
7. Studies with a double blind follow-up of the intervention of interest of less than 3 months

Supplementary Data Search

Following the identification of the trials of interest in the primary data search, additional details for these trials were provided through searches of clinicaltrials.gov and the regulatory reports of the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

OBJECTIVES

• A comparison of the baseline AED composition in the four anti-epileptic drugs (AEDs) approved specifically for the adjunctive treatment of primary generalized tonic-clonic seizures

METHODS

Primary Data Search

A systematic review of RCTs was conducted to identify randomized controlled trials for anti-epileptic drugs approved for the adjunctive treatment of primary generalized tonic-clonic seizures (PGTCS) in adults. The following databases were searched through OVID search platform: EMBASE, MEDLINE, Cochrane Library.

Exclusion Criteria

1. Published in the years: 1989-2014
2. Any of the interventions in the PICOS statement
3. Studies with patients on monotherapy treatment

Supplementary Data Search

Following the identification of the trials of interest in the primary data search, additional details for these trials were provided through searches of clinicaltrials.gov and the regulatory reports of the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

RESULTS

Table 1. Baseline AED Composition

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<th>LEV-X</th>
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<th>CBZ-X</th>
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Figure 1. PRISMA Flow Diagram

Figure 2. Timeline of Trial Enrollment Periods (1-6)

Limited inclusion of trials in the early 1990s

Differences in the minimum age limits (Table 3)

CONCLUSIONS

• The latest trial, the PER-RCT, enrolls patients more than 3 years after the last trial (LTG-XR-RCT) and reasonably allows for up to 3 AEDs at baseline.

• The SOC has evolved with the approval of new PGTCS drugs in a way which favors drugs that have been widely accepted.

• Some drugs have been more widely accepted than others (Table 4), and some drugs have higher minimum age limits.

REFERENCES