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REVIEW

Prognostic factors for medically intractable epilepsy: A systematic review

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Summary
Objective: One third of all epilepsy patients have medically intractable epilepsy. Knowledge of prognostic factors that, in an early therapeutic stage of epilepsy, herald intractability could facilitate patient management. In this systematic review, we examined the evidence for independent prognostic factors of intractability in patients with epilepsy.
Methods: MEDLINE and EMBASE were searched for cohort studies reporting on prognostic factors for medically intractable epilepsy. After selection of abstracts, full-text articles were obtained and their quality was assessed by two reviewers, using the QUIPS checklist. All independent prognostic factors in the individual studies were summarized.
Results: Eleven cohort studies were included, of which ten hospital-based. Younger age at seizure onset, symptomatic etiology, high initial seizure frequency, medical history, epileptic EEG abnormalities, and failure of previous antiepileptic-drugs (AEDs) were documented as independent prognostic factors of intractability in at least 2 of the 11 studies; none of these factors was reported in all 11 studies. None of the studies considered genetic, neurobiological, or immunological factors. The studies were of moderate quality, mostly because they did not provide a conceptual model for the choice of predictors. Heterogeneity in study design, population, candidate prognostic factors, and outcome definitions precluded statistical pooling.

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Conclusions: While potentially relevant prognosticators of medically intractable epilepsy have been identified, the evidence for these factors is not consistent. There is a need for well-designed prognostic population-based cohort studies that also include pharmacological, genetic, neurobiological, and immunological factors. A valid model for the early prediction of medically intractable epilepsy could improve patient management.

Contents

Introduction

Epilepsy, one of the most common neurological disorders (Hauser et al., 1993; Sander, 2003; Shackleton et al., 1997; Siniatchkin and Koepp, 2009), can be classified into symptomatic versus idiopathic or, focal versus generalized forms, based on its etiology (Commission on Classification and Terminology of the International League Against Epilepsy, 1989). This classification is important in determining the appropriate antiepileptic-drug (AED) treatment strategy. Focal epilepsy tends to respond to the majority of AEDs (Luders et al., 2009) but is also more frequently associated with intractability (Devinsky, 1999). Intractability (i.e. refractoriness or pharmacoresistance) is defined as failure of adequate trials of two tolerated, appropriately chosen and used AED schedules to achieve sustained seizure freedom (Kwan et al., 2010). This definition was proposed by a taskforce of the International League against Epilepsy in response to different existing definitions of intractability regarding required number of drug failures, endpoint (e.g., seizure freedom versus tolerable seizure load), and time to achieve this endpoint (Berg, 2009). Overall, it is estimated that a third of all patients have intractable epilepsy (Johnston et al., 2009; Panayiotopoulos, 2007; Sander, 2003) though these patients may experience periods of seizure remission (Munger Clary and Choi, 2011). Intractable patients have a higher risk of premature death, injuries, psychosocial dysfunction, and reduced quality of life (Hao et al., 2011). There are, however, large differences in individual responses to AEDs even between patients with seemingly identical seizure types and epilepsy syndromes (Schmidt and Loscher, 2005).

In clinical practice, intractability is often identified only after several AEDs have been tried. It is difficult to predict at an early stage who will develop intractable epilepsy, except for patients with relatively rare entities such as Lennox—Gastaut syndrome (Berg, 2009). Several clinical, etiological, demographic, pharmacological, and genetic factors may be involved in the development of intractability. Knowledge of those independent factors that predict intractability as early as possible could improve patient management by guiding treatment decisions, such as earlier referral for epilepsy surgery. This may alleviate the medico-social and economic burden of intractable epilepsy (Hao et al., 2011).

The aim of this systematic review was to summarize and qualify the results of published cohort studies designed to find independent prognostic factors of intractability in epilepsy patients.

Methods

Search strategy and selection criteria

A systematic search was conducted using MEDLINE and EMBASE, until June 10, 2010. The search was designed to identify (retrospective or prospective) cohort studies, since this is considered the optimal design for evaluating predictors and outcome (Berg, 2009; Moons et al., 2009). The studies had to be published as full reports in English with the aim of identifying independent prognostic factors of intractability in patients diagnosed with epilepsy. The search