Pharmacoresistance: impact on epilepsy treatment

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INTRODUCTION

Until recently, epidemiological researches on drug-resistant epilepsy were hampered by a lack of defined criteria. In 2010, the International League Against Epilepsy (ILAE) appointed a taskforce to define drug resistant epilepsy as "the failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules to achieve sustained seizure freedom." There is some disagreement over what constitutes a sufficient dosage. As noted in the ILAE study, dogmatically defining the optimal dose for each medication when administered for a specific individual is impracticable. While there is preliminary evidence to support using half of the stated daily dosage as a cut-off in adults, a documented attempt to titrate the dose to a clinically useful dose range should be highlighted. It is also known that medication resistance is dynamic, with some patients experiencing intermittent periods of seizure independence and relapse. As a result, applying the criteria to a particular moment in a patient's history may reflect a snapshot in their epilepsy trajectory. The ILAE definition's inter-rater reliability and validity were found to be positive in comparison to earlier ones, however the evaluation technique was found to be somewhat more time-intensive than other definitions. Since its publication, a recent observational analysis of 1,795 newly diagnosed patients found that only 11% of additional individuals achieved seizure independence with a second antiepileptic medication regimen and 4% with a third regimen attempted. Another recent large multicentre, prospective cohort of treatment-resistant focal epilepsy patients provides additional support based on outcome data from a newly introduced medication in a previously untested combination regimen. Only 12% of patients with a history of two failed previous medicines and 2.6% with a history of six or more treatments achieved seizure independence at the conclusion of the study. The study's strengths included an independent expert panel carefully assessing each patient's drug-resistant condition at enrolment, the administration of suitable medicines and doses, and treatment outcome classification in accordance with the ILAE consensus document. One of the study's limitations was that a high number of patients (41.4%) were Administered Lacosamide as their new AED, despite the fact that some patients may have previously failed to react to AEDs with comparable mechanisms of action (sodium channel modulation).

IMPACT ON TREATMENT

Because 20%-40% of patients referred to video-EEG monitoring units experience non-epileptic seizures, a review of epilepsy diagnosis and exclusion of psychogenic non-epileptic seizures is required when there is a suspicion of pharmacoresistance. An aetiological or syndrome diagnosis should be made, and the appropriateness and efficacy of previously utilised medication trials should be evaluated. Once a patient's pharmacoresistant epilepsy is diagnosed, many methods are examined. Sequential trials of antiseizure medications are generally undertaken, depending on the ease and accessibility of complete epilepsy treatments. Seizure independence is achieved primarily by trial and error in a few of these cases, thus innovative medication additions should not be abandoned prematurely or viewed as necessarily futile. When two or more medicines are used in combination, synergistic, simply additive, or antagonistic interactions can occur. Rational polytherapy is an attempt to enhance seizure outcomes via the art of drug selection. The combination of valproate and lamotrigine continues to provide the greatest evidence for synergism. The hunt for further examples continues. Non-pharmacological methods to journal pre-proofing. However, with increased data, skills, and availability over the last several decades, have been evolved, and these are being sought early given the well-known limits of ant seizure medicines in this patient group. Epilepsy surgery, neurostimulation, and nutritional treatments are commonly available in major centres and play important roles in care. With advancements in genetics and molecular biology, logical ways to understanding and perhaps altering genetically determined variables are being investigated. As a result, patients who meet the ILAE criteria for medication resistance should be referred for assessment as soon as possible. Nonetheless, considering that the majority of patients stay on medicines following these operations, these non-pharmacological methods should not be regarded replacements for appropriate drug management.

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