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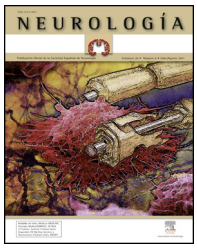

CONSENSUS STATEMENT

Drug-resistant epilepsy: Definition and treatment alternatives☆

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Drug-resistant epilepsy;
Rational combination therapy;
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Deep brain stimulation;
Vagus nerve stimulation;
Ketogenic diet

Abstract
Introduction: Drug-resistant epilepsy affects 25% of all epileptic patients, and quality of life decreases in these patients due to their seizures. Early detection is crucial in order to establish potential treatment alternatives and determine if the patient is a surgical candidate.
Development: PubMed search for articles, recommendations published by major medical societies, and clinical practice guidelines for drug-resistant epilepsy and its medical and surgical treatment options. Evidence and recommendations are classified according to the criteria of the Oxford Centre for Evidence-Based Medicine (2001) and the European Federation of Neurological Societies (2004) for therapeutic actions.
Conclusions: Identifying patients with drug-resistant epilepsy is important for optimising drug therapy. Experts recommend rational polytherapy with antiepileptic drugs to find more effective combinations with fewer adverse effects. When adequate seizure control is not achieved, a presurgical evaluation in an epilepsy referral centre is recommended. These evaluations explore how to resect the epileptogenic zone without causing functional deficits in cases in which this is feasible. If resective surgery is not achievable, palliative surgery or neurostimulation systems (including vagus nerve, trigeminal nerve, or deep brain stimulation) may be an option. Other treatment alternatives such as ketogenic diet may also be considered in selected patients.

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PALABRAS CLAVE
Epilepsia refractaria;
Politerapia racional;
Cirugía epilepsia;
Estimulación cerebral profunda;
Estimulación vagal;
Dieta cetógena

Epilepsia resistente a fármacos. Concepto y alternativas terapéuticas

Resumen
Introducción: La epilepsia resistente al tratamiento médico afecta a una cuarta parte de los pacientes con epilepsia. Como consecuencia de las crisis estos pacientes presentan una peor calidad de vida, por lo que es fundamental su diagnóstico para establecer posibles alternativas terapéuticas e iniciar una valoración prequirúrgica.
Desarrollo: Búsqueda de artículos en PubMed y recomendaciones de las Guías de Práctica Clínica (GPC) y Sociedades Científicas más relevantes, referentes a epilepsia refractaria y al tratamiento médico y quirúrgico. Se clasifican las evidencias y recomendaciones según los criterios pronósticos del *Oxford Centre for Evidence Based Medicine* (2001) y de la *European Federation of Neurological Societies* (2004) para actuaciones terapéuticas.
Conclusiones: La identificación de los pacientes con epilepsia refractaria es importante para optimizar el tratamiento farmacológico. Se recomienda el empleo de una politerapia racional de fármacos antiepilépticos, buscando combinaciones que aumenten la eficacia y minimicen los efectos adversos. Cuando no se consigue el control adecuado de las crisis es necesario realizar una valoración prequirúrgica en un centro especializado, con el fin de resecar la zona epileptógena sin producir déficits al paciente en los casos en los que sea posible. En caso contrario se recurrirá a procedimientos de cirugía paliativa o sistemas de neuroestimulación (vagal, trigeminal o cerebral). Otras alternativas, como la dieta cetógena, también pueden considerarse en pacientes seleccionados.

Introduction

Identifying patients with drug-resistant epilepsy is essential in order to optimise drug treatment, start the evaluation process to determine if they are candidates for surgery, and opt for surgery or other non-pharmacological alternatives on a case-by-case basis.

The methodological steps followed in drafting this chapter of the Official Clinical Practice Guidelines for Epilepsy were described in the first chapter of the guidelines, published as an article in *Neurología*. Classification of the levels of evidence and the grades of recommendation is in accordance with the 2004 European Federation of Neurological Societies guidelines regarding therapeutic actions, and the modified version of the Oxford Centre for Evidence-Based Medicine levels of evidence (2001) for prognostic studies.

Drug-resistant epilepsy

The International League Against Epilepsy (ILAE) defines drug-resistant epilepsy as ''failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom''.[1] Seizure freedom is considered to be sustained when the patient is seizure-free for more than one year, or has sporadic seizures separated by a period three times the longest interval between seizures prior to the treatment, whichever is longer. About 25% of all patients with epilepsy present drug-resistant epilepsy.[2] As a consequence of poor control over their epileptic seizures (ES), they present an increased risk of early death, trauma, and psychosocial alterations, while their quality of life is diminished. Drug-resistant epilepsy may show temporary remission periods (4% of adult cases yearly, with higher rates in children) but ES frequently reappear. Therefore, identifying patients with drug-resistant epilepsy is essential in order to start preparing the presurgical evaluation, and to arrange for possible therapeutic alternatives in specialised units or centres.

Prognostic factors for developing drug-resistant epilepsy

The risk factors associated with a poor prognosis for epilepsy are age-dependent.

- In children (prospective study)[3]: age younger than one year, symptomatic epilepsy, mental retardation or overall developmental delay, pathological neuroimaging study, or a high seizure frequency prior to being diagnosed with drug-resistant epilepsy (level of evidence [LE] II).
- In children (prospective study)[4]: weekly seizures during the first year of treatment, weekly seizures prior to treatment onset, or remote symptomatic epilepsy (LE I).
- In adolescents[5]: focal epilepsy, mental retardation or psychiatric disturbances (LE II).
- In adults (prospective study)[6]: symptomatic focal epilepsy, initial consciousness impairment during seizures, multiple seizure types, tonic-akinetic seizures, or anomalies on the electroencephalogram (EEG) (LE IV).