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Diagnosing and treating epileptic drop attacks, atypical absences and episodes of nonconvulsive status epilepticus

Lennox-Gastaut syndrome (LGS) is a rare and severe epileptic encephalopathy that typically starts in early to mid childhood. Although usually characterised by a triad of features comprising multiple seizure types (including tonic seizures), abnormal EEG with background slow spike-wave and poly-spike abnormalities, and cognitive impairment, the precise limits of the syndrome remain controversial. Accurate diagnosis of LGS is fraught with difficulty, in particular because it can originate from multiple causes, not all of its characteristic features are found in every case, and the features evolve and change over time. Furthermore, in addition to the "typical" characteristics associated with LGS, other types of seizures and EEG features can occur, making it difficult to differentiate from other epilepsy syndromes.

The age at onset of LGS is usually between 1 and 7 years old, peaking at between 3 and 5 (Arzimanoglou *et al.*, 2004). Although onset after 8 years of age is rare, LGS may also be diagnosed in adolescence and adulthood. Since there is currently no cure for LGS, and effective treatment options are limited, the long-term prognosis for most patients is poor. Although usually starting during childhood, LGS persists through adolescence and into adulthood, constituting a major burden for patients and their families. Throughout the course of patients' lives, their medical, educational, psychological and social needs require a multidisciplinary approach, involving cooperation between physicians, psychologists, social workers and specialised agencies.

In an attempt to control the multiple seizure types associated with LGS, antiepileptic drugs (AEDs) are often used in a variety of combinations. However, an AED that is effective in treating one type of seizure may exacerbate another, and the use of polytherapy increases the risk of adverse effects, often aggravating existing co-morbidities. Valproic acid has been recommended as a first-line treatment option for LGS (Wheless *et al.*, 2007), but has yet to be tested rigorously in a controlled trial. Randomised, controlled trials have shown favourable results for adjunctive treatment of LGS with lamotrigine (Motte *et al.*, 1997), topiramate (Sachdeo *et al.*, 1999) and felbamate (Felbamate Study Group, 1993), and the efficacy of these AEDs has also been established in long-term, open-label extension studies (Duchowny *et al.*, 2002; Glauser *et al.*, 2000; Dodson, 1993). However, there are safety concerns with each of these agents, and the majority of LGS patients remain refractory to treatment (Arzimanoglou *et al.*, 2009).

More recently, rufinamide, a triazole derivative that is structurally unrelated to other AEDs, has been investigated as a potential treatment for LGS. A randomised, controlled trial demonstrated rufinamide to be significantly superior to placebo in reducing the frequency of both tonic-atonic drop attacks and total seizures, and to significantly reduce the severity of seizures. Rufinamide was well tolerated, the most common adverse events reported being somnolence and vomiting (Glauser *et al.*, 2008). Efficacy and safety were shown to be maintained over the long term (median 432 days) in an open-label extension to this trial (Kluger *et al.*, 2010). Rufinamide was approved in Europe for the adjunctive treatment of seizures associated with LGS in patients aged $\geq$ 4 years in January 2007, subsequently being approved in the United States for the same indication in November 2008.

The aims of this supplement are, firstly, to show how LGS can be recognised and distinguished from other childhood epilepsy syndromes, outlining the pitfalls and problems associated with accurate diagnosis. Secondly, to demonstrate that LGS affects patients not only during childhood, but also through adolescence and into adulthood, and that successful management of LGS is not limited to seizure control but also requires management of associated co-morbidities and assistance for patients and their carers with the difficult transition from paediatric to adult care environments. Finally, the use of rufinamide in clinical practice in both Europe and the United States will be reviewed, including case reports, to demonstrate that an individualised approach to treatment is required given the diverse features and characteristics of LGS. □

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References

Arzimanoglou A, Guerrini R, Aicardi J. Lennox-Gastaut syndrome. In: *Aicardi's epilepsy in children*, 3rd edition. Philadelphia: Lippincott Williams & Wilkins, 2004, p. 38-50.

Arzimanoglou A, French J, Blume WT, *et al*. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. *Lancet Neurol* 2009; 8: 82-93.

Dodson WE. Felbamate in the treatment of Lennox-Gastaut syndrome: results of a 12-month open-label study following a randomized clinical trial. *Epilepsia* 1993; 34 (Suppl. 7): S18-24.

Duchowny M, Gilman J, Messenheimer J, Womble G, Risner M, & LAMICTAL Pediatric Study Group. Long-term tolerability and efficacy of lamotrigine in pediatric patients with epilepsy. *J Child Neurol* 2002; 17: 278-85.

Felbamate Study Group in Lennox-Gastaut Syndrome. Efficacy of felbamate in childhood epileptic encephalopathy (Lennox-Gastaut syndrome). *N Engl J Med* 1993; 328: 29-33.

Glauser TA, Levisohn PM, Ritter F, Sachdeo RC, & Topiramate YL Study Group. Topiramate in Lennox-Gastaut syndrome: open-label treatment of patients completing a randomized controlled trial. *Epilepsia* 2000; 41 (Suppl. 1): S86-90.

Glauser T, Kluger G, Sachdeo R, Krauss G, Perdomo C, Arroyo S. Rufinamide for generalized seizures associated with Lennox-Gastaut syndrome. *Neurology* 2008; 70: 1950-8.

Kluger G, Glauser T, Krauss G, Seeruthun R, Perdomo C, Arroyo S. Adjunctive rufinamide in Lennox-Gastaut syndrome: a long-term, open-label extension study. *Acta Neurol Scand* 2010; 122: 202-8.

Motte J, Trevathan E, Arvidsson JF, Barrera MN, Mullens EL, Manasco P, & Lamictal Lennox-Gastaut Study Group. Lamotrigine for generalized seizures associated with the Lennox-Gastaut syndrome. *N Engl J Med* 1997; 337: 1807-12.

Sachdeo RC, Glauser TA, Ritter F, *et al*. A double-blind, randomized trial of topiramate in Lennox-Gastaut syndrome. *Neurology* 1999; 52: 1882-7.

Wheless JW, Clarke DF, Arzimanoglou A, Carpenter D. Treatment of pediatric epilepsy: European expert opinion, 2007. *Epileptic Disord* 2007; 9: 353-412.