



Merry Christmas!

PIC QUESTION OF THE WEEK: 12/19/11

Q: Describe the Lennox-Gastaut syndrome and its current therapy.

A: Lennox-Gastaut syndrome (LGS) is a rare type of epilepsy whose onset is typically between the ages of two and eight years. It affects < 200,000 patients and is thus considered an *orphan disease*. The clinical presentation of LGS is quite complex and characterized by frequent episodes of various types of seizures (tonic, atonic, monoclonic, and atypical absence). The uncontrollable seizures associated with LGS tend to diminish as the affected child ages; however, brain function, behavior, and development continue to be problematic. Possible causes of LGS include CNS infection and brain injury incurred during birth, but the cause is unknown in ~ 35% of cases. Complete recovery and/or the elimination of seizures are quite uncommon and the prognosis is highly variable. There are currently six medications that are FDA labeled for the treatment of LGS. These include clonazepam, felbamate, lamotrigine, topiramate, rufinamide, and clobazam (Onfi; Lundbeck, Inc.), the most recently approved agent (10/2011). These drugs are normally used in combination because monotherapy is almost routinely ineffective. Although not specifically labeled for LGS, valproic acid is considered by many neurologists to be quite effective in this disorder, especially when combined with lamotrigine and topiramate. Clobazam is labeled as adjunctive therapy in patients with LGS. It is a benzodiazepine derivative (Schedule IV) that appears to provide improved seizure control and fewer adverse effects (specifically sedation and drooling) than other drugs in this class. Additional adverse reactions include insomnia, constipation, and dysphagia. In clinical trials, clobazam has often been combined with valproic acid, lamotrigine, and topiramate. Dosage is based on weight with maximum daily doses of 20 mg (≤ 30 kg) and 40 mg (> 30 kg). Alternative therapies used concomitantly with pharmacological treatment have included vagus nerve stimulation, surgery, and the initiation of a ketogenic diet. The ketogenic diet consists of meals low in protein and carbohydrate and high in fat (See PIC Question of the Week: 1/04/10). It must be noted that the ketogenic diet may result in elevated serum levels of various drugs and an increase in adverse effects. LGS is one of the more uncommon and severe forms of epilepsy. Hopefully it will be better managed because of the availability of clobazam.

References:

- Michoulas A, Farrell K. Medical management of Lennox-Gastaut syndrome. *CNS Drugs* 2010;24:363-74.
- NINDS Lennox-Gastaut syndrome information page. National Institute of Neurological Disorders and Stroke Web site. Available at: <http://www.ninds.nih.gov/disorders/lennoxgastautsyndrome/lennoxgastautsyndrome.htm>. Accessed November 28, 2011.
- Drugs for epilepsy. *Treat Guidel Med Lett* 2008;6:37-46.
- Tratnor K. Clobazam approved for seizure disorder. *Am J Health Syst Pharm* 2011;68:2204.

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