Efficacy and Tolerability of Vimpat in Patients with Intractable Epilepsy

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Citation

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Abstract

Sir,

Epilepsy is a complex neurological disorder caused by abnormal, sudden, excessive electrical discharges of the neurons in the brain. There are many different seizure types and epileptic syndromes, but all involve abnormal electrical activity. It has been shown that 30% of patients with epilepsy remain medically intractable.¹ For these patients, many of whom have failed multiple classes of antiepileptic drugs (AEDs) and/or surgical procedures, newly FDAapproved drugs are of particular interest.

Vimpat is an antiepileptic drug that was approved in the United States by the FDA in 2008 as an adjunctive therapy in the treatment of partial onset seizures in patients 16 years of age and older. In vitro electrogenic studies have shown that Vimpat exhibits two novel mechanisms of action. It selectively enhances slow inactivation of voltage-gated sodium channels without affecting fast inactivation and also results in the stabilization of hyperexcitable neuronal membranes.²⁻⁴

The efficacy of Vimpat as adjunctive therapy was determined through three multicenter, randomized, placebocontrolled trials of 200 and 400mg/day with a maintenance period of 12 weeks. Vimpat demonstrated a statistically significant reduction in median seizure frequency (23% for placebo, 34% for Vimpat 200mg/day, and 40% for Vimpat 400mg/day). In addition, an open-label extension study demonstrated long-term retention on Vimpat in which 77% of the 370 patients enrolled in the study were still taking Vimpat after one year. Oral Vimpat is rapidly and almost completely absorbed in the gastrointestinal tract and has a high oral bioavailability of approximately 100%. The elimination half-life of Vimpat is approximately 13 hours. When combined with a broad range of AEDs, there were no clinically relevant drug-drug interactions. Additionally, Vimpat exhibits linear pharmacokinetics in the dose ranging from 100mg/day to 800mg/day. Vimpat is generally well tolerated when added to a broad range of AEDs. The most frequently reported adverse events (?10% of treated patients) included dizziness, headache, nausea, and diplopia. The safety and efficacy results from completed clinical trials, as well as the favorable pharmacokinetic profile, suggest that Vimpat may represent a significant advance in antiepileptic drug therapy.

The purpose of this study is to determine the safety and efficacy of oral Vimpat as an adjunctive therapy with multiple AEDs for the reduction of the number of seizures in patients with intractable epilepsy.^{3,4}

METHODS AND RESULTS

A retrospective chart review was performed on all patients with intractable epilepsy who received Vimpat at Scott & White Neurology Clinic/ Texas A&M Health Science Center, Temple, TX between October 2008 and June 2010.

Efficacy was evaluated by comparing seizure frequency of patients with intractable partial epilepsy on their prior antiepileptic drugs to the seizure frequency after adding Vimpat to their treatment regimen.

Subjects were initially treated with 50 mg p.o. b.i.d. of Vimpat . If Vimpat was tolerated and the patient's seizures were not well controlled, the dosage was increased to 100 mg p.o. b.i.d.

Study patients were followed for a period of 3-12 months after the addition of Vimpat.

Data were acquired from electronic medical records.

Approval for this retrospective analysis of patient records was given by the hospital's Institutional Review Board. The demographics are discussed in Table 1.

Figure 1

Table 1: Demographics

n	10	Failed Anticonvulsants	Dilantin: 7(70%)
Age (yrs)	44(16-75)		Phenobarbital: 5(50%)
Gender	Female 7(70%)		Depakote: 5(50%)
	Male 3(30%)		Tegretol: 3(30%)
			Neurontin: 3(30%)
Race	African American: 3 (30%)		Trileptal: 3(30%)
	Caucasian:4(40%)		Mysoline: 2(20%)
	Hispanic:1(10%)		Keppra: 2(20%)
	Unknown: 1(10%)		Topamax: 2(20%)
Age at epilepsy onset (years)*	9.6 (birth-29)		Lamictal: 1(10%)
Type of Epilepsy [#]	partial epilepsy: 10(100%)		Zonegran: 1(10%)
Failed anticonvulsants*	4.1 (1-8)		Felbatol: 1(10%)
			Klonopin: 1(10%)
			Lorazepam: 1(10%)
			Sabril 1 (10%)

Figure 2

Table 2: Mean change in seizure frequency

Number of seizures prior to Vimpat (per month)*	7.3(3-22)	
Number of seizures after Vimpat*	2.5(0-11)	
Seizure free after Vimpat"	2(20%)	
Seizure reduction per month in non-seizure free patients*	64%	
Seizure reduction per month in all patients*	72% (50-100%)	
Side effects	Intermediate Term: 0 Long term: 0	
Duration of follow up (months)*	5.3(3-12)	

*Median: Range

Number of patients: percentage

The data showed that 20% of patients became seizure free following initiation of Vimpat. The 8 patients who were not seizure free on Vimpat showed an average decrease of 64% in the number of seizures per month (Table 2).

The monthly seizure frequency was reduced in all patients by at least 50% (range 50-100%).

No immediate or long term side effects were reported. **CONCLUSION**

In this study, adjunctive Vimpat was safe, efficacious, and well tolerated in significantly reducing seizures in patients with intractable epilepsy who had failed multiple anticonvulsants.

References

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