Seizure disorders affect more than two million Americans with approximately 180,000 new cases diagnosed annually. Partial seizures that begin in localized area of the brain account for up to 70% of seizure disorders and the pharmaceutical companies that develop new antiepileptic drugs (AEDs) usually evaluate them with this seizure type.

Although the seizure disorder experienced by some patients can be effectively managed with just one AED, the use of two or more AED is necessary in many patients and this increases the occurrence of adverse events and drug interactions as well as the potential for noncompliance. Even with the use of multiple AED regimens, the seizure disorder of many patients are not optimally controlled and it is estimated that 30 to 50% of people with epilepsy continue to experience seizures despite treatment with the medication now available.

Following a fifteen year period from 1978 to 1992 in which there were no new AEDs marketed, eight new AEDs have been marketed since 1993, including three in the first 6 months of 2000- levetiracetam, oxcarbazepine and zonisamide. These three agents have been approved for use in conjunction with other AEDs in the treatment of partial seizures and oxcarbazepine also for use as monotherapy in adults. All of the new AEDs represent a very useful addition to the class of agents because they provide alternatives that may be of value in the development of an AED regimen that is more effective and/or better tolerated than the regimen now being used by many patients.

Levetiracetam is a pyrrolidine derivative that is indicated as adjunctive derivative in the treatment of partial seizures in adults with epilepsy. The effectiveness of levetiracetam was demonstrated in three placebo controlled clinical studies in patients who had refractory partial seizures. The addition of levetiracetam to the regimen resulted in a 50% or greater reduction in the frequency of seizures in up to 40% of the patients receiving the new drug, a significantly better response than in a group for whom placebo was added to the regimen. There have been limited studies of levetiracetam in pediatric patients, and patients with generalized seizures.

Like gabapentin, levetiracetam has an advantage over most AEDs because it does not appear to interact via pharmacokinetic mechanisms with other medications. One of the challenges in developing combination regimen for the treatment of epilepsy is that so many of the AEDs interact with each other thereby making it more difficult to predict the response to concurrent therapy and to determine the dosage for individual agents. The recommended dosage of levetiracetam is 500 mg twice a day. The dosage may be increased after a period of at least 2 weeks to 1000 mg twice a day. The maximum recommended dosage is 15000 mg twice a day.

Zonisamide is chemically classified as a sulfonamide and shares certain of the properties of the antibacterial sulfonamide. The antiseizure activity of zonisamide is probably due to various mechanisms, including its ability to block sodium channels and reduced voltage-dependent, transient currents. It also exhibits weak carbonic anhydrase inhibiting activity.

Zonisamide is indicated as an adjunctive therapy in the treatment of partial seizures in adults with epilepsy. Its effectiveness was demonstrated in three placebo controlled clinical studies in patients who had refractory partial seizures. The addition of zonisamide to the regimen resulted in a 50% or greater reduction in the frequency of seizures in up to 42% of patients receiving the new drug, a response that was approximately twice as high as in a group for whom placebo was added to the regimen. The new drug has also been reported to be effective in the treatment of generalized tonic-clonic, tonic myoclonic and atypical absence seizure. The recommended initial dosage of zonisamide is 100 mg once a day. After 2 weeks, dosage may be increased to 200 mg/day for at least 2 weeks. The dosage may be subsequently increased to 300 and 400 mg/day with the dosage stable for at least 2 weeks to achieve steady state at each level. Caution should be exercised in patients with impaired renal or hepatic function, slower dosage titration and more dosage monitoring may be necessary.

Oxcarbazepine is structurally related to carbamazepine and shares certain of its pharmacological action. Its antiseizure activity appears to be similar
to that of carbamazepine, although most of the action of the new agent is attributed to its 10-monohydroxy metabolite (MHD), to which it is rapidly and extensively converted following administration. Oxcarbazepine and MDH are thought to act primarily by producing blockade of voltage sensitive sodium channel.

Oxcarbazepine is indicated for use as monotherapy or adjunctive therapy in the treatment of partial seizures in adults with epilepsy and as adjunctive therapy in the treatment of partial seizures in children ages 4-16 with epilepsy. It is effective as monotherapy in some patients whose partial seizures are not adequately controlled with carbamazepine mono-therapy. There have been limited studies of oxcarbazepine in patients with generalized tonic-clonic seizure and other seizures disorder. Dose is 600 mg twice a day.

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**DRY POWDER INSULIN FOR INHALATION IN DIABETICS**

A 2-year study at the University of Vermont College of Medicine in Burlington, presented at the 97th International Conference of American Thoracic Society In San Francisco indicated the usefulness of inhaled form of insulin to control blood sugar level in type-1 diabetic patients. The study included 140 patients for inhaled insulin therapy. The treatment reduced and controlled the blood glucose level without adversely affecting the lung function of the volunteers. The researchers suggested that the effectiveness of inhaled insulin is comparable to injected insulin, and as good or better than oral diabetic therapy. Inhaled insulin, by providing another way for the body to absorb insulin, may provide an alternative to injections for people with diabetes.


[sent by: S. Chatterjee]