Switching antiepileptic drugs could increase risk of seizures

February 17 2012

The substitution of brand-name antiepileptic drugs with cheaper generic equivalents has been an ongoing point of contention among doctors, federal officials and people with epilepsy.

The U.S. Food and Drug Administration claims generic antiepileptic drugs have the same dosage, purity and strength as their brand-name counterparts and the two are interchangeable. But doctors and people with epilepsy remain concerned, citing widespread reports of individuals suffering seizures after switching medication.

A new comprehensive review by pharmacists and doctors at the University of Connecticut and Hartford Hospital shows that it is not the anticonvulsant drugs themselves, but the switching aspect that may be causing the problem.

In a review of 89 different studies dating back to 1950, the researchers found that the efficacy, tolerability and safety of brand-name and generic antiepileptic medications are virtually the same. But switching from one form to the other may cause patients to have more hospitalizations and longer hospital stays. The study results were first reported in a Comparative Effectiveness Review issued by the Agency for Healthcare Research and Quality (AHRQ) in December 2011.

"If you have epilepsy and want to start on an antiepileptic drug, the evidence is compelling that it doesn't matter if you use a brand- name or a generic product. But if you're already using one version of drug

(generic or brand-name), there may be a concern if you switch to something else," says C. Michael White, a pharmacy professor at the University of Connecticut and director of the federally-designated UConn/Hartford Hospital Evidence-Based Practice Center in Hartford, Conn.

The same concerns apply whether a person switches from a brand-name drug to a generic version or from one generic version to another, White says. While many individuals with epilepsy may not experience any problems switching medications, some people may have complications and the consequences could be severe.

White cautions that the studies showing this increased risk of seizures and complications do not use the strongest study designs and the results are far from definitive. But given the high level of concern regarding different versions of antiepileptic drugs, White says it was important to release these latest findings to inform doctors and patients alike.

"It is in cases like this where opinions are the strongest," White says. "Should you act on worrisome but weak evidence knowing that costs for patients and insurers will go up and make it logistically more difficult for the pharmacies or do you wait for higher quality studies to come out before taking action? We wanted to share our findings so people can make informed decisions about their care."

Finding the right medication therapy is vitally important for people with epilepsy. A seizure-free epileptic who suffers a sudden breakthrough seizure can be seriously injured in a fall or car accident and experience other life-changing consequences that may affect their ability to do such things as drive a car or hold a job.

A number of states including Hawaii, Illinois, Tennessee and Utah, have passed legislation in recent years preventing the substitution of generic

antiepileptic drugs for brand-name products without a patient's consent. Connecticut passed its Patient Prescription Protection Act last year. More than 20 other states have considered passing a law.

"Informed consent is the critical issue here," says Alexandra Finucane, executive vice-president of the national Epilepsy Foundation. "Many people are able to go from one formulation of an epilepsy drug to another, brand to generic, generic to generic. Some however, are at risk for having a breakthrough seizure when switching among different manufacturers' formulations.

"The patient and his or her doctor needs to know and consent in advance when a switch is being considered, as there may be a history of problems with switching and a need for monitoring during the change," Finucane continues. "In some cases, the treating doctor will recommend that the patient stays on the same formulation by the same company. For some people with epilepsy, switching could be a matter of life and death."

Generic equivalents of popular antiepileptic drugs such as carbamazepine, phenobarbital, phenytoin and valproic acid have existed for more than a decade. With generic drugs costing anywhere from a few cents to five dollars less per tablet than brand-name medication, they have become a popular option for patients, health insurers, and pharmacies looking to save money.

Unless a patient is specifically prescribed a brand-name medication only, pharmacists can substitute a generic equivalent without informing the patient or their physician. Patients also may have little or no ability to maintain one specific generic medication at the pharmacy they visit as pharmacies frequently change their generic brands based on market supplies, costs and other factors.

The American Academy of Neurology has issued two position papers

stating that it has concerns with generic antiepileptic medication and that physicians should approve all generic substitutions. The American Epilepsy Society (AES) and the French Chapter of the International League Against Epilepsy have also expressed concerns while the Italian League Against Epilepsy has concluded that while generic medications offer a valuable, low-cost alternative in epilepsy management, generic substitution is not recommended in patients who have achieved remission using a brand-name product.

White says more randomized controlled trials are needed to clarify why switching medication is a problem for some people. The FDA is currently funding three studies that will further explore the efficacy and safety of brand-name and generic antiepileptic medication. The Epilepsy Foundation of America and the AES are also supporting studies regarding the issue.

The clinical trial data reviewed in the UConn/Hartford Hospital study was limited by the small size of the trials reviewed, the short duration of follow-up study and a lack of clarity as to what specific generic products were used. FDA rules require generic drugs to have the same exact amount of active medication as their brand-name equivalent, and that the rate of absorption (e.g., immediate release, delayed release, extended release) be identical. To be equivalent by FDA standards, the amount of drug absorbed must be statistically similar between a generic product and the brand product.

Provided by University of Connecticut