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Antiseizure medications

Brand name vs generic

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For many years, there has been a debate between "brand name" and "generic" medications.[1,2] When a person has an occasional headache and takes acetaminophen to relieve the pain, he or she may have the same relief as if he or she had taken the brand name, Tylenol. However, what if the illness is chronic? Now suppose the illness is something more serious, such as seizures. Is there a difference between generic and brand name? If so, which one is better? Which one will control the seizures better? Which one will have fewer side effects?

When generic medicines are studied, the US Food and Drug Administration (FDA) and the European Medicines Agency require that the generic manufacturer perform a bioequivalence (BE) study to compare the generic and the brand name medication. These studies are usually done with young, healthy volunteers. A single dose of each medication is given. The medications are compared in several ways. For instance, what is the highest level that the medication reaches (also called the concentration max or Cmax)? What is the total absorption of the drug (also called the area under the curve or AUC)? For a generic medication to be approved, the FDA requires that it fall within an acceptable range, namely 80%–125% of the brand name medication.

In their study "Assessing bioequivalence of generic modified-release antiepileptic drugs," Dr. Johnson and colleagues looked at a very specific question: How similar are generic antiseizure medications and brand name antiseizure medications?[3] They focused on a specific kind of antiseizure medications: those with "modified-release" (MR) formulations.

MR medications are often called "extended-release." The medication contained in the pill is the same as that contained in the "immediate-release" version, but the difference is in how quickly the medication dissolves or how quickly the medicine is released from the pill. MR medications use many technologies to accomplish this: special coatings on the pills, slowly dissolving matrices, and specially designed shells around the pills are just a few examples.

MR medications differ from immediate-release medications in another important way: often a person has to take an MR medication only once or twice a day. When compared to the "immediate-release" version of the same medication, this means fewer doses per day. There is a simple advantage: fewer doses means that a person will remember to take it more consistently. Taking the medication consistently means that the seizures (or any illness) will be better controlled.

WHAT WERE THE METHODS? Dr. Johnson and colleagues studied the information available at the FDA's Center for Drug Evaluation and Research. They studied medications that had been approved as of May 2014. There were several antiseizure medications for which MR formulations had been approved: phenytoin, divalproex sodium, carbamazepine, levetiracetam, and lamotrigine. There were 8 MR products for phenytoin, 5 for carbamazepine, 7 for divalproex sodium, 15 for levetiracetam, and 7 for lamotrigine. In total, they were able to compare 42 MR antiseizure medications that had been studied in 3,175 people. In addition to Cmax and AUC, the researchers looked at the time that it took for a medication to reach its maximum level (also called Tmax) and the effects that food had on how the medication was absorbed.

WHAT WERE THE RESULTS? First, the study authors wanted to know more about the 3,175 volunteers. They were all healthy participants. Most were men (86.6%). They were young: the average age was 29.7. Reflecting where the studies were done, 42% were Asian, 35% were Caucasian, 13% were black, and 2% were Hispanic. The mean body mass index (BMI is a measure of body weight to height) was 23.5. In most places, a healthy BMI is 18.5–25, 25– 30 is considered overweight, and 30–35 is considered obese.

When comparing generic to brand name, the AUC (total absorption) was similar in a large majority of the BE studies (88.6%). The Cmax was similar in 74.2% of the BE studies. The total absorption (AUC) varied less in individuals who took their medication with a full stomach. The Cmax was nearly the same whether a person took their pills with food or not. However, in 28.9% of the studies, the Cmax was higher when the person took the medication with food, and this occurred most with the MR formulations of carbamazepine and

divalproex sodium. As one might expect, the time to the maximum blood level (Tmax) was longer in people who took their medications with food. In other words, the food did not prevent all of the medication from getting into the bloodstream, it just took longer to get in.

WHAT DOES THIS MEAN? When comparing generic to brand name MR medications, the majority of the generics were the same. It took longer for the MR medication to reach a maximum blood level when the person took the medication with food. Dr. Johnson and colleagues suggested that patients take their medications consistently. If a person always takes medication with food, keep doing it. If a person prefers to take MR medication on an empty stomach, keep doing it.

A small number of the studies showed that the MR medication differed significantly from the brand name. However, it is not clear what this means in terms of seizure control. Remember, the volunteers in these studies are healthy: they do not have seizures. They are enrolled in these studies to measure how a single dose of medication gets into their body. This is different from a person with epilepsy who takes medicine every day. More studies are needed in order to understand the effectiveness of generic vs brand name medication on seizure control.

REFERENCES

1. Shambora J. The debate about generic drugs. Fortune Magazine June 25, 2009.
2. Greene J. Generic drugs: the same, but not. The Atlantic March 30, 2015.
3. Johnson EL, Chang YT, Davit B, Gidal BE, Krauss GL. Assessing bioequivalence of generic modified-release antiepileptic drugs. Neurology 2016;86:1597–1604.

About epilepsy

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WHAT IS A SEIZURE? The brain is made up of trillions of nerve cells. Nerve cells "talk" to each other constantly. They talk to their neighbors, but they can also talk to cells that are far away, using connections between different parts of the brain. They do this by sending signals and messages to each other. These messages are both electrical and chemical (the chemical messages are called neurotransmitters).

The way that nerve cells talk to each other is critical to how the brain functions. When they are working together well, a person is able to talk, move around, and remember important information (just to name a few tasks). Sometimes, however, brain cells send the "wrong" messages. Our brains have their own autocorrect, but just like a cell phone, sometimes an error still goes through. When the wrong signal is sent, other brain cells respond to the error by sending abnormal signals. If enough brain cells start sending the same wrong message, it results in a seizure.

One way to think of this is that the brain works like an orchestra. There are different sections in an orchestra, each with its own instruments. Although each instrument plays its own part, it is only when they all play together that complex music is made. While playing, each member of the orchestra has to listen to the other members. The best music is made when the orchestra works as a team, playing together and listening to one another.

However, what if one person began playing a different tune? At first, no one would notice that someone was playing the "wrong" tune. Nearby orchestra members would become confused: which tune were they supposed to play? As more members of the orchestra began playing the "different" tune, it would eventually become noticeable. At some point, the "different" tune might become louder than the original music.

This is similar to how a seizure gets started and keeps going. The nearby brain cells start playing the wrong tune, and they encourage other brain cells to do the same thing. Eventually, a person cannot stay aware of what is going on around him or her because too many brain cells are busy playing the wrong tune (having a seizure).

WHAT IS EPILEPSY? Epilepsy is not one illness. There are actually many kinds of epilepsy. Just as there are many kinds of epilepsy, there are many kinds of seizures. Epilepsy is defined as having 2 or more unprovoked seizures in their lifetime.

HOW IS EPILEPSY DIAGNOSED? The first thing a doctor will ask is what happened. It is important to know as much as possible about what happened before, during, and after the seizure. How often do the seizures occur? Is there a warning sign? Does the person remember anything about the seizure? All of these questions help the doctor to better understand the kind of seizures and the kind of epilepsy that the person is experiencing. In addition, asking someone who has seen the seizure to describe it can provide valuable information. If the patient does not remember his or her seizures, the observer may provide information that the patient may not know.

Medical testing can also help to better understand a person's seizures. Electroencephalography (EEG) is a simple and painless study that records the brain's electrical activity. The brain waves are picked up by tiny electrodes that are applied to the person's scalp. The EEG is reviewed to look for specific brain wave patterns that happen during or between seizures in patients with epilepsy. These patterns provide critical information about the person's epilepsy and help with the diagnosis.

Imaging studies are critical in understanding the cause of a person's seizures. The 2 most common studies are magnetic resonance imaging (MRI) and computed tomography (CT). Modern CT and MRI provide very detailed pictures of the brain and are critical for locating tumors, scars, or other abnormalities that may cause seizures.

HOW ARE SEIZURES TREATED? There are many treatments for seizures. Medicines are tried first. If these do not work, your doctor may consider special diets, brain surgery, or devices for the treatment of seizures. Usually the physician tries to stop all seizures while causing no side effects. It is very important to tell your doctor about the kinds of problems you experience while on a medication (or any treatment). Together, you will make the best choice of treatment(s).

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