Multiple sclerosis drug has clinical benefits

April 5 2010

A drug whose clinical benefit in treating multiple sclerosis was discovered at Rush University Medical Center was approved by the Food and Drug Administration on January 22 and is now available in the U.S.

The drug, called dalfampridine, is the first therapy for multiple sclerosis that can be taken orally. It is also the first FDA-approved therapy to treat impaired walking, a debilitating symptom of the disease limiting patients' independence and ability to accomplish the most basic tasks of daily living. While other multiple sclerosis drugs work by decreasing the inflammation that causes damage to the central nervous system, dalfampridine is designed to allow conduction of nerve impulses despite the damage.

Research that led to the discovery of dalfampridine's therapeutic value dates back to the 1960s, when Dr. Floyd Davis, then a neurologist in training and later a physician at Rush, became intrigued by an unusual clinical observation: many multiple sclerosis patients fare better when their body temperature is slightly lowered, even by just two- or three-tenths of a degree.

"In multiple sclerosis, the protective myelin sheath that wraps around nerve fibers in the brain and spinal cord is damaged, essentially causing a short circuit," said Davis, who is now retired. "Somehow, lower body temperature enabled the electrical pulse to continue its travel along the nerve fibers. I was completely transfixed by the significance of that fact."

It was important because it showed "that the damaged nerve fibers were not doomed, as previously believed," said Dr. Dusan Stefoski, director of the Rush Multiple Sclerosis Center, who teamed up with Davis in 1978, shortly after completing neurology training at Rush.

Davis launched a series of laboratory studies to understand the mechanism that explained the noticeable improvement in symptoms.

He then looked for a compound that could mimic some of the effects of lower body temperature and learned of 4-aminopyridine, or dalfampridine, which blocks the potassium ion channels in nerve fibers.

"The chemical was commonly used in physiology laboratories where scientists were studying normal nerve conduction, but at the time it was used clinically only by physicians in Bulgaria, then a Communist-block country," Davis said. "They didn't know how it worked, but they used it to help patients recover from anesthesia-induced paralysis more quickly."

In 1983, in a small proof-of-concept study, Davis and Stefoski injected the drug in 11 patients whose motor function and eyesight were impaired because of multiple sclerosis.

"It was stunning," Stefoski said. "After a single intravenous dose, the patients could walk better and see better."

Rush was granted market exclusivity by the FDA under the Orphan Drug Act of 1983 and licensed worldwide rights for dalfampridine first to Ireland-based Elan Corporation and subsequently to Acorda Therapeutics, Inc., located in Hawthorne, New York. This month, Acorda began marketing dalfampridine in the U.S. under the brand name Ampyra.

In two Phase III clinical trials conducted by Acorda, the drug yielded a consistent improvement in walking speed. Walking speed increased by about 25 percent in 35 percent of patients in one trial and in 43 percent of patients in the other, as measured by a standard test called the Timed 25-Foot Walk. Study participants who took the drug also experienced greater leg strength than those who took a placebo.

Stefoski said that although the drug has been approved specifically for the treatment of impaired walking, it also relieves other symptoms of multiple sclerosis, since it restores signal conduction in all the affected nerve fibers.

Multiple sclerosis is a chronic, often disabling autoimmune disease. According to the National Multiple Sclerosis Society, more than 2.5 million people worldwide and 400,000 people in the U.S. have been diagnosed with the disease. Symptoms include, in addition to difficulty walking, but fatigue, lack of balance, and problems with eyesight and memory, and heat sensitivity.

Multiple sclerosis takes several forms. The relapsing remitting form, the most common, is characterized by unpredictable acute attacks followed by periods of months to years of remission, with no new signs of disease. In secondary progressive and primary progressive forms of the disease, there is a steady, permanent neurological decline with no periods of remission. Tests have shown that dalfampridine works for all forms of multiple sclerosis.

Provided by Rush University Medical Center