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Drug improves mobility for some MS patients

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The experimental drug fampridine (4-aminopyridine) improves walking ability in some individuals with multiple sclerosis (MS). That is the conclusion of a multi-center Phase 3 clinical trial, the results of which were published today in the journal The *Lancet*.

"This study indicates that fampridine could represent an important new way to treat multiple sclerosis and perhaps become the first drug to improve certain symptoms of the disease," said neurologist Andrew Goodman, M.D., chief of the Multiple Sclerosis Center at the University of Rochester Medical Center (URMC) and lead author of the study. "The data suggest that, for a sub-set of MS patients, nervous system function is partially restored while taking the drug."

The study evaluated a sustained-release formulation of the drug, Fampridine-SR, which is being developed by Acorda Therapeutics, Inc. The company, which funded the study, submitted a new drug application to the U.S. Food and Drug Administration earlier this month. Goodman has been a consultant and advisor to Acorda for its fampridine studies in MS.

Multiple sclerosis is a disease of the central nervous system and is the most common cause of neurological disability in young adults. Worldwide it is estimated that more than a million people are affected by MS which is typically characterized by recurrent relapses followed by periods of remission early in its course. The symptoms of the disease vary from person to person, but commonly consist of muscle weakness,

gait difficulties, numbness or tingling in arms and legs, difficulty with coordination and balance, blurred vision, and slurred speech. Over time, the effects of the disease tend to become more permanent and debilitating.

While the precise cause is unknown, it is understood that the immune system in individuals with MS attacks myelin, a fatty tissue in the central nervous system that wraps the fibers - or axons - that connect nerve cells. Similar to the insulation on an electrical wire, myelin allows for the efficient conduction of nerve impulses. When myelin is lost or damaged in the disease, signals between nerve cells are delayed, disrupted, or even blocked.

It is believed that fampridine improves the transmission of signals in the central nervous system of some MS patients by blocking potassium ion channels. These channels serve as gates on the surface of cells and regulate the normal electrical activity. In laboratory experiments involving nerve fibers with myelin that was damaged in a manner that mimics MS, scientists found that blocking these channels results in a recovery of signal conduction.

In the Phase 3 study published today, the effects of Fampridine-SR were tested in 301 adult MS patients at 33 locations in the U.S. and Canada over a 14-week period. Three quarters of the participants took the drug and the rest were given a placebo.

Typically, MS drugs have been evaluated based on the ability to prevent relapses. Because the goal of this study was to assess changes in function, the researchers instead sought to evaluate participants' mobility and muscle strength - as opposed to the disease process. In prior studies, Goodman and his URMC colleague, the late Steven Schwid, M.D., had validated new methods to measure changes in gait, or walking speed over distance. Employing these methods in The *Lancet* study, they found that

34.8% of those receiving the drug experienced an improvement (an average of about 25% increase) in the speed they could walk 25 feet compared to only 8.3% in the placebo group.

"During the course of the disease, many MS patients experience a decline in mobility and this disability has a major impact in terms of quality of life," said Goodman. "As a clinician, I can say that improvement in walking speed could have important psychological value; it may give individuals the potential to regain some of the independence that they may have lost in their daily lives."

Several other drugs have been approved to treat MS. These treatments either counter the nervous system inflammation that is a characteristic of the disease or suppress the immune system generally. While these drugs can be effective at preventing new relapses and slowing the progression of the disease, there are no treatments currently available that improve impaired function, such as mobility problems, for people with MS. Participants in the trial were allowed to continue to take most other medications for MS and researchers did not observe any negative interactions. However, a total of eleven patients (4.8%) in the fampridine-treated group discontinued the study due to side effects. Only two of these were considered by the investigators to be possibly related to treatment.

Source: University of Rochester Medical Center

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