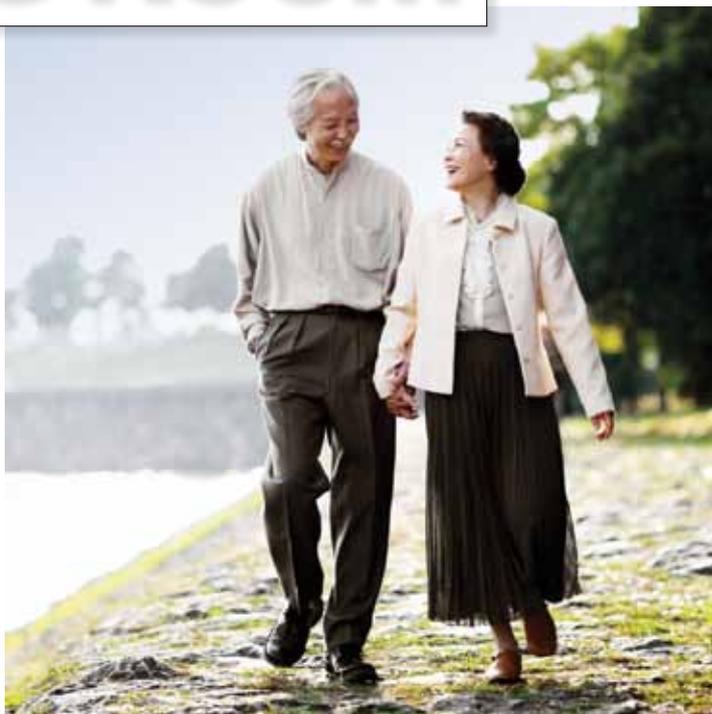


THE WAITING ROOM

THIS WAY IN

Drug Infusion Reduces “Off Time” in Parkinson’s Disease

BY GINA SHAW



Continuously infusing a steady dose of levodopa gel into the small intestine reduces medication “off time” in people with advanced Parkinson disease (PD), according to a rigorous trial presented at the Annual Meeting of the American Academy of Neurology (AAN) in April.

A person with PD wants to have as much “on time” as possible, when the medications taken to control PD symptoms are working effectively. Off time occurs as one dose of PD medication begins to wear off, before it’s time to take the next dose. As the disease advances, many patients experience increasing off time between doses of their medications, during which symptoms such as impairment of voluntary movements and dyskinesias may flare up. (Dyskinesias are involuntary movements such as tics and spasms.)

During the past decade, researchers have tried a number of strategies to reduce off time in people with PD, such as giving smaller doses of levodopa drugs at more frequent intervals and extended-release medications. But the new levodopa gel represents “the most significant improvement in off time in a randomized, controlled trial for any treatment we’ve looked at to date,” says lead investigator C. Warren Olanow, M.D., the Henry P. and Georgette Goldschmidt Professor and Chairman Emeritus of the department of neurology and professor of neuroscience at the Mount Sinai School of Medicine in New York.

“For that five percent to 10 percent of patients whose symptoms are not well-controlled with oral drugs, this is really important.”

—C. WARREN OLANOW, M.D.

A randomized, controlled trial produces the most reliable scientific evidence. Such a trial usually enrolls large numbers of people who are randomly assigned (as by flip of a coin) to receive the new therapy or a placebo (a treatment that looks just like the new therapy but has no active ingredients). All study subjects go through the same process, and no one involved in the study—researchers or study subjects—knows who is in the active therapy or placebo group.

In this study, 37 patients received the levodopa infusion plus placebo drug capsules, and 34 patients received placebo gel infusion plus levodopa-carbidopa immediate-release tablets. Patients were given the infused drug through a tube inserted in the stomach, much like a feeding tube.

Patients who received the gel infusion had a decrease in off time of four hours per day on average. Patients taking tablets only had a decrease in off time of 2.09 hours per day on average. Both groups had similar levels of adverse events, most commonly complications of inserting the device and abdominal pain.

“These results are significant and could provide an enormous improvement in the quality of life for many patients,” says Cheryl Waters, M.D., Albert B and Judith L. Glickman Professor of Clinical Neurology at Columbia University Medical Center in New York, Fellow of the AAN, and one of the study investigators.

In fact, says Dr. Waters, should these results be confirmed in larger trials, eventually some people with advanced PD who receive the le-

STEVE COLE/ISTOCKPHOTO

Treating Infantile Spasms

The American Academy of Neurology (AAN) has released an updated, evidence-based guideline for the treatment of infantile spasms, a type of seizure disorder that develops during the first year of life.

Infantile spasms are usually very brief, lasting just a few seconds, and involve sudden, involuntary movements of the upper body, neck, arms, and legs.

“When we issued our first guideline on infantile spasms in 2004, not enough studies existed to tell us whether or not treatment in the short term affected long-term outcomes in these children,” says Cristina Y. Go, M.D., a neurologist at Toronto’s Hospital for Sick Children and the lead author of the updated guideline.

After reviewing an additional eight years’ worth of evidence, the AAN found that the data still pointed to only two effective treatments for infantile spasms: adrenocorticotrophic hormone (ACTH), an injectable medication that may work by stimulating the body to produce natural hormones like cortisol, and the antiepileptic drug (AED) vigabatrin.

The new AAN guideline reports that lower doses of ACTH appear to be equally effective at controlling the spasms, with fewer side effects such as infections and high blood pressure. This is particularly important because such side effects can be severe, and even fatal.

With eight more years of data, the researchers were also able to study the development of babies treated for infantile spasms as they grew. Two types of infantile spasms exist: those with a known cause, such as a neonatal stroke or tuberous sclerosis (a genetic disorder in which non-cancerous tumors grow on the brain and other vital organs); and those labeled “cryptogenic” because the baby appears developmentally normal before the spasms start and tests find no underlying cause.

“Overall, we found no difference in developmental outcomes between children treated with ACTH and those treated with vigabatrin,” says Dr. Go. “But in the cryptogenic group, those who received hormonal therapy had much better developmental outcomes at four years of age than those who received vigabatrin.”

No matter which treatment they received—hormonal therapy or vigabatrin—children treated within one month of the time their seizures first appeared had better outcomes than those treated much later. “If a child is suspected of infantile spasms, it’s important to quickly get proper assessment and treatment,” says Dr. Go. “Many times infantile spasms get missed, or are mislabeled as colic or reflux, until the child starts losing milestones months down the line. We might still successfully treat the spasms then, but the long-term outcomes won’t be as good.”

If you think your baby may be showing signs of infantile spasms, go to infantilespasmscenter.org/infantile-spasms-questionnaire.



vodopa gel infusion might be able to stop taking several of their other medications, which can be liberating. “And even if a person is just on levodopa but has to take it eight to ten times a day, the medication regimen can still interfere with daily life—plus, it can be difficult to predict exactly when the drugs will work,” she says.

There are downsides to the gel infusion. It is an operation, which can involve complications such as infection and inflammation. In some cases, those complications can be severe, including intestinal blockages and perforation leading to peritonitis. “The majority of subjects in this trial actually had some side effects associated with the procedure,” said Robert G. Holloway Jr., M.D., M.P.H., Fellow of the AAN, and professor of neurology at the University of Rochester Medical Center in Rochester, NY.

Also, batteries to the infusion device must be changed, tubes can get kinked, and patients have to carry a fanny pack with a three-pound gel pump around with them.

But Dr. Olanow notes that only three of the study subjects dropped out—one in the gel infusion group and two in the levodopa-carbidopa group. “After the trial, everyone wanted to stay on the infusion for the extension study we did, which is now ongoing,” he says.

And for people whose advanced PD symptoms are increasingly hard to control with oral medications, abdominal surgery may be a slightly less drastic step than the other approach that offers improved control of off time: deep brain stimulation, with its requirement of brain surgery.

The new treatment will probably only be suitable for a fairly small number of PD patients—about five percent to 10 percent, Dr. Olanow says. “We’re getting better with regular meds at preventing motor problems in PD. But for that five percent to 10 percent of patients whose symptoms are not well-controlled with oral drugs, this is really important.”

The study’s leaders plan to present their results to the U.S. Food and Drug Administration (FDA) soon. “There’s a pre-NDA [New Drug Approval] meeting planned this summer,” Dr. Olanow says. “If the FDA is willing, it’s conceivable that this could be presented within a few months and potentially be approved within a year.”

If the FDA does approve levodopa drug infusion, it won’t be available at every hospital everywhere. “It does require a team of people with experience and knowledge, and there is a fair amount of work to do educating patients,” says Dr. Waters. “Also, I’m afraid it will be more expensive than deep brain stimulation. But it’s a truly viable option for people who are suffering with PD fluctuations, and I hope we can offer it to our patients soon.”

This clearly isn’t a therapy for everybody, says Dr. Holloway. “But it expands our treatment options for very advanced, debilitated patients. Although there are some risks associated with it, my sense is that this therapy is going to be moving forward.”