Parkinson disease and duodenal levodopa infusion: why patients withdraw the treatment?

Parkinson disease is a chronic and progressive movement disorder associated to degeneration of neurons in the brain, particularly in a region called *substantia nigra*. These neurons produce dopamine, a neural transmitter that is involved in the control of movement and behavior. It is reckoned that over 6 million people in the world are affected by Parkinson disease. Although the cause is only partially known, there are numerous treatment that markedly improve symptoms of the disease. Medical treatments aim to replace dopaminergic function; levodopa is a precursor of dopamine and the most effective antiparkinsonian medication.

When given orally, levodopa may provide insufficient benefit, particularly in the advanced disease stages, as patients may experience periods of reduced mobility or involuntary movements. Under these circumstances, the normal emptying of the stomach may be delayed and unpredictable. This problem may be circumvented by delivering a stable, concentrated, levodopa gel directly into the duodenum via a percutaneous endogastric gastrostomy and an external infusion pump. This duodenal levodopa infusion is currently approved in the European Economic Area, Switzerland, Canada, Australia and USA. It requires applying an infusion device through a percutaneous endoscopic gastrostomy (called PEG) to reach the duodenum. Usually the infusion is applied during waking hours and stopped overnight; standards of care require daily hygiene and a periodic intestinal tube replacement.

Long-term data indicate that approximately 31% of patients with levodopa infusion discontinue therapy These figures raised our concern, particularly because the causes of withdrawal were still poorly known. We therefore performed an observational study on patients with Parkinson disease who received a duodenal levodopa infusion to determine which adverse events caused treatment discontinuation and the timing of its occurrence. We reviewed all consecutive patients implanted from October 2006 until June 2014. Surgery-related events were defined as related to the surgical procedure, device related events were defined as related to intestinal tube, stoma, or pump complications; infusion-related events referred to delivery and administration of levodopa intestinal gel. At the end of the study, 21 patients (60%) were still on treatment and had efficacious motor control. Discontinuation was most frequently caused by device or infusion-related adverse events.

There were 2 main causes of withdrawal: stoma infection and worsening of dyskinesias not manageable by a reduction of the infusion rate. In most patients, discontinuations occurred during the first year after implant. Risk of discontinuation was related to age at implant. We therefore focused attention on the first year after implant and suggested that training of patients and caregivers, and gentle changes in the infusion schedule would reduce the dropout rate. Programmed recalls during the first year after implant may be warranted. Finally, replacement of the infusion tube should be performed by centers expert on duodenal infusion of levodopa.

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