## Off time will disappear with longer acting levodopa formulations

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Capsule: The so called "Honey Moon" period of good response to levodopa (LD) in PD disappears after 5-7 years. It has been suggested that, long-acting medications should prolong the good response, but of controlled-release LD formulations did not prolong the smooth response. The mechanisms responsible for the loss of smooth response are complex and include gastric emptying as well as pharmacokinetic and pharmacodynamic factors. Could a better LD formulation solve the problem? Pro: Diego Santos García, CHUAC (Complejo Hospitalario Universitario de A Coruña), A Coruña, Spain. Summary: Levodopa remains the most effective treatment for Parkinson's disease and is considered the gold standard therapy. However, disease progression and changes in the gastrointestinal tract result in a declining window of treatment response in a majority of patients. Efforts have been made recently to improve levodopa bioavailability either by developing more effective oral formulations or by innovating routes of administration (intestinal infusion, transcutaneous or inhaled levodopa). Some examples are IPX066, the 'accordion pill' (AP09004), ND0612, and CVT-301. Other novel formulations have been discontinued, including DM-1992, which is a bilayer formulation containing an IR LD/CD layer and an ER LD/CD layer with gastroretentive properties, and XP21279, a novel oral levodopa prodrug that is absorbed from the small and large intestine by high-capacity nutrient transporters expressed throughout the gastrointestinal system. A very important aspect is the fact that in the future, the scenario in which new levodopa formulations will be used, probably will be different. PD will be diagnosed earlier and there could be drugs for stopping progression of the disorder. Moreover, drugs for improving levodopa bioavailability will be used. In this context, control of motor symptoms and motor fluctuations would be a reality.