INTRODUCTION
Initiating levodopa treatment is usually followed by a significant improvement in Parkinsonian symptoms (“Honeymoon Period”) (1); the response to an individual levodopa dose wears off slowly (2). However, with disease progression, most patients experience a gradual shortening in the duration of levodopa’s beneficial effect End of Dose Wearing Off [EODWO] (3). Patients may suffer motor abnormalities, anxiety, dysthymia, double vision, numbness and excessive perspiration related to EODWO (2, 4, 5). Herein, we describe two patients on levodopa therapy for Parkinson’s disease (PD) who developed EODWO-related abdominal pain.

CASE REPORTS
Case 1
NV, a 61-year-old right-handed male, was diagnosed with PD at the age of 58 years. His initial symptoms included rigidity and bradykinesia on the right side of the body. The patient was initially started on levodopa/carbidopa 100/25 mg three times daily, which resulted in a significant improvement of bradykinesia and rigidity. After four years on levodopa, however, he began to experience EODWO 90 minutes prior to each scheduled dose of levodopa/carbidopa. He reported significant slowness in activities of daily living and stiffness...
in his body. Moreover, he would complain of severe abdominal pain as each dose of levodopa/carbidopa wore off; this abdominal pain would improve on taking levodopa. The abdominal discomfort was a feeling of severe intra-abdominal cramping without any nausea or vomiting. Although he was examined in the emergency department several times, the cause of his abdominal pain could not be identified. Abdominal CT, MRI spine and chest X-ray were all normal. Analgesics and spasmolytics were ineffective in addressing his abdominal discomfort. Eventually, the patient consulted his neurologist with respect to the recurring episodes of intense abdominal pain at the end of each levodopa dose. The addition of controlled-release levodopa successfully ameliorated the abdominal pain, the rigidity and bradykinesia. Delaying the scheduled dose of levodopa would cause the return of EODWO symptoms, including abdominal pain.

Case 2
A 71-year-old right-handed male was diagnosed with Parkinson’s disease at the age of 67 years. His initial symptoms included drooling, micrographia, bradykinesia and loss of facial expression. MRI brain and EMG/NCS were both unremarkable. He was started on levodopa/carbidopa 100/25 mg three times daily; subsequently, the patient noticed a marked improvement of bradykinesia and drooling. The levodopa dosage was gradually increased to 100/25 mg, two tablets four times daily. Entacapone was later added to alleviate EODWO. Roughly three years into levodopa/carbidopa therapy, the patient began to experience intense abdominal pain around 3 am – six hours after his last scheduled dose of levodopa/carbidopa – as the evening dose of levodopa/carbidopa wore off. The patient would achieve relief of this abdominal discomfort only upon taking his next scheduled dose of levodopa/carbidopa at 5 am. Upon being informed of these nightly bouts of abdominal pain, the patient’s neurologist surmised that his symptoms were related to a wearing off effect of the evening dose of levodopa. Addition of a bed-time dose of controlled-release levodopa/carbidopa at 11:30 pm successfully ameliorated the patient’s abdominal pain. The patient has continued on levodopa/carbidopa treatment without episodic abdominal pain.

DISCUSSION
Patients on prolonged Parkinson’s disease levodopa therapy frequently suffer EODWO. In fact, according to Nutt et al (4), nearly 50% of all patients will experience one or more EODWO symptoms after an average of five to six years of levodopa use. Wearing-off symptoms are extremely diverse and may include a variety of psychological, emotional, autonomic and sensory abnormalities. Severe abdominal pain resulting from EODWO may lead to hospitalization and an erroneous diagnosis of acute abdomen as described by Kułakowska et al (2). Patients may undergo extensive investigations, such as abdominal ultrasound, CT scans or GI endoscopy to identify the cause of the pain. In rare cases, patients may be subjected to exploratory laparotomy. Recurrent abdominal pain may be a key indicator of the development of EODWO in patients on levodopa therapy. Careful history taking may allow physicians to relate the levodopa dosing schedule to the manifestation of abdominal pain. Increasing the frequency of levodopa treatment may resolve EODWO symptoms. For some patients, controlled-release levodopa preparations may relieve EODWO. With controlled-release therapy, the plasma concentration of levodopa may be maintained at sufficient concentrations so as to preclude the manifestation of wearing off symptoms (including abdominal pain) for over 8 hours (6). Lees reported that patients on controlled-release therapy may require considerably larger doses of levodopa (6). The work of Hauser in 2004 and Hauser et al in 1998 supports adding a cathechol O-methyltransferase inhibitor such as Entacapone or monoamine oxidase-B inhibitor such as Selegiline to alleviate EODWO (7, 8). Entacapone and Selegiline inhibit the enzymatic degradation of levodopa, thereby prolonging levodopa’s half-life and preventing premature EODWO.

REFERENCES