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Short communication

Oral L-dopa solution therapy of menstrual-related fluctuations in Parkinson's disease

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In 1986 Quinn and Marsden reported menstrual-related fluctuations in women with Parkinson's disease (PD) [1]. There have been other reports of this phenomenon, but almost all of them are in abstract form [2–6]. However, their cause remains unclear and only a few treatments have been recommended [2,4]. We present a perimenopausal PD patient whose perimenstrual motor fluctuations showed a good response to an oral L-dopa solution taken hourly.

A 50 year-old woman who had been diagnosed with PD at the age of 40 presented with right-hand tremor and stiffness. She had been treated for 1 year with carbidopa/L-dopa, amantadine and selegiline, with an excellent response. At the age of 44 she suffered severe motor fluctuations, wearing-off phenomenon and peak-dose dyskinesia; she was currently taking 500 mg of L-dopa a day in five divided doses of 100 mg. Four years later, coinciding with the onset of her menopause, she experienced a progressive worsening of all the parkinsonian symptoms around the time of her menses. These fluctuations proved to be refractory to any therapy applied and the patient was admitted to hospital for assessment. We noted that, starting at day 19 of her menstrual cycle and for the next 5–6 days her parkinsonian symptoms were much worsened, with off-periods up to 10 h/day and an UPDRS while 'off' of 62; after menstruation and for 18 days her off periods lasted 2 h/day. When she was not in a menstrual period her UPDRS 'on' was 16, but when she was examined around the time of her menstrual period, her UPDRSS on was 25. Conventional therapy with L-dopa (700 mg/day), bromocriptine (40 mg/day) and selegiline (10 mg/day) was not effective in controlling the menstrual parkinsonian fluctuations despite increasing the frequency of dosage of L-dopa and bromocriptine. She did, however, note a substantial improvement when taking a L-dopa/carbidopa/ascorbic acid solution orally at hourly intervals (13 intakes/day). Seven and a half tablets of Sinemet® 25/100 and 2 g of crystaline ascorbic acid (vitamin C, Redoxon®) were dissolved to 1 l of water to give a solution of 0.75 mg/ml levodopa, 0.185 mg/ml carbidopa, and 2 mg/ml ascorbic acid (so the patient took, 76.9 ml/h of the solution, i.e. 57.6 mg of L-dopa/h). She started this treatment 5 days before her period, continuing throughout it and for 5 days after. Bromocriptine and selegiline were kept unchanged. The day she finished her period she returned to conventional treatment with L-dopa tablets. On this regimen her menstrual-related fluctuations improved dramatically and she experienced only 2 h off for a day and her UPDRS while this off was much less severe (UPDRS 22). Her on periods also improved on this regimen and the on UPDRS, during the menstrual period, was 18.

PD usually begins between 50 and 60 years of age, but its incidence increases with age with a peak between 60 and 64 years of age [7]. Menopause onset occurs about 51 years of age and can last for 10–15 years [8]. Therefore, the majority of women suffer the onset of PD when they are climateric. That is why the number of parkinsonian menstruating women is low and the cyclic changes in their parkinsonian symptoms are not well recognized. Indirect clinical evidence suggests that estrogens may influence the course of the disease because menstrual worsening coincides with a presumed nadir in both estrogen and progesterone levels, and it is known that estrogens can modify the activity of the mesoestriatal, mesolimbic and mesocortical dopaminergic pathways both biochemically and behaviorally The only study that has examined the issue of parkinsonian motor symptoms and menstrual pattern in a meticulous and systematic manner, however, did not find a direct relationship between hormonal menstrual fluctuations and those of PD [6]. On the other hand, several studies suggest that

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clinical fluctuations of PD are directly related to changes in plasmatic L-dopa levels [9]. Wald et al. [10] demonstrated that gastrointestinal transit time is significantly prolonged in the luteal phase, when progesterone levels are higher than in the follicular phase in menstruating women. Hutson et al. [11] showed that sexual hormones have inhibitory effects on gastric emptying in premenopausal women. Parkinsonian patients have also an impaired gastric emptying and abnormal motility of the upper gastrointestinal tract [12]. All these conditions can result in an erratic absorption of levodopa and they might be the cause of 'random' fluctuations in parkinsonian mobility [13]. The treatment with L-dopa solution may allow a better intestinal absorption because its gastric emptying occurs continuosly. Therefore, seric drug levels may become more stable and thus, the dopaminergic stimulation, more continuous than with L-dopa tablets. Our case is another example of the tight relationship between the menstrual period and the motor fluctuations of PD. We suggest that treatment with L-dopa oral solution might be helpful in some of these patients.

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