The Effect of Bromocriptine (BCT) on the On-Off Phenomenon*

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Summary

Twenty-three patients with idiopathic Parkinson disease with classic "on-off" phenomena were studied prospectively during treatment with bromocriptine (BCT). Patients were evaluated for an average of 6 to 12 months and received an average of 56.5 mg of BCT. Nine patients (39%) showed improvement in terms of "on-off". When evaluated retrospectively, it appeared that the only difference between the responders and non-responders was a younger mean age (57.1 to 63.2).

Three major types of relatively sudden fluctuations in performance are seen in parkinsonian patients. These are:

1. Episodic freezing episodes, which occur on initiation of large muscle movements such as walking or standing up and can be seen in patients almost anytime in the course of the disease.
2. End of dose akinesia ("wearing off" phenomenon).
3. Classic "on-off", where there is no clear cut temporal relationship between dose and onset of akinesia.

Episodic freezing episodes were described prior to the advent of levodopa therapy but they do appear to be accentuated by this drug in some patients (Fahn et al., 1979). However, the latter 2 problems are only seen in patients treated with long-term dopaminergic therapy.

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and must be considered major side effects and limitations of the currently available antiparkinsonian drugs. The relative effects of the newer antiparkinsonian agents on wearing off and on-off have been only partially studied. Reports on the efficacy of bromocriptine have been variable and some differences may be due to different definitions of the on-off phenomenon (Fahn et al., 1979; Parkes et al., 1976a; Kartzinel and Calne, 1976; Kartzinel et al., 1976; Parkes et al., 1976b; Calne et al., 1978; Lieberman et al., 1979) as well as the fact that some studies were not specifically designed to address the particular issue of on-off.

In fact, only one of the prior studies (Kartzinel and Calne, 1976) was specifically designed to evaluate BCT and this phenomenon, but the type of fluctuation was not clearly stated.

This study was designed to evaluate the effect of BCT in 23 patients with classic (true) “on-off” phenomenon. Patients with the “wearing-off” phenomenon and sudden freezing were excluded.

Choice of Patients and Description of Study

Twenty-three patients with idiopathic Parkinson disease were studied. All patients had classic “on-off” phenomena and all found this distressing and disabling in terms of daily living. Typically, the patient would turn “on” approximately 1/2 hour after taking levodopa containing medication, remain “on” for some period of time and then over a period of a few minutes, return to the akinetic state. This would last from 5—30 minutes and then, independently of the patient taking further medication, the “on” or kinetic state would return. This cycle could be repeated throughout the day although many patients described a predilection for either morning or afternoon periods. The average duration of disease was 12.5 years with a range from 4 to 20 years. During their periods of maximum motor ability, 19 patients were classified as Stage III disease, according to the Hoehn and Yahr classification (Hoehn and Yahr, 1967). Three patients were Stage IV and 1 patient Stage II. All patients advanced at least one, and sometimes two stages during the “off” phase. Patients were evaluated for an average duration of 12.6 months on BCT. One patient was followed for 3 months but follow up in the rest ranged from 6 to 20 months. The “on-off” phenomena were evaluated by having the patient keep a daily log of “on-off” periods. The number of fluctuations per day as well as their relationship to medicine ingestion was also recorded. All patients were taking a levodopa/carbidopa (Sinemet®) combination at the time of entry