EDITORIAL

Excessive Sleepiness in Parkinson's Disease: A Wake-Up Call

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Sleep impairment in Parkinson's disease (PD) has been recognized since James Parkinson's original description in An Essay On The Shaking Palsy in 1817 in which he stated that not only are nocturnal sleep disturbances common, but that "constant sleepiness" is a feature of advanced disease. The neurological community was re-alerted to the importance of excessive daytime somnolence (EDS) and to the possible contribution from dopaminergic medication in 1999 with the report of sudden onset of sleep episodes occurring in patients receiving pramipexole or ropinirole, which are both D2/D3 agonists.[1] In Canada, the result of this report and others of EDS was the recommendation from the manufacturers of pramipexole and ropinirole, made in cooperation with the Therapeutic Products Programme of Health Canada, that patients receiving these medications be warned not to drive or engage in other activities where impaired alertness could put themselves or others at risk of serious injury or death.[2]

In 2002, the Canadian Movement Disorders Group (CMDG) reported that 51% of 638 PD patients treated with dopaminergic therapy exhibited features of EDS.[3] Concomitants of EDS can include fatigue, tiredness, lack of energy, or exhaustion and can lead to frequent naps, sometimes occurring at inappropriate times such as during meals, conversation, or driving. The CMDG found that 3.8% of the patients surveyed had experienced at least one episode of sudden onset of sleep while driving,[3] although there is considerable debate regarding the very concept of "sudden onset of sleep" since the amnestic nature of sleep may remove any perception of sleepiness preceding its onset.[4] The neurodegenerative process itself, involving brainstem neurons in the regions of the pedunculopontine nucleus, dorsal raphe and locus coeruleus associated with sleep mechanisms, may be partially responsible for sleep abnormalities in PD, though it is also well established that levodopa and dopamine agonists can be associated with excessive drowsiness. While Frucht had originally documented a relationship in PD to pramipexole and ropinirole,[1] it has subsequently become clear that EDS can be associated with all dopaminergic agents, including levodopa. In the CMDG study, there was no significant difference in the risk for sleep episodes among the different dopamine agonists.[3] Interestingly, in patients with restless leg syndrome, dopaminergic drugs may actually reduce rather than increase the risk of sudden onset of sleep, at least at relatively low doses.[5] Although it is likely that EDS is of multifactorial origin in PD, it is also likely that dopaminergic treatment is at least partially involved, perhaps by enhancing an underlying tendency to excessive sleepiness in PD patients.[6]

In this issue of the Journal, de Bie and colleagues[7] report the results from an online survey designed to assess Canadian neurologists' practice concerning driving advice given to PD patients starting a dopamine agonist. Although there was a disappointing "voter turnout" of less than 20%, raising concerns regarding the generalizability of the results, the reported observations are interesting with only 4.4% of respondents following the manufacturers' recommendations of advising patients not to drive. The results from the questionnaires reported in this article also indicate, however, that the majority of the responding neurologists assess patients for the presence of EDS after starting dopamine agonists, although on a somewhat variable and often informal basis. Of some concern is the small number of neurologists who appear to be unconcerned by this important potential medication-related side effect.

Reasons behind this apparent widespread disregard for the manufacturers' recommendations are unclear. Evidently some Canadian neurologists feel this advice does not have adequate evidence-based support and the recommendation that patients be advised not to drive solely on the basis of a diagnosis PD and treatment with dopamine agonists is too rigid. They may prefer guidelines such as those in the United Kingdom, where the recommendation is that PD patients taking dopaminergic medications be warned of the risk for sleepiness and sleep episodes and be advised not to drive if they experience such events or to stop driving if they are feeling sleepy.[4] Indeed, one might suspect that many of us have already chosen to follow this recommendation. The call that de Bie and colleagues make for a revision of the Health Canada guidelines is not unreasonable, although their data suggest the existing recommendations are having little impact on neurological practice. Perhaps it would be more effective to establish clear practice guidelines, based on evidence-based principles of neurological practice, for the management of this vexing clinical problem. We should consider this a wake-up call for the need to rationalize patient management based on both medical and societal issues.

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