Sleep benefit in Parkinson’s disease

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Many patients with Parkinson’s disease wake in the morning “off”. Patients with sleep benefit wake “on”. This sleep benefit gradually wears off over a variable period, usually about 30 to 60 minutes. Little is known about sleep benefit. Previous reports have produced conflicting results. No objective study has been undertaken to confirm whether sleep benefit exists or to document patients’ subjective reports that they wake in the “on” state. The aims of this study were to investigate the existence of sleep benefit, to identify the characteristics of the patients who reported it, and to measure its duration.

Methods

The study comprised two parts.

INPATIENT STUDY

A consecutive series of 20 patients with Parkinson’s disease admitted to the National Hospital for Neurology and Neurosurgery (NHNN) was studied by one of us (DEB). These patients were rated using the motor unified Parkinson’s disease rating scale (UPDRS) as follows:

(1) Immediately on waking before any medication.
(2) “On” after medication.
(3) “Off” after medication.

These ratings were consecutive on the same day. The patients also completed an activities of daily living (ADL) proforma at these times. The ADL rating scale is a 25 item questionnaire and patients were asked to complete measures of their capacities according to his or her own best” (w−b> 12=sleep benefit).

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Sleep benefit (w−b&gt;12)</th>
<th>No of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa treatment</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td>Dopamine agonists (bromocriptine)</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Selegiline</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>Artane or other anticholinergic</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Hoehn and Yahr (mean daily on):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>Stage 2</td>
<td>37</td>
<td>21</td>
</tr>
<tr>
<td>Stage 3</td>
<td>24</td>
<td>12</td>
</tr>
<tr>
<td>Stage 4</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Stage 5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Motor fluctuations</td>
<td>80</td>
<td>43</td>
</tr>
<tr>
<td>Confirmed by ADL scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective sleep benefit</td>
<td>66</td>
<td>40/66</td>
</tr>
<tr>
<td>No objective sleep benefit</td>
<td>23</td>
<td>4/18 (no forms nine patients)</td>
</tr>
<tr>
<td>Uncertain regarding sleep benefit</td>
<td>24</td>
<td>5/24 SB present</td>
</tr>
<tr>
<td>Total sleep benefit</td>
<td>49/113</td>
<td>43</td>
</tr>
</tbody>
</table>

The purpose of this part of the study was to confirm the existence of sleep benefit and to measure its size and duration.

OUTPATIENT STUDY

To obtain information from outpatients, a questionnaire was devised and given to a consecutive series of 150 outpatients attending the Parkinson’s disease clinic at the National Hospital for Neurology and Neurosurgery, the Royal United Hospital, Bath, and members of the South West Young Onset (YAPPs) Parkinson’s disease group. The questionnaire asked for appropriate details of the patients’ Parkinson’s disease. Three identical ADL rating scales were also included with the questionnaire and patients were asked to complete each of these individual rating scales on the same morning at the following times:

(1) Immediately on waking before any medication.
(2) At their best before any medication.
(3) At their worst before any medication.

The purpose of these measurements was to confirm the occurrence of sleep benefit and to measure its magnitude and duration.

The results were analysed using Student’s t test. This was two tailed and a level of significance was set at p<0.05.

Results

INPATIENT STUDY

Sleep benefit was confirmed in six out of the 16 (38%) patients who were studied from the moment of waking. When they awoke these patients performed as well as when they were “on” due to medication. Subsequently they spontaneously turned “off” to an identical state to “off” after medication. There was a strong correlation between the motor UPDRS scores and the self rated ADL scores (p<0.001).

OUTPATIENT QUESTIONNAIRE STUDY

One hundred and thirteen questionnaires were returned from the 150 patients circulated. Twenty eight of these were incomplete in some respects. The table summarises the results.

The absolute scores on the ADL scale were not comparable between patients as each rated their capacities according to his or her own

Answers to questionnaire regarding medication, Hoehn and Yahr stage, the presence of motor fluctuations, and sleep benefit in 113 patients with Parkinson’s disease related to sleep benefit determined by ADL scores of “worst”−“best” (w−b> 12=sleep benefit).
subjective baseline. However, the difference in scores for “worst—best” and “worst—on waking” for each patient was comparable. The measure of sleep benefit was taken as the value on the rating scales of “worst—best”. A change in ADL score of 12 was deemed sufficient to confirm sleep benefit representing a possible change in category for half the 25 items of the scale.

Forty nine patients out of 113 (43%) had sleep benefit confirmed by the rating scales. The duration of sleep benefit estimated subjectively by the 66 patients with Parkinson’s disease varied from 10 minutes to >150 minutes (mean (SD) 57 (46) minutes). However, the duration of sleep benefit demonstrated objectively using the ADL scores in the 40 patients with Parkinson’s disease was longer (mean (SD) 87 (58) minutes).

There was a negative correlation between the presence of sleep benefit and age of onset—that is, patients with young onset were more likely to have sleep benefit ($r=-0.31$, $t=-2.96$; $p<0.01$). There was a correlation between sleep benefit and duration of disease (time for which patient had had Parkinson’s disease)—that is, those with longer duration of disease were more likely to have sleep benefit ($r=0.26$, $t=2.45$; $p<0.05$). There was no correlation between sleep benefit and the concurrent Hoehn and Yahr stage rating determined by the answers to the questionnaire ($r=0.10$, $t=0.95$; NS).

Differences in mean sleep benefit scores were correlated with type of medication, “yes” to the question “Do you have sleep benefit?” and motor fluctuations. Those patients with motor fluctuations and those taking bromocriptine were more likely to describe sleep benefit ($p<0.01$). The mean sleep benefit score for those answering “yes” to the question “Do you have sleep benefit?” was also significantly greater ($p<0.01$). There was no significant difference in mean sleep benefit score for those on benzhexol (artane) and selegiline.

**Discussion**

The good correlation between the objective motor UPDRS ratings and the patients’ own ADL scale ratings indicates that the ADL scales are a reliable measure of “on” and “off” disability for each individual patient. The ADL scale was therefore used in the second part of this study to confirm more objectively the prevalence and duration of sleep benefit rather than simply relying on the patient’s own estimation.

The outpatient series was not a homogenous or representative series of patients with Parkinson’s disease and incomplete ascertainment may also have caused bias. Although some patients had difficulty understanding some of the questions, some results indicated that most patients were capable of recognising sleep benefit as defined by the authors. There was a good individual correlation between the answer of “yes” to the question “Do you have sleep benefit?” and the presence of this objectively estimated on the rating scales. Sixty one per cent of those answering “yes” to the question “Do you have sleep benefit?” had this objectively confirmed by the ADL scores of “worst—best” and the ADL scores of those answering “no” were in agreement in 71%. The mean sleep benefit score for group answering “yes” (mean of ADL scores of “worse—best” of the two groups) was also significantly different ($p<0.01$).

The study showed that the mean duration of sleep benefit was 87 minutes, which is an appreciable period of early morning benefit, allowing such patients to get up and have breakfast before requiring medication, avoiding the need to wait for the medication to work or require help to get out of bed and dressed. It also enables the start of medication to be delayed, extending the useful day.

The results suggest that sleep benefit is not related to the severity of Parkinson’s disease as there was no relation between current Hoehn and Yahr stage and sleep benefit. There was, however, a significant relation between the age of onset of Parkinson’s disease and sleep benefit so that patients with younger onset were more likely to have sleep benefit. Our study also showed a significant relation between duration of disease and the presence of sleep benefit so that those with longer duration of disease were more likely to have sleep benefit. This must of necessity be explained by the association of sleep benefit with age of onset and further strengthens the validity of this result. Other differences between young onset and older onset patients have been described, possibly indicating a different disease process or compensatory mechanisms of a younger nervous system.

The significant relation between the use of bromocriptine and sleep benefit was not explained by an association with use in predominantly younger patients; nor could the association be explained by the duration of action of bromocriptine as this is too short. Bromocriptine itself does not cause sleep benefit, as the benefit was present even in untreated patients and those on levodopa alone. It is possible, therefore, that bromocriptine and other dopamine agonists may prolong sleep benefit. A study of the effect of antiparkinsonian drugs, particularly other dopamine agonists, on sleep benefit would be worthwhile and might point to alternative strategies for some patients with Parkinson’s disease.

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