Mortality Abstract 241M1

MORTALITY IN PATIENTS WITH PARKINSON'S DISEASE TREATED WITH DOPA

Richard B. Singer, MD

Reference


Objective of This Study

To determine comparative mortality in Parkinson patients treated with dopa after classification by interval from onset of symptoms to start of treatment.

Subjects Studied

Common diagnostic criteria were used by physicians at four University medical centers to identify 359 patients with Parkinson's Disease initially treated with dopa starting in 1968-1977. The centers were the UCLA School of Medicine, Los Angeles, CA, the University of Colorado, Denver, CO, Cornell University Medical School, New York NY, and the Mayo Clinic, Rochester, MN. About 95% of the patients had idiopathic Parkinson's Disease, the others had postencephalitic parkinsonism. A few early misdiagnoses were identified and excluded from the study group. Patients were restricted to those with onset of their disease less than 10 years prior to enrollment for treatment with dopa, which first became available for widespread use in 1968. The patients were classified solely on the basis of the interval from onset of symptoms to the date of enrollment for dopa treatment: Group 1, 1-3 years; Group 2, 4-6 years; Group 3, 7-9 years. Mean ages in the groups at onset of Parkinson's Disease were 56.8, 55.5, and 54.4 years, respectively, in Groups 1, 2, and 3. These and other basic data in the three groups are given in Table 1A. Note that the order of mean age is reversed when this is adjusted to age at start of follow-up, by use of the mean interval from onset to enrollment, 2 years in Group 1, 5 years in Group 2, and 8 years in Group 3. Male patients outnumbered female in all three groups. Most of the patients were enrolled in the entry years 1968 through 1970, especially in Groups 2 and 3. No classification was reported for severity of the disease or disability at the time of enrollment, but it can be presumed that cases with a longer duration from onset were apt have more severe findings on enrollment.

Follow-up

Since all patients were being managed with dopa therapy they were presumably followed regularly by their physician at one of the four medical centers. No details are given, except that after partial follow-up 12 patients were lost to observation in Group 1, 10 patients in Group 2, and 11 patients in Group 3. Overall follow-up was therefore 91% complete. Cutoff date was October, 1985.

Expected Mortality

Expected deaths (d')were calculated for each patient as the cumulative mortality from age at entry to age at termination of observation (death, loss to follow-up or end of follow-up). The authors describe the calculation as, in effect, d' = (e-t)/e, where e is the life table number of survivors at entry age, e, (out of a cohort of 100,000 born alive), and t the survivors at termination age, t. (The authors use a different symbol for t.) This provides a value of individual d' derived as individual Q', rather than the sum of the individual annual q' rates for all durations. At long durations and higher ages cumulative mortality rate (Q') will be appreciably smaller than with the customary actuarial method of basing each year's d' as the product of q' and a full year of exposure. However, in this series any difference of this sort would have only a small impact on the comparative mortality results, especially in terms of excess death rate (EDR). Aggregate expected deaths, d', were not reported in the article. They have been calculated as the quotient of the observed deaths, d, and the decimal mortality ratios, MR (the latter are given in the text to two decimal places, and shown in bar graphs).

Results

These are shown in Table 1B for the full observation period to 1985 for each group. The slight differences in mean follow-up are attributable to the larger numbers of deaths in Groups 2 and 3. In patients with early Parkinson's Disease (Group 1, onset less than 4 years prior to entry) the aggregate mortality ratio was 143%
and the EDR 9 per 1000 per year. This was for a mean follow-up of 11.0 years, with a range from 8 to 17 years. Excess mortality was higher in Group 2, with an EDR of 30 per 1000, and still higher in the longest disease duration Group 3, EDR 44 per 1000; mortality ratios were 244% and 295%, respectively. If dopa is effective in reducing mortality in patients with parkinsonism, it is more effective when started less than 4 years after onset of symptoms.

The authors attempted to standardize the interval from onset to end of follow-up by cutting off observation in 1982 for Group 2 and 1979 for Group 3. This does give a maximum interval from onset to end of observation of 17 years for all groups, but further truncates duration of follow-up in Groups 2 and 3 (the years from onset to entry are not years of follow-up). The aggregate experience for Group 3 can be divided into two consecutive observation periods, 1968-1979 (data in the article), and 1979-1985 (by subtraction for E, d and d'). Results for these two periods are shown on lines 4 and 5 of Table 1B. It is apparent that there is a marked trend for excess mortality to rise with increasing duration of follow-up: the mortality ratio increasing from 263% to 340%, and EDR from 37 to 72 per 1000 per year. It is also apparent that treatment with dopa did not prevent this increase in excess mortality with duration of the disease while patients were under continuing treatment.

Cause of death information was provided in 111 of the 171 total deaths observed. The authors classified 51, or 46%, as due to Parkinson's Disease, parkinsonism, or the probably related conditions of pneumonia and inanition, and 60 deaths as due to other causes unrelated to Parkinson's Disease. The classification was based on death certificate information alone, which the authors acknowledge as being incomplete for this classification. The percentage of parkinsonism-related deaths was lowest in the Group I patients, who had the shortest average duration from disease onset to death.

### Table 1A

*Three Groups of Patients with Parkinson's Disease, Classified by Interval from Onset to Start of Treatment with Dopa*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years from Onset to Start of FU</td>
<td>1-3</td>
<td>4-6</td>
<td>7-9</td>
</tr>
<tr>
<td>Number of Patients</td>
<td>130</td>
<td>133</td>
<td>96</td>
</tr>
<tr>
<td>Entry into FU 1968-70</td>
<td>52%</td>
<td>77%</td>
<td>80%</td>
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<tr>
<td>Male/Female Numbers</td>
<td>87/43</td>
<td>89/44</td>
<td>54/42</td>
</tr>
<tr>
<td>Mean Age at Onset - Years</td>
<td>56.8</td>
<td>55.5</td>
<td>54.4</td>
</tr>
<tr>
<td>Mean Age at Entry - Years</td>
<td>58.8</td>
<td>60.5</td>
<td>62.4</td>
</tr>
</tbody>
</table>

### Table 1B

*Comparative Mortality, Patients with Parkinson's Disease, Treated with Dopa, Classified by Interval from Onset to Start of Treatment, 1968-85*

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1 (1-3)</td>
<td>11.0</td>
<td>130</td>
<td>1435</td>
<td>41</td>
<td>28.7</td>
<td>143%</td>
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<tr>
<td>2 (4-6)</td>
<td>10.1</td>
<td>133</td>
<td>1341</td>
<td>69</td>
<td>28.3</td>
<td>244</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (7-9)</td>
<td>9.5</td>
<td>96</td>
<td>913</td>
<td>61</td>
<td>20.7</td>
<td>295</td>
</tr>
<tr>
<td>68-79*</td>
<td>7.4</td>
<td>96</td>
<td>712</td>
<td>42</td>
<td>16.0</td>
<td>263</td>
</tr>
<tr>
<td>79-85**</td>
<td>---</td>
<td>---</td>
<td>201</td>
<td>19</td>
<td>4.7</td>
<td>340</td>
</tr>
</tbody>
</table>

* Basis of expected deaths: 1980 Abridged U.S. Life Tables.
* Group 3, experience from 1968 to 1979 (see text).
** Group 3, experience from 1979 to 1985 by difference (see text).