Activities of Daily Living – Outcome During Three Years in Donepezil Treated Alzheimer Patients.

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ACTIVITIES OF DAILY LIVING – OUTCOME DURING THREE YEARS IN DONEPEZIL TREATED ALZHEIMER PATIENTS

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Objectives
To analyse and present the outcome of longitudinal change in ADL function and cognition in patients treated with donepezil for three years.

Methods and Subjects
The Swedish Alzheimer Treatment Study (SATS) is an open, long-term, multicentre study in a routine clinical setting. Patients with the diagnosis of Alzheimer’s disease received the cholinesterase inhibitor donepezil. The 435 patients were assessed with several functional and cognitive rating scales including IADL, PSMS, FAST, MMSE and ADAS-cog at baseline and every 6 months for a total period of three years. A mathematical correction of the sum of the IADL scores was performed to ensure that activities more commonly done by women did not affect the result between genders.

The expected rate of IADL decline in untreated patients was calculated using a linear equation as presented by Green et al.[1, 2]:

$$\Delta \text{IADL} = 10,124 - 0.332 \times \text{IADL}_{\text{bas}}$$

in which $\Delta \text{IADL}$ is the annual rate of decline of IADL and $\text{IADL}_{\text{bas}}$ is the IADL score at baseline.

A two-step cluster analysis was performed to reveal any natural groupings (clusters) of the patients based on the ADL scores at baseline.

Baseline characteristics
- Number of patients (n): 435
- Gender (males/females): 35% / 65%
- Donepezil mean dose during study, mg/day: 6.5 – 8.3
- 3 year completion rate: 38%
- Age at start of donepezil treatment*: 74.6 ± 6.5
- Illness duration, years*: 3.1 ± 2.3
- MMSE*: 22.0 ± 4.6
- ADAS-cog (0-70)*: 20.7 ± 10.0
- IADL*: 15.9 ± 5.8
- PSMS*: 7.4 ± 2.2
- FAST*: 4.0 ± 1.3

*mean ± SD

Results

Fig A PSMS, FAST

After three years of donepezil treatment the total mean decline from baseline in PSMS score was 6.1 ± 5.4 (mean ± SD) points. Using the mathematical model by Green et al[1, 2] patients in this study would be expected to decline approximately 15.8 ± 5.6 points on ADL scale after 3 years. The IADL changes from baseline show a strong linear relationship (p < 0.01) with cognition at all assessments between 12 and 36 months. None of the ADL scales showed significant differences between gender at baseline, but after three years the IADL mean decline from baseline was significantly worse among females 7.0 ± 5.7 (p < 0.01) compared to males 4.5 ± 4.6.

Fig B IADL

After three years of donepezil treatment the total mean decline from baseline in IADL score was 6.1 ± 5.4 (mean ± SD) points. Using the mathematical model by Green et al[1, 2] patients in this study would be expected to decline approximately 15.8 ± 5.6 points on ADL scale after 3 years. The IADL changes from baseline show a strong linear relationship (p < 0.01) with cognition at all assessments between 12 and 36 months. None of the ADL scales showed significant differences between gender at baseline, but after three years the IADL mean decline from baseline was significantly worse among females 7.0 ± 5.7 (p < 0.01) compared to males 4.5 ± 4.6.

Fig C

The 10 most significant variables between the two groups, in order of significance, were:

<table>
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<tr>
<th>Variable</th>
<th>ΔIADL</th>
<th>PSMS</th>
<th>FAST</th>
<th>MMSE</th>
<th>ADAS-cog</th>
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<tr>
<td>Number of patients</td>
<td>435</td>
<td>435</td>
<td>435</td>
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<td>Gender (males/females)</td>
<td>35% / 65%</td>
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<tr>
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</tr>
<tr>
<td>Age at start of donepezil treatment*</td>
<td>74.6 ± 6.5</td>
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<tr>
<td>Illness duration, years*</td>
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<tr>
<td>MMSE*</td>
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<tr>
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<tr>
<td>IADL*</td>
<td>15.9 ± 5.8</td>
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<td>15.9 ± 5.8</td>
</tr>
<tr>
<td>PSMS*</td>
<td>7.4 ± 2.2</td>
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<tr>
<td>FAST*</td>
<td>4.0 ± 1.3</td>
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</tr>
</tbody>
</table>

A cluster analysis showed two subgroups that significantly differed in age (p < 0.001), illness duration (p < 0.05) and cognition (p < 0.001) at baseline. No significant difference in gender, apoE4-carriers or mean dose of donepezil was observed. The cluster 1 patients decline significantly faster in the long-term outcome of PSMS score compared to the other group.

Conclusions
Increasing strength in the linear correlation between the three ADL scales as well as cognition was observed during the three years of the study. The IADL scale showed a decline of function less than expected compared with untreated patients in a mathematical model.

Long-term instrumental activities scores deteriorated significantly faster in the female gender than in the male, thus the result was mathematically corrected for gender-dependent activities.

Cluster analysis based on ADL scores at baseline, identified two subgroups: with different mean age and cognitive ability and dissimilar rate of change in basic functional decline.