Plasma concentration of galantamine - influence of dose and body mass index in Alzheimer’s disease.

Wattmo, Carina; Jedenius, Erik; Minthon, Lennart; Wallin, Åsa

2010

Document Version:
Publisher’s PDF, also known as Version of record

Link to publication

Citation for published version (APA):

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.
Plasma concentration of galantamine in Alzheimer’s disease - influence of dose and body mass index

Wattmo C*, Jedenius E*, Minthon L*, Wallin Å K*
*Clinical Memory Research Unit, Department of Clinical Sciences, Malmö, Lund University, Sweden.
*Alzheimer Disease Research Center, Department NVS, Karolinska Institutet, Stockholm, Sweden.

Background and objectives
Patients with Alzheimer’s disease (AD) are at present treated with galantamine without actual knowledge of plasma concentration levels. The aim of this presentation is to analyse the relationship between galantamine plasma concentration, dose, demographic factors and body mass index (BMI).

Methods and subjects
The Swedish Alzheimer Treatment Study (SATS) is a 3-year ongoing, open-label, non-randomized, prospective, multicentre study in a routine clinical setting. A total of 84 AD patients treated with galantamine and recruited at the Memory Clinic in Malmö were included in this study. They were assessed with several cognitive and functional rating scales at baseline and every 6 months over the course of 3 years. After 180 of these assessments, blood samples were obtained for the analysis of plasma galantamine concentration. Efficacy measures including Mini Mental State Examination (MMSE), Instrumental activities of daily living scale (IADL) and BMI were simultaneously evaluated. The dose, as well as the time from drug intake to plasma extraction was investigated.

One-way Analysis of Variance (ANOVA) with Bonferroni correction was used to compare the mean differences between the groups based on galantamine dose, and T-test was computed for analyses between genders. Pearson’s correlation coefficient was calculated investigating any linear associations between plasma concentration and the variables dose, age and BMI, respectively. A general linear model with plasma concentration as the dependent variable was used to study the multivariate impact on the independent variables.

Conclusions
Galantamine plasma concentration demonstrated a strong relationship with dose. The dose did not differ between genders, whereas the impact of body mass index on plasma concentration was important only among the males.

Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>84</td>
</tr>
<tr>
<td>Gender (males / females)</td>
<td>29% / 71%</td>
</tr>
<tr>
<td>Age at onset</td>
<td>73.9 ± 7.1</td>
</tr>
<tr>
<td>Age at start of treatment</td>
<td>76.7 ± 7.0</td>
</tr>
<tr>
<td>Illness duration, years</td>
<td>3.0 ± 1.8</td>
</tr>
<tr>
<td>MMSE, range 0 - 30a</td>
<td>22.7 ± 4.0</td>
</tr>
<tr>
<td>IADL, range 8 - 31a, b</td>
<td>13.4 ± 5.0</td>
</tr>
</tbody>
</table>

*a mean ± SD, b IADL – 8 (no impairment) to 31 (severe impairment).

Results

Fig 1 Association between galantamine plasma concentration and daily dose.

Mean galantamine plasma concentration demonstrated strong positive linear association with dose (r = 0.51, p < 0.001). The mean ± SD plasma concentration levels (µmol/L) differed significantly between the patients with the respective daily doses; 8 mg: 0.163 ± 0.073, 16 mg: 0.261 ± 0.105, 24 mg: 0.368 ± 0.145 (p < 0.001). No gender differences regarding dose were observed.

Fig 2 Galantamine plasma concentration level depending on time from drug intake.

The galantamine plasma concentration level showed a steady decline over the time from drug intake to plasma extraction. The patients with a daily dose of 24 mg indicated a more rapid decline in plasma concentration.

Fig 3 Relationship between galantamine plasma concentration and body mass index

There was no linear relationship between galantamine plasma concentration and body mass index (BMI) in the entire cohort. When investigating the impact of gender, a negative linear association (r = -0.45, p = 0.001) between concentration and BMI was found in the male group but not in the female. Larger men showed lower plasma concentration levels.