A single-center, double blind, randomized, controlled study to evaluate the relative efficacy of sublingual and oral vitamin B complex administration in reducing total serum homocysteine levels

Yuka Yazaki, Gigi Chow, and Mark Mattie, M.D., Ph.D.*

Abstract

Objective: Reports correlating total homocysteine (tHcy) concentrations with arteriosclerosis have become a matter of interest amongst healthcare professionals and the public. Several commercial preparations of vitamin B complexes have been marketed as supplements intended to reduce elevated levels of tHcy. Among these preparations are those that have been specifically designed for sublingual administration. This study is designed to evaluate the relative efficacy of sublingually vs. orally delivered vitamin B complex in reducing serum tHcy levels.

Design: Forty-one subjects, between the ages of 50-80 years with total serum tHcy concentrations exceeding 11 µmol/l, were treated with a six-week regimen of vitamin B complex. Each B complex consisted of 1000 µg vitamin B12 (as methylcobalamin), 400 µg folate (as folic acid), and 5 mg vitamin B6 (as pyridoxine HCl). Participants in the study were randomized into two groups designated, retrospectively, as SL and PO. Members of the group SL were given a sublingually delivered vitamin B complex and a matching orally delivered placebo. Members of group PO were given a orally delivered vitamin B complex and a matching sublingually delivered placebo. A statistically significant reduction in tHcy values was observed in both groups upon completion of the six-week protocol.

Materials and Methods

Inclusion criteria:
• must sign an informed consent form
• must be between the ages of 50-80 years
• must have a fasting serum tHcy level greater than or equal to 11 µmol/l

Exclusion criteria:
• must have a fasting serum tHcy level less than or equal to 11 µmol/l
• serum tHcy level is < 11 µmol/l
• is pregnant or breast feeding
• has had surgery within 30 days
• has had a myocardial infarction
• has had a stroke within the last 6 months
• has clinically overt peripheral vascular disease
• has unstable angina
• has had a previous antiarrhythmic medication
• is receiving any heart disease-related medication
• started less than three months prior to the study
• has been diagnosed or demonstrates consistent with congestive heart failure
• has clinically overt peripheral vascular disease
• has been diagnosed or demonstrates symptoms
• has had a myocardial infarction
• has unstable angina
• has had a stroke within the last 6 months

Results: The dropout rate was 2.4% (1/42). The SL and PO groups were assigned a total of 20 and 21 subjects, respectively. There were no statistically significant differences between the two groups with respect to gender distribution, mean age, or compliance. Mean serum tHcy concentrations of subjects before and after treatment are listed in Table 1. A statistically significant reduction in tHcy values was observed in both groups upon completion of the six-week protocol. There was no statistically significant difference in serum tHcy concentrations between groups either before or after treatment.

The serum tHcy concentrations of three subjects from the SL group and three subjects from the PO group were measured weekly. In both groups, the most significant decline in tHcy concentrations occurred during the first three to four weeks of therapy with changes in levels thereafter becoming asymptotical. Serum tHcy concentrations are plotted as a function of time in Figure 1.

Conclusions: The efficacy of vitamin B complex therapy used in the treatment of hyperhomocysteinemia is well established. The purpose of this study was to assess treatment dependence on the route of administration by comparing reductions in serum tHcy in subjects given vitamin complex orally to those given the same complex sublingually. When a vitamin complex preparation, consisting of 1000 µg vitamin B12 (as methylcobalamin), 400 µg folate (as folic acid), and 5 mg vitamin B6 (as pyridoxine HCl), was administered to subjects using oral and sublingual routes of administration, no difference in effect following a six-week treatment period was observed in middle-aged to elderly subjects with hyperhomocysteinemia who were otherwise healthy.

Results:

Table 1. A statistically significant reduction in tHcy values was observed in both groups upon completion of the six-week protocol.

<table>
<thead>
<tr>
<th></th>
<th>SL Group</th>
<th>PO Group</th>
<th>Between P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline tHcy</td>
<td>14.0 ± 2.6</td>
<td>13.7 ± 2.0</td>
<td>NS</td>
</tr>
<tr>
<td>6 Weeks tHcy</td>
<td>8.9 ± 1.6</td>
<td>8.7 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Within P value</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.05</td>
<td></td>
</tr>
</tbody>
</table>

Table #1. tHcy concentrations of groups before and after treatment. tHcy values are expressed in µmol/l and displayed as mean ± SD. NS = Not Significant.

Figure 1. Total serum homocysteine concentrations of six subjects plotted as a function of time. Solid line: Average of PO group (squares), Dotted line: Average of SL group (circles), …. SL Group, ___ PO Group.