SHORT REPORT

Improvement of Parkinsonian features correlate with high plasma levodopa values after broad bean (Vicia faba) consumption

J M Rabey, Y Vered, H Shabtai, E Graff, A D Korczyn

Abstract
Five healthy volunteers and six patients with Parkinson’s disease (PD) ate 250 g cooked broad beans after 12 hours without treatment. During the next four hours a substantial clinical improvement was noted, three patients showed severe dyskinesias, and plasma levodopa concentrations rose.


Levodopa was identified in the seedlings, pods and beans of the broad bean (Vicia faba—VF) by Guggenheim in 1913. Although anecdotal cases of PD improvement after ingesting broad beans have been presented, we are not aware of any studies which have systematically examined this question.

Patients and methods
Six patients with PD participated in the study, after signing written consent (mean age 63.5 years; mean disease duration 13 years; stage III, Hoehn and Yahr scale; mean daily dose of broad beans 541 mg and 54.1 mg carbidopa; 3 also took bromocriptine and 3 took lisuride hydrogen maleate (table 1). Three of the patients also had moderate drug-induced dyskinesia. Five healthy volunteers (mean age 49 years) also participated in the study after giving their written consent. The trial was approved by the hospital Helsinki Committee.

After 12 hours off medication, six PD patients had breakfast at 7 am consisting of tea or coffee with biscuits or a slice of bread. At 8–8.30 am they ate 250 g of cooked VF. Blood samples were obtained before eating VF (time 0) and every 30 minutes thereafter for four hours. Clinical evaluation was scored according to the Webster scale. Dyskinesia was evaluated on a separate scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Five days later, the same patients were given orally 125 mg levodopa plus 12.5 mg carbidopa at time 0, after 12 hours off medication. Blood samples were then obtained at time 0 and each 30 minutes thereafter for four hours. The clinical evaluation was performed as described above. Five healthy volunteers also ate 250 g cooked VF at 8–8.30 am. Blood samples were obtained at time 0 and every 30 minutes for four hours.

DOPA MEASUREMENTS
Plasma concentrations of levodopa were determined by an HPLC-ECD method. Catecholamines were absorbed onto acid washed alumina at pH 8.5 directly from plasma. After being shaken with the alumina, the residue plasma was aspirated. Catecholamines were then eluted from the alumina by a small volume of 0.1 M HCl. The HPLC system consisted of an LDC/Milton Roy high pressure pump, a rheodyne injector, and RP chromatographic column (BAS ODS column, 4 x 250 mm, 5 μm) and an electrochemical detector (LC-4, BAS) equipped with a TL-5 glassy carbon electrode. The applied potential at the working electrode was +0.6-0.6 V. The mobile phase consisted of monochloroacetate buffer containing 2 mM EDTA and an ion pair agent (SO3, 50 mg/L). The lower limit of detection was 200 pg/mL and the intertest coefficient of variation was 5%.

Statistical analysis for the comparison of clinical performance and levodopa plasma levels in the PD group while eating VF versus levodopa was performed using Wilcoxon and Student’s paired t tests.

Table 1  Patients’ characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/age</th>
<th>Disease duration (y)</th>
<th>Stage (Hoehn-Yahr)</th>
<th>Treatment (mean daily dose mg)</th>
<th>Dyskinesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/60</td>
<td>9</td>
<td>III</td>
<td>500 LD</td>
<td>+ + + +</td>
</tr>
<tr>
<td>2</td>
<td>M/65</td>
<td>10</td>
<td>III</td>
<td>750 LD</td>
<td>+ + + +</td>
</tr>
<tr>
<td>3</td>
<td>M/70</td>
<td>15</td>
<td>III</td>
<td>500 LD</td>
<td>+ + + +</td>
</tr>
<tr>
<td>4</td>
<td>F/56</td>
<td>12</td>
<td>III</td>
<td>625 LD</td>
<td>+ + + +</td>
</tr>
<tr>
<td>5</td>
<td>M/66</td>
<td>20</td>
<td>III</td>
<td>500 LD</td>
<td>+ + + +</td>
</tr>
<tr>
<td>6</td>
<td>F/64</td>
<td>12</td>
<td>III</td>
<td>375 LD</td>
<td>+ + + +</td>
</tr>
</tbody>
</table>

LD—levodopa, Bro—bromocriptine, Lis—lisuride.
Dyskinesia (see method).

Results
PD patients showed a significant improvement in their motor features after eating VF which was similar to the improvement measured after receiving 125 mg of levodopa plus 12.5 mg of carbidopa (table 2). Moreover, in three patients we observed after VF ingestion severe dyskinesias which were similar to those observed after levodopa administration (table 3). Plasma levodopa levels increased substantially (although somewhat less) after the broad beans compared with levodopa in PD.
patients (figure 1). The mean (SD) Cmax was also not significantly different ([Cmax (VF) 0.84 (0.2) µg/ml vs Cmax (levodopa) 1.22 (0.31)µg]). The mean (SD) AUC was similar ([VF 2.95 (0.85) µg/ml/H°⁻⁴ vs levodopa 3.21 (0.59) µg/ml/H°⁻⁴]). The mean Tmax was also similar.

Five volunteers also showed an increase in plasma levodopa levels after eating broad beans which were similar although considerably lower than the levels measured in PD patients after they had eaten broad beans (fig 2).

**Discussion**

Three natural potential precursors for dopamine synthesis which can be supplied in the diet, already exist in the brain: phenylalanine, tyrosine and levodopa. Phenylalanine hydroxylase has not been found in the brain but phenylalanine may be a substrate for tyrosine hydroxylase and can be converted to tyrosine by this enzyme. High doses of phenylalanine, however, reduce catecholamine synthesis, perhaps due to inhibition of tyrosine hydroxylase. Several investigators found that dl-phenylalanine either had no effect or exacerbated Parkinsonism.

Tyrosine is the normal precursor for catecholamine synthesis. Tyrosine administration does not affect dopamine synthesis in normal animals. However, if the dopaminergic system is lesioned, the increased firing rate of the remaining neurons will require more tyrosine and in this case, tyrosine administration will enhance dopamine synthesis. Administration of tyrosine to Parkinsonian patients increased the CSF concentration of the dopamine metabolite homovanillic acid (HVA) by 75%. If, however, tyrosine hydroxylase was severely depleted, as in more advanced Parkinsonism, tyrosine addition would be of little benefit.

The levodopa content of the normal diet is very low or absent. The low concentration of levodopa found in the plasma apparently reflects the activity of peripheral tyrosine hydroxylase in sympathetic neurons rather than dietary intake.

In our study, plasma levodopa levels induced in PD patients were higher than the levels measured in healthy volunteers after eating the same amount of broad beans. This difference may be due to the previous treatment of the patients with carbidopa, a potenti peripheral decarboxylase inhibitor with a prolonged plasma half-life.

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Table 2 Cumulative Motor Score (Webster) (n = 6)

<table>
<thead>
<tr>
<th>Minutes</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>150</th>
<th>180</th>
<th>240</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF</td>
<td>140</td>
<td>114</td>
<td>97</td>
<td>95</td>
<td>96</td>
<td>105</td>
<td>123</td>
<td>130</td>
</tr>
<tr>
<td>LD</td>
<td>136</td>
<td>119</td>
<td>99</td>
<td>100</td>
<td>102</td>
<td>115</td>
<td>124</td>
<td>132</td>
</tr>
</tbody>
</table>

VF = Vicia faba ingestion, LD = 125 mg levodopa + 12.5 mg DCI.

Table 3 Cumulative Dyskinesia Score (n = 3)

<table>
<thead>
<tr>
<th>Minutes</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>150</th>
<th>180</th>
<th>240</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF</td>
<td>0</td>
<td>6</td>
<td>12</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>LD</td>
<td>0</td>
<td>5</td>
<td>12</td>
<td>10</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

VF = Vicia faba ingestion, LD = 125 mg levodopa + 12.5 mg DCI.

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8 Nagatsu T, Levitt M, Videnfriend S. Tyrosine hydroxylase: The initial step in norepinephrine biosynthesis. J Biol

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Figure 1 Plasma levodopa levels measured after the ingestion of VF and levodopa in six PD patients.

Figure 2 Plasma levodopa levels measured after the ingestion of VF in six PD patients and five healthy volunteers.
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Jacques Dubois, 1478-1555,
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Sylvius and Francisco
some tremors were always present but
others appeared only with movement. He explored the
concept of thermal and tactile senses, had an understand-
ing of ductless glands and was one of the first to propose that the pancreas produced a juice, which together
with saliva and a form of fermentation, aided digestion. He was the first to describe tubercles and the process of
cavitation. The Netherlands honoured him with this stamp
in 1937 (Stanley Gibbons no 470, Scott no B95).