Effect of Nimodipine on Blood Pressure in Acute Ischemic Stroke in Humans

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Nimodipine is currently under investigation for the treatment of acute stroke. Although relatively specific for the cerebrovasculature, acute reductions in blood pressure after a dose may adversely affect neurologic outcome. We studied 29 consecutive acute ischemic stroke patients treated with placebo (n = 9) or either 120 (n = 10) or 240 (n = 10) mg/day of nimodipine. Blood pressure was recorded before and 30 and 60 minutes after a dose for the first 8 days. Ten neurologic physicians were asked to predict the treatment group (placebo or drug) of randomly selected patients based on blood pressure results. Only those patients on 240 mg/day of nimodipine had significant decreases in blood pressure after a dose (p < 0.001); however, these were minimal (average 10 mm Hg systolic). Only 26 of 48 treatment predictions (54%) were correct. At the studied doses, nimodipine has a minimal effect on blood pressure in the acute stroke period. (Stroke 1988;19:401-402)

Nimodipine is a calcium channel antagonist that has relative specificity for the cerebral vasculature in vitro. The drug has been studied in the treatment of various cerebrovascular disorders. In subarachnoid hemorrhage, treatment with nimodipine decreased the severity of the neurologic deficit without causing significant adverse effects. In patients suffering from common or classic migraine headache, nimodipine decreased the frequency and duration of headaches and produced minimal adverse effects. Significant hypotension was not noted in either study although it was not specifically studied.

In acute stroke, systemic blood pressure must be monitored very closely. Under normal conditions, cerebral blood flow is preserved over a wide range of systemic blood pressures. In ischemic brain tissue, autoregulation is impaired and cerebral blood flow becomes pressure-dependent. It is important, then, to avoid a precipitous reduction in systemic blood pressure, which may increase infarct size. We studied the effect of nimodipine on blood pressure in patients with acute ischemic stroke.

Subjects and Methods

All patients studied were part of a larger, double-blind, randomized clinical trial to evaluate the safety and efficacy of nimodipine in the treatment of acute ischemic stroke (Study no. D83-049-01, a 21-day randomized, double-blind trial of nimodipine vs. placebo in acute ischemic brain infarction, Miles Pharmaceuticals, West Haven, Connecticut, unpublished data). Patients over 45 years of age were recruited for the study. The diagnosis of acute ischemic stroke was confirmed by history and neurologic examination. Informed consent to participate was obtained from each patient before entry into the trial.

Patients were randomized to receive placebo or either 120 or 240 mg/day of nimodipine in six divided doses. All patients were treated for 21 days. Before each morning dose and 30 and 60 minutes after the dose for the first 7 days, brachial blood pressure was taken and recorded. The only drugs that were disallowed during the investigation were other calcium channel antagonists and antihypertensive agents other than β-blockers. Administration times of concurrent medications were always separated from study drug administration by at least 2 hours.

After completion of the trial, 10 neurologic physicians were asked to predict the treatment group (placebo or drug) of randomly selected patients by evaluating the effect of the dose on blood pressure as recorded on data sheets. Differences in mean arterial pressure (MAP) and systolic pressure (SP) before and 30 and 60 minutes after placebo or nimodipine were analyzed using one-way analysis of variance.

Results

Nine patients received placebo and 10 patients each received either 120 or 240 mg/day of nimodipine. The three groups did not differ in age, sex, and risk factors, and there was no significant difference in pretreatment blood pressures (Table 1).

Acute Effects on Blood Pressure

When MAPs recorded before and 30 and 60 minutes after the 10 AM dose were compared, there was no difference between the three readings in the patients receiving placebo. In patients receiving either 120 or 240 mg/day of nimodipine, statistically significant yet clinically insignificant differences in MAP were seen before and after the dose (Table 1, Figure 1). When SPs...
TABLE 1. Average Mean Arterial and Systolic Blood Pressures Before and 30 and 60 Minutes After Dose of Placebo or Nimodipine

<table>
<thead>
<tr>
<th>Group</th>
<th>Before Mean arterial pressure</th>
<th>30 min Mean arterial pressure</th>
<th>60 min Mean arterial pressure</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>102 ± 21</td>
<td>99 ± 13</td>
<td>102 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Nimodipine 120 mg/day</td>
<td>102 ± 14</td>
<td>99 ± 11</td>
<td>97 ± 13</td>
<td>0.03</td>
</tr>
<tr>
<td>Nimodipine 240 mg/day</td>
<td>100 ± 11</td>
<td>93 ± 10</td>
<td>93 ± 12</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Before Systolic pressure</th>
<th>30 min Systolic pressure</th>
<th>60 min Systolic pressure</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>143 ± 23</td>
<td>141 ± 24</td>
<td>143 ± 33</td>
<td>NS</td>
</tr>
<tr>
<td>Nimodipine 120 mg/day</td>
<td>142 ± 21</td>
<td>139 ± 22</td>
<td>136 ± 21</td>
<td>NS</td>
</tr>
<tr>
<td>Nimodipine 240 mg/day</td>
<td>142 ± 16</td>
<td>133 ± 17</td>
<td>133 ± 19</td>
<td>0.0009</td>
</tr>
</tbody>
</table>

Data are mean±SD in mm Hg. NS, not significantly different from before dose.

taken before and 30 and 60 minutes after the 10 AM dose were compared, there were no differences in either the placebo group or the group receiving 120 mg/day of nimodipine. Only 240 mg/day of nimodipine was found to have a significant effect on SP. This was minimal (average 10 mm Hg) and not clinically significant (Table 1, Figure 2). Although no significant changes in blood pressure occurred in the patients receiving placebo, there was a great deal of variability in recorded pressures. Changes in SP ranged from 2 to 70 mm Hg at 30 and 60 minutes after a dose.

**Chronic Effects on Blood Pressure**

Although blood pressure tended to decrease over time in all three groups, there was no difference when lowest daily MAPs in the nimodipine groups were compared with the placebo group.

**Assessment of Blindedness of Study**

Of the 48 predictions of treatment made by the participating physicians, only 26 (54%) were correct. With a 50% likelihood (placebo vs. drug) of guessing correctly, the 54% accuracy rate was no better than chance. With respect to peripheral blood pressure, the blind was considered successful.

**Discussion**

The lack of a pronounced effect of nimodipine on blood pressure in the stroke patients we studied may be a concentration- or dose-dependent phenomenon. A more pronounced effect may be evident at higher doses that achieve higher serum concentrations of nimodipine. In patients with impaired hepatic function, decreases in MAP were seen after the administration of nimodipine in doses that produced no change in the blood pressure of an age-matched control group. This was attributed to the higher nimodipine concentrations in patients with hepatic disease.

Wide fluctuations in MAP and SP were found in the stroke patients participating in our study, irrespective of treatment group. In a recent report by Britton et al, patients admitted to the hospital for acute stroke experienced a spontaneous decline in blood pressure in the first 4 days of their hospital stay. In that report, only one measurement per day was analyzed so assessment of within-day fluctuation could not be made. In our study, MAP and SP tended to decrease over time in all three groups, but this decline did not reach statistical significance.

In conclusion, at the doses currently used in the treatment of acute ischemic stroke, nimodipine has a minimal effect on blood pressure.

**References**


**Key Words**
- Blood pressure
- Calcium channel blockers
- Cerebrovascular disorders
- Nimodipine
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World Wide Web at:
http://stroke.ahajournals.org/content/19/3/401