Letters to the Editor

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Pentoxifylline Alters the Natural Course of Acute Nonhemorrhagic Stroke

To the Editor:

Recently Hsu et al reported the results of a placebo-controlled, double-blind trial in patients with acute nonhemorrhagic stroke using pentoxifylline.1 The authors state that although pharmacologic effects were present during the first few days, the clinical benefits were small and not sustained.

This study shows a change in the natural course of stroke using pentoxifylline infusion therapy in contrast to a placebo group. To our knowledge, this is the first time that an improvement has been demonstrated in the acute phase of stroke using a rheologically active drug.

Consciousness, motor and cranial nerve functions, and total neurologic deficit scores improved significantly in the patients treated with pentoxifylline infusion. These variables deteriorated in the placebo group during the first 3 days, which partially reflects the very early entry of the patients (within 12 hours after onset of symptoms) into the trial. The significant differences between placebo and pentoxifylline therapy could not be maintained in the subsequent oral treatment period (after 3 days), although initial improvements due to pentoxifylline were sustained. These findings may be related to the different pentoxifylline plasma levels following the intravenous or oral route of administration.

We recommend further clinical investigations to substantiate the role of pentoxifylline infusion treatment in acute cerebral ischemia.

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The following is in response:

To the Editor:

We thank Drs. Ott, Chandra, and Hartmann for their thoughtful comments about our observations of pentoxifylline’s effects on acute stroke. We discussed the potential differences in pentoxifylline pharmacokinetics between intravenous and oral routes in the unabridged version of our paper, available from NAPS (c/o Microfiche Publications, PO Box 3513, Grand Central Station, New York, NY 10163-3513 [NAPS Document No. 04557, 54 pages]) and others.1

Furthermore, the pharmacokinetic differences between administering pentoxifylline intravenously and by controlled-release tablet have been studied by the clinical trial sponsor. While the multicenter controlled trial in acute stroke was ongoing, a study of the pharmacokinetics of the stroke trial intravenous regimen was carried out in 15 healthy volunteers. Summary comparisons of mean drug and metabolite steady-state plasma concentrations between intravenous administration (1,200 mg/day, 24-hour continuous infusion) and controlled-release tablet (400 mg t.i.d.) are shown in Table 1.

Clearly, the plasma concentrations of pentoxifylline and metabolite I are about 3 times higher during intravenous dosing compared to oral administration. The pentoxifylline metabolites are all considered to be hemorheologically active. It is possible that the higher concentrations of pentoxifylline and metabolite I present during intravenous dosing may produce more pharmacologic effects than an equal dose administered orally. If so, greater pharmacologic effects might account for the significant differences between drug and placebo noted during intravenous dosing for the first 3 days after stroke.

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Reference


Neurosarcoidosis and Stroke

To the Editor:

Brown et al1 recently reviewed the issue of sarcoidosis and stroke. Given the relatively common occurrence of vascular disease and microscopic infarction in neuropathologic studies of sarcoidosis involving the brain,2 the paucity of stroke cases is surprising. It is often difficult to substantiate the diagnosis of central nervous system (CNS) sarcoidosis and define the underlying pathophysiology of stroke syndromes. We report a case of CNS sarcoidosis presenting with stroke and an incidental suprasellar mass.

A 38-year-old white male with sarcoidosis was admitted with acute onset of left hemiparesis following a 2-week history of transient ischemic attacks. The patient had had biopsy-proven sarcoidosis since age 25 with ocular, skin, lymph node, and pulmonary involvement. He required corticosteroid treatment for control of his systemic disease and was taking triamcinolone (4 mg twice daily) at the time his neurologic symptoms developed. On admission, the patient related a history of 10 minutes of left

**TABLE 1. Mean Steady-state Plasma Concentrations (ng/ml)**

<table>
<thead>
<tr>
<th></th>
<th>Intravenous</th>
<th>Controlled-release tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentoxifylline</td>
<td>155</td>
<td>59</td>
</tr>
<tr>
<td>Metabolite I</td>
<td>561</td>
<td>185</td>
</tr>
<tr>
<td>Metabolite IV</td>
<td>55</td>
<td>76</td>
</tr>
<tr>
<td>Metabolite V</td>
<td>609</td>
<td>620</td>
</tr>
</tbody>
</table>


1. Interestingly, the authors state that although pharmacologic effects were present during the first few days, the clinical benefits were small and not sustained.

2. The authors state that although pharmacologic effects were present during the first few days, the clinical benefits were small and not sustained.

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Pentoxifylline alters the natural course of acute nonhemorrhagic stroke.
E Ott, B Chandra and A Hartmann

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World Wide Web at:
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