Isoniazid-Induced Reduction of Serum Cholesterol

To the Editor:

During a randomized, double blind, crossover, placebo-controlled clinical trial of oral isoniazid (isonicotinic acid hydrazide, INH), serum cholesterol was measured during the sixth week of treatment of both phases of placebo and the drug in five men. The ages of the patients ranged from 28 to 65 years, with a mean of 45 years. The dosage of isoniazid was 300 mg thrice daily (15 mg/kg body weight, approx). One hundred mg per day of pyridoxine (vitamin B6) was given during the drug phase to prevent isoniazid-induced pyridoxine-depleted peripheral neuritis. Lactose was used as placebo. No dietary restrictions were imposed during the study. None of the patients had any family history of lipid abnormalities nor any associated diseases that could cause abnormal levels of serum cholesterol. Cholesterol was measured by the enzymatic method using kinetic discrete analyzer.

Table 1—Isoniazid-Induced Reduction of Serum Cholesterol*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age in Years</th>
<th>Placebo</th>
<th>Isoniazid</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>171</td>
<td>138</td>
<td>-29</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>195</td>
<td>150</td>
<td>-45</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>265</td>
<td>154</td>
<td>-111</td>
</tr>
<tr>
<td>4</td>
<td>53</td>
<td>260</td>
<td>175</td>
<td>-85</td>
</tr>
<tr>
<td>5</td>
<td>65</td>
<td>189</td>
<td>159</td>
<td>-30</td>
</tr>
</tbody>
</table>

n = 5 (SD) 45 ± 16 216 ± 43 155 ± 14† -61

*mg percent; †Significant (p<.01) by two tailed, paired t-test

On treatment with isoniazid, there was a mean decrease of 61 mg/dl of cholesterol with a range of 29 to 111 mg/dl which occurred in all five patients. This reduction was significant (p<.01) by the two tailed, paired t-test. The individual values are given in the Table. The results suggest that isoniazid has a lipid-lowering effect. The dosage used in this study was about three times that used in the treatment of tuberculosis. Review of the literature indicated that pyridoxine has no significant effect on cholesterol levels. Animal experiments have shown that prior to development of a tuberculous lesion, there was an increased level of cholesterol in the lungs and this was inhibited by isoniazid treatment. It is further shown that isoniazid reduces incorporation of radioactive (3H) into bound lipid and phospholipid. Thus, the reduction of cholesterol appears to be due to direct action of isoniazid.

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References


Acute Thrombophlebitis following IV Amiodarone Administration

To the Editor:

Dr. Aravanis et al pointed out (Chest 1982; 82:515) the onset of acute thrombophlebitis as an acute side effect of IV administration of amiodarone, this event is not negligible because sometimes it requires the discontinuation of the drug infusion. We use IV amiodarone at a lower attack dose than Dr. Aravanis: 2-4 mg/kg instead of 7.5-10 mg/kg, but also in our patients the early onset of severe inflammation of the perfused vein created difficulties in continuing the drug infusion. IV amiodarone was given in 36 cases of supraventricular and ventricular arrhythmias, resistant to the conventional anti-rhythmic drugs; in 33 patients it was infused in a peripheral vein and in the last three patients through the subclavian vein. In 24 of the first 33 patients (73 percent) pain, redness and swelling were present in the site of the infusion a few hours after the beginning of treatment, and these findings rapidly became worse. In order to avoid this painful side effect, 1,000 units of heparin or 10 mg of hydrocortisone were added to the 5 percent glucose solution containing amiodarone, but both procedures were ineffective. In the three patients in whom amiodarone was infused with the central venous catheter, no sign of local reaction was seen. According to our experience, we think an effective way to prevent thrombophlebitis following IV amiodarone therapy is to employ central vein perfusion.

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To the Editor:

Dr. Aravanis reported on the occurrence of a severe local reaction consisting of pain, redness, swelling and acute thrombophlebitis following intravenous infusion of amiodarone. Although the exact incidence was not reported, three cases in which the reaction occurred were presented. Amiodarone was given in doses of 7.5-10 mg/kg as a 300 mg bolus injection followed by a 600 mg infusion. Dr. Aravanis concluded that it would be advisable to administer amiodarone through a central venous catheter to avoid these local reactions. Because the occurrence of thrombophlebitis is localized at the infusion site, it is unlikely to be a hypersensitivity reaction and is probably dependent on the concentration and infusion rate. Unfortunately, these parameters were not reported. At our institution, amiodarone is administered as an intravenous infusion of 5 mg/kg diluted in 100 ml of dextrose in water and infused over 30 minutes. Using this method of administration in 16 infusions, we have not encountered acute thrombophlebitis.

We conclude that acute thrombophlebitis following the intravenous infusion of amiodarone may be avoided by adequate dilution and appropriate infusion rate and the need for central venous administration may be unwarranted.

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Communications to the Editor