Absence of an Effect of Chronic Administration of Growth Hormone on Serum Lipids

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Human growth hormone (hGH) was administered to a group of osteoporotic patients at two dosage levels for a period of 6 mo each. The first dose employed was 2 units subcutaneously daily, and the second dose was 0.2 W^{1/4} units (where W is body weight expressed in kg) daily. There was no significant change in serum-cholesterol or triglyceride concentration despite the production of hyperglycemia and soft-tissue swelling on the higher dosage regimen.

A number of factors may account for the conflict between our findings and a previous report in which hGH administration had a hypocholesterolemic, hyperglycemic effect. These factors include differences in sex, age, dosage, and duration of treatment. Nonetheless, it is clear that from a therapeutic vantage, even if hGH were readily available, it would not be a useful hypocholesterolemic agent.

An EFFECT of growth hormone on serum-lipid levels is suggested by a number of observations. The rise in serum cholesterol following hypophysectomy in the rat is prevented only when growth hormone is administered in addition to thyroid hormone. Serum-cholesterol levels are increased in dwarfs with monotropic deficiency of human growth hormone (hGH). In addition, the subacute administration of hGH (1 wk) to hypercholesterolemic and normcholesterolemic human subjects results in a reduction in serum-cholesterol and an elevation of serum-triglyceride levels.
Table 1. Effect of hGH

<table>
<thead>
<tr>
<th></th>
<th>Pre*</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Post*</th>
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<tbody>
<tr>
<td><strong>Low Dose</strong></td>
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<tr>
<td>CHOL</td>
<td>252 ± 61</td>
<td>264 ± 50</td>
<td>273 ± 71</td>
<td>269 ± 78</td>
<td>258 ± 70</td>
<td>250 ± 55</td>
<td>240 ± 72</td>
<td>242 ± 69</td>
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<td>(N = 7)</td>
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<tr>
<td>TRIG</td>
<td>119 ± 66</td>
<td>156 ± 66</td>
<td>144 ± 87</td>
<td>146 ± 94</td>
<td>135 ± 85</td>
<td>130 ± 72</td>
<td>135 ± 104</td>
<td>143 ± 98</td>
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<tr>
<td>FBS</td>
<td>100 ± 15</td>
<td>101 ± 4</td>
<td>102 ± 12</td>
<td>99 ± 14</td>
<td>99 ± 11</td>
<td>102 ± 0</td>
<td>98 ± 13</td>
<td>104 ± 14</td>
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<tr>
<td><strong>High Dose</strong></td>
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<tr>
<td>CHOL</td>
<td>245 ± 63</td>
<td>242 ± 48</td>
<td>247 ± 63</td>
<td>241 ± 43</td>
<td>256 ± 73</td>
<td>247 ± 68</td>
<td>272 ± 63</td>
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<td>(N = 6)</td>
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<tr>
<td>TRIG</td>
<td>126 ± 105</td>
<td>156 ± 106</td>
<td>143 ± 78</td>
<td>160 ± 106</td>
<td>152 ± 102</td>
<td>130 ± 85</td>
<td>184 ± 113</td>
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</tr>
<tr>
<td>FBS</td>
<td>99 ± 15</td>
<td>100 ± 18</td>
<td>104 ± 18</td>
<td>96 ± 13</td>
<td>105 ± 19</td>
<td>105 ± 12</td>
<td>107 ± 15†</td>
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</tbody>
</table>

*Pre indicates values obtained prior to therapy, and Post indicates values 2–3 mo following discontinuation of therapy.
†p < .02; others not significantly different from baseline.
It is the purpose of the present study to examine the effects on serum-lipid constituents of chronic administration of hGH to adult human subjects.

MATERIALS AND METHODS

The patients were participants in a program for the treatment of osteoporosis with hGH. The study was divided into two treatment periods in which a daily morning dose of 2 units of hGH was given subcutaneously and a higher daily dose period in which 0.2 units W \(0.75\) (where W represents body weight expressed in kg) of hGH was used (mean dose 4.2 ± 0.8 units). Each regimen was carried out for 6 mo. All but one of the patients were females. The mean age was 62 ± 7 yr. Serum-cholesterol and triglyceride levels were obtained after an overnight fast on a monthly basis in most patients. They were performed on an outpatient basis, except for the baseline values and the values obtained after 1 yr of treatment. The patients were questioned on each visit concerning food ingestion, and when it was determined that they were not fasting for 12 hr, the values were discarded.

RESULTS

Two patients had type IIb hyperlipoproteinemia initially. Following the administration of 2 units of hGH daily, there was no significant change in mean cholesterol, triglyceride, or fasting blood glucose (Table 1). Mean body weight was unchanged.

Following the high dose regimen of hGH administration, there was again no significant change in mean serum-cholesterol or triglyceride values, although at the end of 6 mo, the mean fasting blood glucose was significantly elevated (Table 1). A number of other metabolic effects of hGH were noted during the high dose period, including increased calcium turnover and hydroxyproline excretion. Moreover, the patients developed symptoms and signs of hyper-somatotropism, such as soft-tissue swelling, joint stiffness, and the carpal-tunnel syndrome.

DISCUSSION

We have previously noted that the incidence of hypercholesterolemia is not increased in acromegalic individuals. The incidence of hyperglyceridemia was felt to approximate that prevalent in the American population (20%). This is consistent with the findings in the present study that chronic administration of hGH had no effect on serum-cholesterol and triglyceride levels.

The findings in the present study are in conflict, however, with those of Byers and Friedman who reported that the administration of 5 mg of hGH twice daily for 7 days resulted in a decrease in serum cholesterol and an increase in serum triglycerides in both normocholesterolemic and hypercholesterolemic patients.

There are several factors that may explain these divergent findings. Even the high dose regimen in our patients was considerably less than the 10 mg daily dosage employed in the study of Byers and Friedman. Their patients were treated for only 1 wk, whereas the first post-treatment lipid analysis was obtained in our patients following 4 wk of therapy. Thus, the subacute and chronic effects of hGH administration may differ.

Our patients were much older than those studied by Byers and Friedman. Resistance to the effects of hGH with increasing age has been noted for a number of metabolic parameters and could also apply to the effect on serum lipids.
However, on the high dose regimen, certain metabolic effects were achieved, as indicated by the soft-tissue swelling, increased calcium turnover, and hyperglycemia.

An additional consideration is that there is a sex-related difference in lipid response to hGH administration, since all of Byers and Friedman's patients were men whereas all but one of our patients were female. Also worthy of further investigation is the possibility that sex-hormone deficiency (as seen in post-menopausal women) prevents the metabolic effects of hGH on lipid metabolism.

From a therapeutic vantage, it is evident that even if a higher dosage of hGH (i.e., ≥10 mg/day) had a hypolipidemic effect, its prolonged administration would produce the unacceptable side effect of the production of acromegaly.

ACKNOWLEDGMENT

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REFERENCES


3. Friedman M, Byers SO, Rosenman RH, Li CG, Neuman R: Effects of subacute administration of human growth hormone on various serum-lipid and hormone levels of hypercholesterolemic and normocholesterolemic subjects. Metabolism 23:905-911, 1974


