Effects of Interleukin-4 Administration on Endocrine Function and Lipid Profile of Patients With Malignant Diseases

To the Editor:

Interleukin-4 (IL-4) is a novel pleiotropic lymphokine that is currently being studied in clinical trials as an antineoplastic agent. Our understanding of the potential endocrine effects of endogenous IL-4 is limited at present, but available literature suggests that IL-4 may interfere with hepatic lipogenesis, osteoclastic bone resorption and prolactin action. Given the complex interaction between IL-4 and the endocrine system, it is important to carefully define the impact of exogenous IL-4 given in pharmacologic doses as treatment for cancer to avoid potential adverse endocrine effects.

We monitored serum hormone and lipid levels in 31 patients with malignant diseases who received IL-4 within the context of a phase I clinical trial conducted by ABM. Serum hormone and lipid levels were measured in the morning before IL-4 administration and at regular intervals during treatment. None of the patients had a known history of dyslipidemia or hormone imbalance. Glucocorticoid administration was omitted throughout the study. All patients received IL-4 for at least 1 week. Twenty two patients were treated for at least 30 days, 14 patients for at least 60 days, and 9 patients for more than 90 days. IL-4 was administered three times weekly at doses ranging from 20 mcg/sqm/day (5 patients) to 600 mcg/sqm/day (2 patients) in seven doubling increments. Written informed consent was obtained from all patients according to institutional guidelines.

Administration of IL-4 was generally well tolerated; no differences in hormone or lipid levels could be attributed to IL-4 dose intensity: accordingly, the data were pooled for all dose levels. There was no significant change in patient weight (initial, 80 ± 4 kg, mean ± SEM v final 81 ± 3 kg), serum albumin (3.9 ± 0.1 mg/dL v 3.8 ± 0.1 mg/dL) or serum glucose (103 ± 4 mg/dL v 112 ± 10). In addition, there were no significant changes in serum corticotropin, cortisol, thyrotropin, thyroxine, total cholesterol, or triglyceride levels (Table 1), which remained within the normal range throughout the study. Serum prolactin levels were also normal, 13.5 ± 1.5 ng/mL during the study.

Within our expanding understanding of immune-endocrine communications, it has become increasingly clear that complex interactions exist between the two systems. Physiologically, cytokines participate extensively in the regulation of multiple hormonal/metabolic pathways. Clinically relevant hormone dysregulation has been described for interferon and IL-2 but not for IL-1a. The present study shows that IL-4, as currently used in clinical studies does not create significant endocrine dysfunction.

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REFERENCES


Table 1. Effect of IL-4 on Hormonal/Metabolic Parameters

<table>
<thead>
<tr>
<th>Measure</th>
<th>Basal (n)</th>
<th>30 d (n)</th>
<th>60 d (n)</th>
<th>&gt;90 d (n)</th>
<th>(Normal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH</td>
<td>47 ± 9 (21)</td>
<td>47 ± 7 (19)</td>
<td>54 ± 8 (12)</td>
<td>71 ± 22 (7)</td>
<td>(0-52 pg/mL)</td>
</tr>
<tr>
<td>Cortisol</td>
<td>16 ± 1 (25)</td>
<td>15 ± 2 (22)</td>
<td>15 ± 3 (11)</td>
<td>14 ± 2 (9)</td>
<td>(4-29 mcg/dL)</td>
</tr>
<tr>
<td>TSH</td>
<td>2 ± .2 (26)</td>
<td>2 ± .4 (21)</td>
<td>2 ± .5 (14)</td>
<td>2 ± .9 (9)</td>
<td>(0.3-5 mU/mL)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>8 ± 3 (19)</td>
<td>8 ± 4 (18)</td>
<td>8 ± 5 (14)</td>
<td>8 ± 3 (9)</td>
<td>(4-12 mcg/dL)</td>
</tr>
<tr>
<td>Chol</td>
<td>171 ± 9 (28)</td>
<td>168 ± 7 (24)</td>
<td>174 ± 10 (7)</td>
<td>156 ± 9 (10)</td>
<td>(120-280 mg/dL)</td>
</tr>
<tr>
<td>TG</td>
<td>163 ± 15 (28)</td>
<td>180 ± 16 (22)</td>
<td>189 ± 24 (17)</td>
<td>181 ± 18 (10)</td>
<td>(35-160 mg/dL)</td>
</tr>
</tbody>
</table>

Abbreviations: ACTH, adrenocorticotropin (pg/mL); TSH, thyrotropin (mU/mL); chol, total cholesterol (mg/dL); TG, triglycerides (mg/dL). Cortisol in mcg/dL, thyroid, Total thyroxine in mcg/dL; (n), number of patients.
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