PHYSIOLOGY AND REPRODUCTION

Effect of Recombinant Human Insulin-Like Growth Factor-II on Weight Gain and Body Composition of Broiler Chickens

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ABSTRACT Osmotic minipumps containing either saline or recombinant human insulin-like growth factor-II (IGF-II) were implanted into 4-wk-old female broiler chickens such that the treated chickens received 0.5 mg IGF-II/kg body weight per d. At the end of the trial, no differences in body weight gain or bone length were detected between the treated and control groups. Similarly, there were no differences between the two treatments with respect to heart, spleen, liver, or bursa of Fabricius weight. The relative weight of the abdominal fat pads was greater (P < 0.05) in the birds treated with IGF-II than in the controls, whereas the weight of breast muscle was reduced (P = 0.06) in the birds treated with IGF-II. There was no effect of IGF-II treatment on feed intake or feed conversion efficiency. Plasma growth hormone (GH) levels were acutely depressed by 15 min after IGF-II administration; and also after 2 wk of IGF-II treatment. Plasma triiodothyronine (T3) concentrations were significantly depressed by IGF-II treatment. These results suggest that IGF-II may not stimulate growth in chickens, but can act as a nutrient partitioning agent, either directly or indirectly through altering plasma GH or T3 concentrations.

(Key words: insulin-like growth factor-II, chicken, growth, body composition, fat)

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INTRODUCTION

There is considerable circumstantial evidence to suggest that the insulin-like growth factors (IGF) mediate the actions of growth hormone (GH) in stimulating growth in both mammals and birds. However, a number of recent studies have cast doubt on the physiological role of circulating IGF-I on growth in normal birds (Huybrechts et al., 1992; Tixier-Boichard et al., 1992) and mammals (Zapf et al., 1989; Kerr et al., 1990; Spencer et al., 1991a). Insulin-like growth factor-II has been considered to be a fetal somatomedin, and of minor importance in postnatal animals. However, it is also now well established that in mammals other than rodents (Zapf et al., 1981) and in birds (Decuypere et al., 1993) postnatal plasma IGF-II concentrations are at least as high as IGF-I concentrations. There are much fewer data available on the in vivo effects of IGF-II on growth and body composition. Results from fetal pigs (Spencer, 1986) and rodents (Schoenle et al., 1985; van Buul-Offers et al., 1988; Conlon et al., 1995) suggest that purified IGF-II has, at best, only weak growth-promoting activity. There are no reports on the effects of IGF-II administration to chickens, but differences in circulating IGF-II levels between lines of chickens with different growth characteristics have been reported (Scanes et al., 1989; Decuypere et al., 1993). The present paper provides the first report on the effects of continuous infusion of recombinant human IGF-II on growth and body composition in chickens.

MATERIALS AND METHODS

Twenty female Ross broiler chickens were used. The birds were housed individually in cages at an ambient temperature of 22 C. They all had ad libitum access to water and to a commercial broiler ration containing 3,200 kcal ME/kg and 23% CP.³ The total feed consumed by each bird throughout the experiment was recorded. At 4 wk of age, the birds were weighed and allocated to one of two groups such that the groups were balanced with regard to body weight. Ten birds were implanted with an osmotic minipump, filled with a solution containing 10 mg of IGF-II such that the birds received approximately 0.5 mg/kg per d of IGF-II (recombinant human IGF-II), for 14 d, whereas 10 control birds received saline alone. Another group of 6
birds was slaughtered at the beginning of the experiment to provide initial carcass energy data. Two weeks after the start of the treatment, blood was collected by brachial vein puncture into heparinized tubes and the birds were then euthanized by cervical dislocation. The carcasses were immediately weighed and dissected. Liver, spleen, heart, and bursa of Fabricius were removed and weighed. The abdominal fat pads and the breast muscle on one side of the bird were also removed and weighed. One leg was removed, and the shank-toe length (from the proximal end of the tibia to the tip of the third metatarsal) was measured. Liver GH receptors and energy balance, heat production, and energetic efficiency were measured as described elsewhere (Spencer et al., 1995).

Acute hormonal responses to IGF-II administration were measured in heparinized blood collected by brachial vein puncture both before, and at 15-min intervals for 1 h after i.v. administration of IGF-II (100 μg) or saline, in otherwise untreated birds. In this acute study (which was undertaken to confirm that IGF-II administration was able to alter hormone concentrations) the birds were 7 wk of age and weighed 2.05 ± 0.06 kg (seven chickens per treatment). The blood samples were centrifuged and the plasma frozen at -20 C for later assay of hormone concentrations. Growth hormone was measured by homologous radioimmunoassay using a monoclonal antibody (Berghman et al., 1987). Thyroxine (T4) was assayed using a commercially available kit, and 3,3',5-triiodothyronine (T3) by radioimmunoassay using a commercially available antiserum, as described elsewhere (Huybrechts et al., 1992). Plasma IGF-I levels were measured by radioimmunoassay after acid-ethanol extraction (Huybrechts et al., 1985).

Differences between groups were compared statistically by t test (SAS Institute, 1986). The GH data were log transformed before analysis. Hormonal data from the acute study were analyzed by ANOVA for repeated measures (SAS Institute, 1986).

**RESULTS**

Neither body weight nor relative growth rate was affected by IGF-II treatment when compared with the saline-treated controls (Table 1). Similarly, IGF-II administration did not significantly influence the weight of liver, heart, or spleen. The absolute weight of abdominal fat was greater (P = 0.06) in the birds treated with IGF-II, and this was reflected in a significantly (P < 0.05) greater relative amount of abdominal fat when expressed as a percentage of carcass weight. In contrast, the weight of the breast muscle was lower (P = 0.06) in the IGF-II-treated birds. There was no effect of IGF-II treatment on shank length. Treatment with IGF-II did not affect appetite (Table 2) and also had no significant effect on feed efficiency (body weight gain:weight of feed consumed), energy retention, or heat production; however, energetic efficiency was increased (P < 0.05) with IGF-II treatment. There was an acute fall in plasma GH concentrations of chickens treated with IGF-II that reported for IGF-I administration to normal chickens (McGuinness and Cogburn, 1991; Huybrechts et al., 1995).

**DISCUSSION**

The results of these studies indicate that administration of recombinant human IGF-II does not stimulate overall somatic growth (either in terms of weight gain or shank length) in broiler chickens; however, administration of IGF-II causes a decrease in plasma GH concentrations. The age and sex of the birds were chosen to maximize the possibility of finding an effect of treatment. Although slower growing female broilers were used rather than males, and although growth rate is slowing at 4 to 6 wk of age, administration of IGF-II did not affect weight gain. Such a lack of effect is similar to that reported for IGF-I administration to normal chickens (McGuinness and Cogburn, 1991; Huybrechts et al.,

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This concurs with the results using partially purified IGF-II (Kasuga et al., 1982; Canfield and Kornfeld, 1986). It has been reported that in chicken tissues the cation-independent mannose-6-phosphate receptor does not bind IGF-II (van Buul-Offers et al., 1998), and in the fetus (Spencer, 1985; Tixier-Boichard et al., 1992). These reciprocal effects with the opposite treatments strongly suggest a real effect of IGF-II in regulating fat deposition.

It has been shown previously (Decuypere et al., 1987) that T₃ is closely associated with abdominal fat deposition in chickens. Moreover, these reduced T₃ levels may also explain the lower heat production of the birds treated with IGF-II, as circulating T₃ levels are positively correlated with heat production (Buyse et al., 1992). The decreased plasma T₃ concentrations associated with IGF-II administration in the present study suggest that the changed fat deposition and heat production may be attributed to an indirect effect of IGF-II through thyroid hormone metabolism. Interestingly, it has been shown previously (Decuypere et al., 1990) that administration of exogenous IGF-I resulted in increased plasma T₃ concentrations and a corresponding decrease in fatness (Huybrechts et al., 1992). These data provide the interesting observation that IGF-I and IGF-II appear to have opposite effects on T₃ and body composition in chickens, though apparently working through a single receptor. This does not seem to be a result of compensatory decreases in IGF-I, but there are a number of possible explanations for this result. There may be another, as yet unidentified, receptor for IGF-II in the chicken; evidence for a third type of IGF receptor with preferential binding of IGF-II has been reported in deer antler (Elliott et al., 1993). Another possibility is that the increased amounts of plasma IGF-II, decreases the number of binding sites available for IGF-I to bind to the receptor.

The lack of effect of IGF-II administration on heart and liver are consistent with the reported lack of effect of IGF-I on growth of these organs (Skottner et al., 1989; Tixier-Boichard et al., 1992). However, IGF-I administration can increase spleen and thymus weight in hypophysectomized rats (Guler et al., 1988; Skottner et al., 1989; Binz et al., 1990), and mice selected for high plasma concentrations of IGF-I had higher spleen and thymus weights than their counterparts selected for low IGF-I levels (Siddiqui et al., 1992). In the present study, there was a nonsignificant increase in spleen weight and

### TABLE 2. Effect of insulin-like growth factor-II (IGF-II) administration for 14 d on feed intake, appetite, feed efficiency, total carcass energy, heat production, and energetic efficiency in female broilers

<table>
<thead>
<tr>
<th>Item</th>
<th>Controls</th>
<th>IGF-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feed intake, g</td>
<td>1,253 ± 40.7</td>
<td>1,206 ± 64.4</td>
</tr>
<tr>
<td>Appetite, g.g BW</td>
<td>0.83 ± 0.02</td>
<td>0.80 ± 0.04</td>
</tr>
<tr>
<td>Feed efficiency (BW:intake)</td>
<td>0.61 ± 0.03</td>
<td>0.62 ± 0.03</td>
</tr>
<tr>
<td>Carcass energy, Mcal</td>
<td>4.11 ± 0.23</td>
<td>4.49 ± 0.21</td>
</tr>
<tr>
<td>Energy retention, Mcal</td>
<td>1.50 ± 0.21</td>
<td>1.90 ± 0.23</td>
</tr>
<tr>
<td>Heat production, Mcal</td>
<td>3.11 ± 0.21</td>
<td>2.79 ± 0.39</td>
</tr>
<tr>
<td>Energetic efficiency</td>
<td>0.26 ± 0.03</td>
<td>0.36 ± 0.03*</td>
</tr>
</tbody>
</table>

1Values are means ± SEM (n = 10).
*P < 0.05.

### TABLE 3. Plasma concentrations of growth hormone (GH), triiodothyronine (T₃), thyroxine (T₄), and hepatic GH receptor binding in chickens given insulin-like growth factor-II (IGF-II) and control birds given saline

<table>
<thead>
<tr>
<th>Item</th>
<th>Controls</th>
<th>IGF-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone, ng/mL</td>
<td>17.0 ± 4.2</td>
<td>9.3 ± 1.2*</td>
</tr>
<tr>
<td>T₃, ng/mL</td>
<td>0.94 ± 0.10</td>
<td>0.57 ± 0.09*</td>
</tr>
<tr>
<td>T₄, ng/mL</td>
<td>16.3 ± 1.8</td>
<td>17.3 ± 1.8</td>
</tr>
<tr>
<td>GH binding, %/mg protein</td>
<td>18.8 ± 1.9</td>
<td>16.3 ± 2.1</td>
</tr>
</tbody>
</table>

*iValues are means ± SEM (n = 10).
*P < 0.05.
no effect on the bursa. These results leave yet unresolved the question of whether IGF-II, like IGF-I, can influence the growth of the organs of the immune system.

The decrease in plasma GH following administration of IGF-II is consistent with the elevation in plasma GH that has been seen following immunoneutralization of IGF-II in chickens (unpublished data). These data suggest a role for IGF-II in regulating GH-negative feedback, a finding that has also been reported in sheep (Spencer et al., 1993).

In conclusion, administration of recombinant human IGF-II to chickens at a dose of 0.5 mg/kg per d had no effect on growth rate, but was associated with increased carcass fatness and decreased plasma T₃ concentrations. Whether a higher dose of IGF-II would stimulate weight gain, or whether IGF-II would be effective in a growth-retarded line of chickens, remains to be established.

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REFERENCES


