《Research Note》

Effects of Thyroidectomy on Serum Levels of Growth Hormone, Insulin-Like Growth Factor (IGF)-1 and IGF-Binding Activity in Dwarf and Normal Chickens

Sadao HOSHINO, Tomoko NAGAI, Daisuke MORISHITA
and Masaaki WAKITA

Faculty of Bioresources, Mie University, Tsu-shi 514

Surgical thyroidectomy tended to increase circulating concentrations of growth hormone (GH) in normal Rhode Island Red chickens (Gifu 15 line) but not in dwarf ones (Gifu 20 line). The operation significantly reduced serum IGF-1 concentrations in normals but resulted in an increasing tendency in dwarfs. Serum IGF-binding activity decreased following thyroidectomy in dwarfs. Basal levels of IGF-binding activity were 3-times higher in dwarfs than in normals, presumably reflecting low basal concentrations of IGF-1 in dwarfs. The results suggest that circulating concentrations of IGF-1 as well as those of GH are influenced by thyroid status and dwarfing gene *dw*.

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Key words : thyroidectomy, dwarf, GH, IGF-1, IGF-binding activity

Introduction

The hormonal characteristics of the sex-linked dwarf chicken have been extensively investigated and it is well established that the dwarf chicken lacks GH receptor in the liver (BURNSIDE *et al.*, 1991), which in turn results in an impaired IGF-1 production and a low circulating IGF-1 concentration (HOSHINO *et al.*, 1982 ; HUYBRECHTS *et al.*, 1985). Further, a low triiodothyronine (T_3) concentration and/or rather a high thyroxine (T_4) concentration inherent to this strain (SCANES *et al.*, 1983) are known to have a profound influence on GH secretion and IGF-1 status in the circulation. However, studies on serum IGF-binding proteins and their activities in dwarf chickens are scarce. These studies would serve the understanding of growth mechanisms, because of important roles of binding proteins for hormonal clearance and actions in the target tissues.

Recently we found that T_4 supplement to propylthiouracil-induced hypothyroid cockerels provoked a marked increase in serum IGF-binding activity (MORISHITA *et al.*, 1991). In view of the hormonal situation of the dwarf chicken, it seems of interest to investigate serum IGF-binding activity in dwarf chickens and its responses to surgical thyroidectomy (Tx) in comparison with normal chickens.

Materials and Methods

One-day-old dwarf (Gifu 20 line) and normal (Gifu 15 line) Rhode Island Red male chicks were reared with free access to a commercial formula feed (21% CP, 2,950 ME/kg) and water in a temperature controlled battery until 4 weeks of age and thereafter in an unheated brooder. At 4 weeks of age birds were weighed and surgically thyroidectomized under pentobarbital (25 mg/kg) anesthesia. The success of surgery was examined at autopsy by gross visual observation and only those birds successfully thyroidectomized were included in the results of experiments. The control group of birds underwent a sham operation. At 6 weeks of age, 14 days after operation, all birds were weighed and then killed to collect blood samples. The blood samples were centrifuged ($600 \times g$, 15 min) after clotting at room temperature and the sera separated and stored at -80°C to await analyses.

Concentrations of serum T_4 , GH and IGF-1 were determined by radioimmunoassays as described before (WAKITA *et al.*, 1991; MORISHITA *et al.*, 1991). Serum IGF-binding activity was determined as described by LEE *et al.* (1989). Serum total proteins and albumin were measured following the methods of LOWRY *et al.* (1951) and DOUMAS *et al.* (1971). Statistical treatment of the results was done by a two-way analysis of variance and significance of differences between means was assessed by Student's *t*-test.

Results

When compared to sham-operated groups, body weights in Tx groups were significantly decreased 2 weeks after the operation. Serum T_4 concentrations were also decreased by Tx in both lines. Despite the presence of a small amount of T_4 in Tx birds, the results may indicate the success of surgery, because of a possible presence of extrathyroidal tissue that produces thyroid hormones (HADDAD and MASHALY, 1989). The dwarf line had a slight, but not significant, lower body weight than the normal line at 6 weeks of age, though 30% reduction in mature dwarf chickens is known (HOSHINO *et al.*, 1992).

Serum GH concentrations in dwarfs tended to decrease following Tx, but those in normals showed a tendency to increase. The responses in serum IGF-1 concentrations to Tx also were reverse in the lines. Serum IGF-binding activity in dwarfs, but not in normals, showed a significant decrease following Tx. Concentrations of serum total proteins in normals were increased by Tx, while there were no significant differences in albumin concentration between control and Tx birds of both lines.

Circulating basal concentrations of GH were significantly higher and those of IGF-1 lower in dwarf birds than in normal birds. Serum basal IGF-binding activity was extremely high in dwarfs. These differences in basal concentrations of GH and IGF-1 and IGF-binding activity between lines disappeared following Tx (Table 1).

Discussion

Circulating concentrations of GH showed a tendency to increase following Tx in

Table 1. Effects of thyroidectomy (Tx) on body weights (BW), serum concentrations of thyroxine (T₄), growth hormone (GH), insulin-like growth factor (IGF)-1, total proteins and albumin, and on IGF-binding activity (IGF-BA) in dwarf and normal cockerels (Mean±SE, n = 5)

	Dwarf		Normal		Analysis of variance		
	Control	Tx	Control	Tx	Strain	Tx	Inter-action
BW : Initial (g)	221±13	224±8	225±5	213±7	NS	NS	NS
Final (g)	423±24	318±15**	461±10	325±20***	NS	**	NS
T ₄ (ng/ml)	11.73±0.67	0.97±0.18***	9.62±0.74	1.88±0.45***	NS	**	**
GH (ng/ml)	174.8±11.7†††	112.0±48.7	70.7±12.3	158.7±76.1	NS	NS	NS
IGF-1 (ng/ml)	2.19±0.96†††	5.03±0.97	20.51±2.59	10.50±2.25*	**	NS	**
IGF-BA (%)	40.3±3.9††	12.5±1.2**	12.0±0.6	12.1±0.8	**	**	**
Proteins (mg/ml)	40.1±1.9	38.0±1.4	36.0±1.1	43.9±2.7*	NS	NS	**
Albumin (mg/ml)	22.2±0.4	22.4±1.0	24.4±1.3	22.9±1.9	NS	NS	NS

* P<0.05, ** P<0.01, *** P<0.001 vs control (Student's t-test)

† P<0.05, †† P<0.01, ††† P<0.001 vs normal (Student's t-test)

NS : not significant (ANOVA), ** P<0.01 (ANOVA)

normal birds, in accordance with the previous finding (HARVEY *et al.*, 1983). This seems highly likely to reflect thyroïdal inhibition of circulating GH concentrations in the fowl, a peculiar effect not observed in mammals (HARVEY *et al.*, 1990). A possible increase in thyrotropin releasing hormone (TRH) following Tx may also be concerned with serum GH levels. However, this trend was not clear in dwarf birds, suggesting a different response in GH secretion to thyroid hormones. A higher basal level of GH in dwarfs may have modified the thyroïdal effect on synthesis, release and clearance rates of GH.

Responses in IGF-1 concentrations and binding activity in dwarfs following Tx also contrast to those in normals in a striking way. Apart from the well recognized low IGF-1 levels in dwarfs (HOSHINO *et al.*, 1982 ; HUYBRECHTS *et al.*, 1985), it should be noted that the basal IGF-binding activity was 3-times higher in dwarfs than in normals, and Tx reduced it to normal levels without notable changes in serum concentrations of total proteins and albumin. Serum IGF-binding activity generally increases when circulating concentrations of IGF-1 are decreased by experimental treatments, such as fasting and hypophysectomy (MORISHITA *et al.*, 1993). Accordingly, the increased basal IGF-binding activity in dwarfs would be attributable to low circulating IGF-1 concentrations.

In the present study, changes in circulating concentrations of IGF-1 and GH following Tx suggest that IGF-1 concentrations are not entirely dependent on GH status. In addition, it is likely that IGF-1 levels as well as GH levels in the circulation are affected by thyroid state, the influence of which is modified by the

presence of dwarfing gene *dw*.

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