REPRODUCTIVE
BIOLOGY

The interaction of the thyroid gland, pineal gland and immune system in chicken

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Received: 7 October 2005; accepted: 15 September 2006

SUMMARY

The interaction of immunological system, thyroid and pineal gland was studied in 5-week old males of *Gallus domesticus*. Several morphometrical parameters in pineal and thyroid glands were measured after bird immunization with human red blood cells and/or treatment with melatonin or seduxen, a melatonin receptor blocker. The peak of the thyroid activity was found on Day 7 after immunization. The immune system appears to directly activate the thyroid gland only in the presence of certain level of melatonin. We suggest that the melatonin mechanism of action includes the enhancement of thyroid gland sensitivity to immune factors. Seduxen prevented the stimulatory influence of the immune system on the thyroid gland. *Reproductive Biology 2006, 6, Suppl. 2:79–85.*
Key words: thyroid gland, immunization, pineal gland, melatonin, seduxen

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INTRODUCTION

Interrelationships of the endocrine, nervous and immune systems attract a lot of scientific attention [3]. Thyroid hormones (thyroxine: T_4; triiodothyronine), in addition to involvement in controlling energy production and protein and carbohydrate metabolism, stimulate the metamorphosis of lower vertebrates, control tissue growth and development, intensify oxidation and heat production as well as influence the functioning of the nervous system. Thyroid hormones also activate components of the immunological system including NK cells, K cells and macrophages [10]. Physiological doses of T_4 (1.4-3 nmol/l) stimulated antibody production by B cells and thymulin synthesis by thymic epithelial cells. The pineal gland, on the other hand, is a neuroendocrine organ that converts external photoperiodic information into an internal hormonal messenger - melatonin, which in an endocrine manner regulates its peripheral targets [11]. It is established that among other numerous actions, melatonin is also an immunomodulator [15]. The purpose of the experiment was to study the interaction between the thyroid and pineal gland during the immune response development, and the effect of melatonin on the functional status of thyroid epithelial cells.

MATERIALS AND METHODS

The experiment was carried out on 192 male 5-week old *Gallus domesticus* which are characterized by the presence of the mature hypothalamic-thyroid axis. Birds were maintained under a 24-h light/dark cycle with lights on/off at 6 pm and 10 am, respectively. The birds were divided into three groups: 1/ control group treated *per os* with placebo; 2/ melatonin group treated *per os* with melatonin (23.5 μg/100 g bw/day); 3) seduxen group treated *per os* with a seduxen, a melatonin receptor blocker (diazepam, 39 μg/100 g bw/day). After one week of the treatment, half of the birds from each group were immunized with human red blood cells (HRBC). Each

bird was i.v. injected with 0.5 ml of 10% HRBC in the middle of the dark phase. The development of the thyroid and pineal gland response to the treatment was measured on Days 1, 3, 7 and 9 after immunization in eight randomly selected birds from each group. Seduxen, a benzodiazepine derivative, melatonin receptor blocker in mammals, was also shown to inhibit the avian pineal gland function [2]. Doses of melatonin and seduxen used in this experiment were based on Shmidt-Nielsen`s study [14] concerning correlations between human and bird metabolism.

Birds were decapitated in the middle of the dark phase. Pineal and thyroid glands were dissected and submitted to the histological procedure. After fixation in the Bouin solution, both glands were dehydrated through a graded series of alcohol and benzol, embedded in paraffin and sectioned at 5 μm. Slides were stained in hematoxiline and eosine [5, 6]. To study the thyroid activity we used the height of secretory epithelium and the diameter of follicles. To evaluate the pineal gland activity, the pinealocyte's nuclear diameter was measured. Student`s t-test was used to determine differences ($p \leq 0.05$) between control and experimental groups.

RESULTS AND DISCUSSION

The significant increase in pinealocyte nuclei diameter was observed on Day 7 post-immunization (fig. 1) suggesting an increase in the biosynthetic activity of the pineal gland. This coincides with the time of immune reaction development described earlier in chickens [7, 8]. Moreover, the results of the experiment (fig. 1) show that the effect of the pineal gland activation by immunization is maintained when birds are treated with seduxen and especially melatonin. Both, melatonin and seduxen treatments did not influence the thyroid gland activity measured by the height of the secretory epithelium (fig. 2). Immunization caused an increase in the secretory epithelium height on Days 7 and 9. The melatonin treatment did not significantly affect the influence of immunization while the seduxen treatment significantly reduced this effect. Similar changes were observed when the

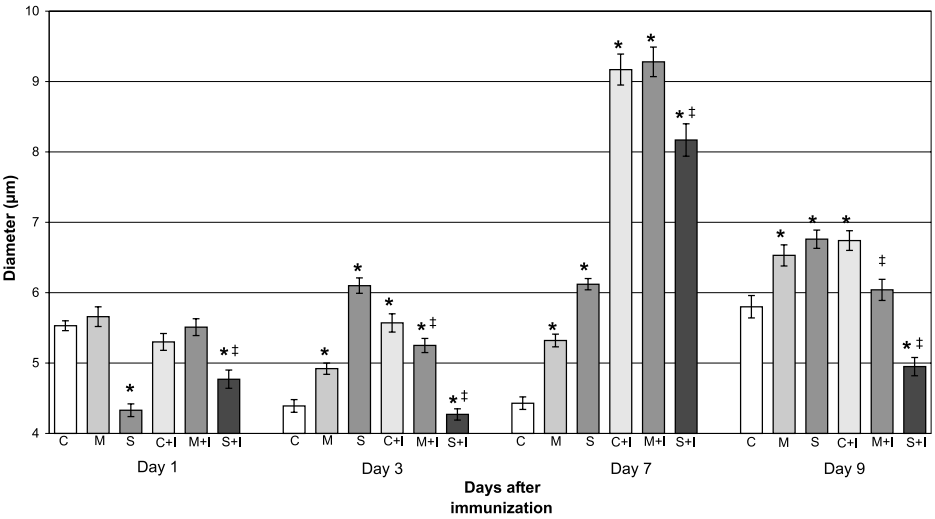

Figure 1. Diameter of pinealocyte nuclei in control (C), melatonin-treated (M) and seduxen-treated (S) male birds (*Gallus domesticus*). After one week of the treatment animals were immunized with human red blood cells (C+I, M+I, S+I groups). Following immunization, melatonin and seduxen treatments were continued for one, three, seven or nine days, and then, the diameters were assessed histologically in birds from each group (n=8 per group). *designates the significant difference compared to corresponding control group (C), ‡designates the significant difference compared to corresponding immunized control group (C+I)

inner diameter of the thyroid follicles was examined. Seduxen treatment reversed the effect of immunization. After melatonin treatment, the stimulatory effect of immunization on the inner diameter of follicles was observed as early as Day 1 (fig. 3).

The thyroid hormones are able to influence the intensity of immune response [1], and cytokines produced by immune cells may directly affect the thyroid gland function [13]. The results presented in this paper are in agreement with this notion. Melatonin usually decreases the thyroid gland activity in mammals [9, 12]. Our results demonstrated that the treatment with exogenous melatonin potentiated the activation of thyroid gland caused by immunization in chickens. Seduxen substantially prevented the activation of the thyroid gland by the stimulated immune system. It is known that seduxen

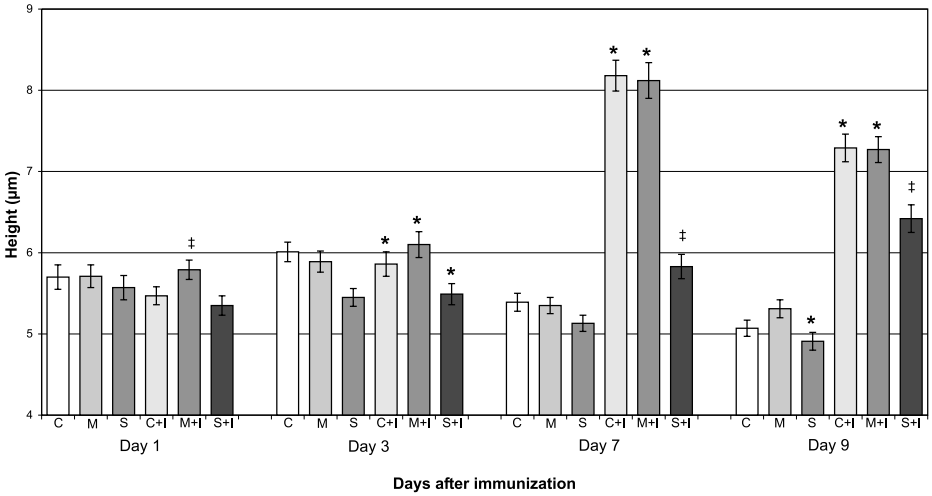

Figure 2. Height of secretory epithelium of thyroid gland in control (C), melatonin-treated (M) and seduxen-treated (S) male birds (*Gallus domesticus*). After one week of the treatment animals were immunized with human red blood cells (C+I, M+I, S+I groups). Following immunization, melatonin and seduxen treatments were continued for one, three, seven or nine days, and then, the diameters were assessed histologically in birds from each group (n=8 per group). *designates the significant difference compared to corresponding control group (C), ‡designates the significant difference compared to corresponding immunized control group (C+I)

is able to influence the sensitivity of target tissues to thyroid hormones [4]. Also there are some reports showing an altered reaction to seduxen in different functional conditions of the thyroid gland [16].

We suggest the following sequence of the interactions of immune system, pineal gland and thyroid gland in immature chickens. Immunization leads to the activation of the thyroid gland. Melatonin does not directly affect the thyroid gland but it increases the thyroid gland sensitivity to the activating influences of the immune system-derived factors. The stimulatory effect of the activated immune system on the thyroid gland is not observed without a certain level of melatonin synthesis in the pineal gland. Thus, the developing immune response also activates the pineal gland. Exogenous melatonin does not change the

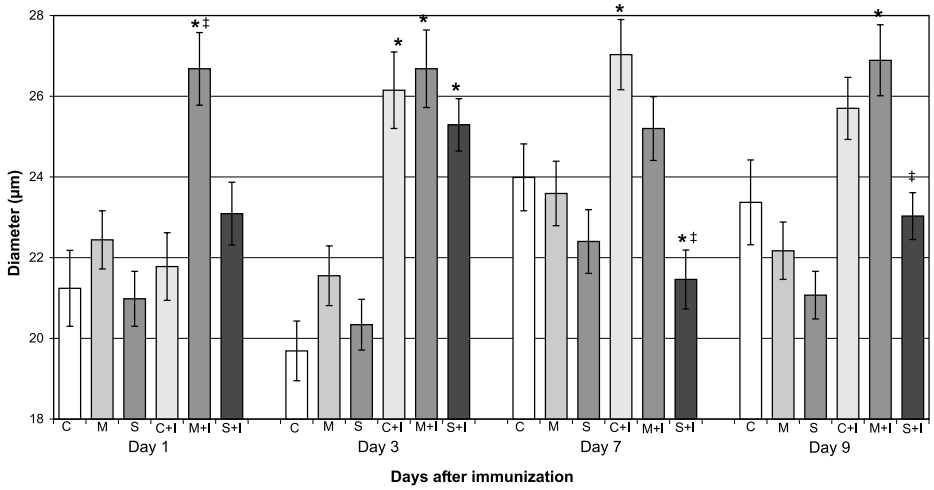

Figure 3. Inner diameter of follicles of thyroid gland in in control (C), melatonin-treated (M) and seduxen-treated (S) male birds (*Gallus domesticus*). After one week of the treatment animals were immunized with human red blood cells (C+I, M+I, S+I groups). Following immunization, melatonin and seduxen treatments were continued for one, three, seven or nine days, and then, the diameters were assessed histologically in birds from each group (n=8 per group). **designates the significant difference compared to corresponding control group (C), ‡designates the significant difference compared to corresponding immunized control group (C+I).

interaction between the thyroid gland and immune system but accelerates the process of the thyroid activation. Seduxen, the melatonin blocker, prevents the stimulatory influence of the immune system on the thyroid gland.

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