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Changes in blood levels of prolactin, growth hormone and immunoglobulins during immune response*

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Objective In this study, in order to establish the relationship between immune system and neuroendocrine system, we aimed to identify the changes on serum prolactin (PRL) and growth hormone (GH) levels during immune response *in vivo*.

Method The study was performed on 32 New Zealand white rabbits. First, the rabbits were divided into two groups. The first group contained 16 rabbits which were immunized by intraperitoneal injection of 5 ml of sheep red blood cells (SRBC) suspension. The other group contained 16 rabbits which were injected 5 ml of saline intraperitoneally. Blood samples that obtained on 3rd, 5th, 7th and 10th days from the rabbits of both two groups were examined. The serum levels of IgG, IgM, prolactin and growth hormone were measured. Then the interactions between the parameters were analyzed.

Results It has been observed that the serum levels (up to twice of normal range) of IgG, IgM in the immunized rabbits were increased when compared to controls ($p<0.01$). Similarly, there has been a statistically significant increase of serum prolactin and growth hormone levels in the immunized group when compared to controls ($p<0.01$),

Conclusion Finally, we came to a conclusion that the cytokines that come into existence by immune response increase serum prolactin and growth hormone levels by affecting the pituitary gland.

Key words Immune response, prolactin and growth hormone.

Introduction

The neuroendocrine and immune system all contribute to maintenance of homeostasis. These systems operate independently to a certain degree, each with their own collection of highly specific cells and regulatory factors. However, they depend on each other for normal development and function (1,2).

Similar studies have demonstrated that the nervous, endocrine, and immune systems are interconnected with each other for normal functioning. The dialog underlying this complex network of communication consists of signalling molecules (hormones, cytokines, interleukins, neuropeptides, neurotransmitters) and their specific receptors (3). For instance, an anterior pituitary hormone, prolactin, affects the activation state of thymocytes and lymphocytes as well as the secretion of the thymic hormone "thymulin". Conversely, cytokines such as interleukin-1 and interleukin-6 (IL-1, IL-6) stimulate the secretion of anterior pituitary hormones and can be produced by non-immune cells including those of the pituitary gland (1,4). Evidence implicating possible roles of PRL or GH in the regulation of the immune system has been reported. Hypophysectomized animals have deficiencies in both cell mediated and humoral immunological functions and either PRL and GH corrects these deficiencies (5).

In this study, the serum PRL and GH levels were determined during the experimental immune response

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Material and Method

Thirty two five months old male New Zealand white rabbits weighing 1400 ± 50 g were used in the study. The animals were placed in an environment 22 ± 3 °C and were given food and water ad lib.

Rabbits were divided into two groups, each consisting of 16 animals. The animals in the first group were immunized by a single intraperitoneal injection of 2,5 x 10^{10} sheep erythrocyte suspension. Non-immunized animals in the second group were given 5 ml of saline (% 0.9 NaCI) alone.

The animals in two groups were taken 2 ml of blood samples intracardiacally on 3rd, 5th, 7th and 10th days under 25 mg/kg of ketamine anesthesia. Serum samples were stored at -20 °C .

PRL and GH levels were determined by chemiluminescent enzyme immunoassay method, using "Immulite Hormone Analyzer". Ig G and Ig M levels were measured by using "Turbox Analyzer" (Orion Diagnostica). Liquid-phase immunoprecipitation determination in serum was performed by nefolometric method.

Results were expressed as mean ± SEM. Student's t test and correlation analysis test were used with computer statistical program of SPSS for windows in the study.

Results

A significant increase was observed in serum Ig M and Ig G levels of immunized group as compared to controls (Fig.1-2) ($p<0.01$). And also, a significant increase was observed in serum GH and PRL levels of immunized group as compared to controls (Fig.3-4) ($p<0.01$). There was a positive correlation between the increase in Ig G and GH levels in immunized group ($r = 0.95$, $p<0.01$). And, a positive correlation was found between the increase in Ig G and PRL levels in immunized group ($r = 0.86$, $P<0.01$). There was a positive correlation between the increase in Ig M and PRL levels in immunized group. ($r = 0.50$, $p<0.05$). But, a negative correlation was found between the increase in IgM and GH levels in immunized group ($r = 0.86$, $P<0.01$).

The ımmunoglobulin levels have been shown in Table I and serum levels of PRL and GH have been shown in Table II. And also, correlation coefficients were shown in Table III.

Table I. The serum levels of IgM and IgG in immunized and control groups.

	IgM (g/l) n=16		IgG (g/l) n=16	
Days	Control	Immunized	Control	Immunized
3	0.58±0.10	1.13±0.10*	7.43±1.07	11.00±0.98*
5	0.50±0.08	1.43±0.10*	7.05±0.65	13.85±1.11*
7	0.48±0.13	1.88±0.10*	7.10±0.88	19.58±0.83*
10	0.50±0.08	1.38±0.15*	6.00±1.01	23.98±1.45*

(*:p<0.01)

Table II. The serum levels of prolactin and growth hormone in immunized and control groups.

	Growth h. (ng/ml) n=16		Prolactin (ng/ml) n=16	
Days	Control	Immunized	Control	Immunized
3	9.48±0.54	12.00±0.70*	5.68±0.38	6.13±0.61*
5	10.13±0.94	14.47±0.40*	5.25±0.13	18.03±0.54*
7	8.85±0.59	16.45±0.66*	6.15±0.13	18.90±1.02*
10	9.52±0.48	20.10±1.63*	6.35±0.39	24.35±0.65*

(*:p<0.01)

Table III. Correlation coefficients of immunized group.

	GH	PRL	İgG	İgM
GH	1			
PRL	0.897**	1		
İgG	0.949**	0.862**	1	
İgM	0.306	0.501*	0.442	1

**:p<0.01 *:p<0.05

Discussion

Cytokines, leukocyte derived peptides, influence pituitary hormone release.The immune system influence the endocrine system, since individuals lacking thymus have a number of endocrine system imbalances. The involvement of anterior pituitary hormones with the immune system had its beginnings from observation in hypophysectomized animals and in animals and humans with deficiencies in anterior pituitary hormones (5-7). One of the earliest known indications that pituitary hormones regulate the immune system stems Smith's original observations (8) that in hypophysectomized rats, the thymus gland is atrophic .

Edward et al. (9) reported that IL-1 acted directly on pituitary cells to stimulate the release of ACTH , LH, TSH, and GH while simultaneously inhibiting the release of PRL . Although IL-1 appears to act directly on pituitary cells, it is also possible that it may act indirectly on pituitary secretion through hypothalamic factors.

It has been shown that intravenously administered IL-6 increased the plasma level of PRL, and decreased the levels of FSH and LH (10).

PRL and GH can both serve as an immunomodulatory factors. It has been shown that PRL treatment stimulated thymulin release by the thymic epithelium. In contrast, suppression of PRL release by bromocryptine, a drug that specifically blocks PRL release, (a dopaminergic receptor agonist) evoked a significant reduction in the circulating levels of thymulin. GH also stimulated the release of thymulin by thymic epithelial cells *in vitro* (11). It was reported that an extract of bovine thymus, thymosin fraction 5, stimulated the release of PRL and GH (11,12).

In addition to thymic factors, Basedovsky et al. reported that immunization of animals with SRBC resulted in increased antibody and serum corticosterone concentration caused an increase in serum IL-1 levels (13).

Specific receptors for IL-1 and IL-6 are found in the anterior pituitary and the IL-6 receptor m RNA is also localized to the dorsomedial and ventromedial portions of the hypothalamus.

In this study , the IgG levels indicate the occurrence of immunization after SRBC injection. There were significant changes in serum GH and PRL levels during immune response in the animals. The maximum increase in serum GH and PRL levels occurred on day 10^{th}. The Table II demonstrates a four fold increase in serum PRL and a two fold increase GH levels as compared to controls .

Dougles and et al. (14) reported that mononuclear leukocytes could synthesize and secrete GH releasing hormone (GHRH) in vitro. It is similar to hypothalamic GHRH in terms of bioactivity, antigenicity, and molecular weight. Their findings dmonstrate a potencial regulatory loop between the immune and neuroendocrine tissues.

There were a statistically correlation between IgG and hormone levels in this study. Our study has shown that in the course of immune response to SRBC in rabbits, major changes occurred in the blood levels of GH and PRL . Thus, PRL and GH release are activated during immune response via cytokines released by immune cells. In the light of these findings, it can be said that immune system can influence neuroendocrine function via the cytokines such as IL-1 and IL-6 . Hypothalamic and pituitary receptors may also play an important role in this effects. Also, we can say that the immune and hormonal change during immune response may also be very important in immunoregulation. From the evidence available, it is apparent that PRL and GH have an important function in the immune system and future investigations should be directed toward elucidating their sites of action.

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