EXPERIMENTAL METHODS FOR CLINICAL PRACTICE

Changes in Thymosin-α_1 Content in Patients with Nonspecific Gynecologic Diseases Depending on Inflammation Type and Efficacy of Antiinflammatory and Immunomodulating Therapy

A. V. Shurlygina, G. I. Litvinenko, T. I. Dergacheva, and V. A. Trufakin*

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Plasma content of thymosin-α_1 and its circadian variations in patients with inflammatory gynecologic diseases differ from those in healthy donors and depend on the type of inflammation and efficacy of treatment. It is concluded that not only the absolute content of thymic hormones, but also their biorhythmic variations are important for immune regulation.

Key words: *biorhythms; inflammation; thymic hormones*

Thymosin-α_1 belongs to the family of thymic immunoregulatory peptides controlling T cell differentiation, cytokine production, and activation of antiviral, antimycotic, and antitumor immunity [7,9,13,15]. Changes in the production and/or plasma concentration of this factor negatively influence some stages of T cell differentiation both in the thymus and peripheral organs and impair T-cell immunity. Changes in plasma thymosin-α_1 content usually accompany tumor growth, acute radiation sickness, and aging [1,6,12].

Nonspecific inflammatory diseases of the uterus and adnexa are usually accompanied by secondary immunodeficiency correlating with the type, stage, and severity of the inflammation [3]; T cell response is often impaired.

In this connection, it is of interest to study endocrine function of the thymus in different types of inflammation and against the background of antiinflammatory and immunomodulating therapy.

Institute of Clinical and Experimental Lymphology; *Institute of Physiology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk. ***Address for correspondence:*** A.V.Shurlygina@iph.ma.nsc.ru. Shurlygina A. V.

MATERIALS AND METHODS

Fifteen healthy donors, 30 patients with acute salpingitis, and 30 patients with chronic salpingitis were included in the study. Laboratory tests and physical examination were performed in all women. In some cases, laparoscopy, ultrasound investigation of the small pelvis, and cytomorphological examination of cervical and vaginal smears were performed, immune and endocrine status and lymphocyte sensitivity to thymic immunomodulators were additionally evaluated [5]. Antiinflammatory, antibacterial and immunomodulating drugs were administered according to standard schemes. Treatment efficacy assessed by clinical and laboratory parameters was expressed in terms of recovery, improvement, or no effect [3].

Plasma thymosin-α_1 was measured by radioimmunoassay [1]. Taking into account diurnal fluctuations of thymic endocrine function [10], the blood was collected twice a day (at 8.00 and 20.00).

The data were processed statistically using nonparametric Wilcoxon—Mann—Whitney test.

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RESULTS

In healthy donors plasma content of thymosin-α_1 showed moderate but significant diurnal fluctuation: it was 1.58±0.03 μg/ml in the morning and 1.85±0.04 μg/ml in the evening ($p<0.05$).

In patients with acute salpingitis similar biorhythms were observed but both the morning and evening concentrations of the peptide increased compared to the corresponding values in donors. During acute inflammation, variations in thymosin-α_1 level became more pronounced than in donors.

In patients receiving antiinflammatory therapy, blood concentration of thymosin-α_1 and its diurnal fluctuations correlated with the efficacy of treatment: recovery and significant improvement was associated with an increase in peptide content and high diurnal variability of this parameter, while inefficient treatment was attended by smoothening of diurnal fluctuation due to decreased evening concentration of thymosin-α_1 (Fig. 1, *a*).

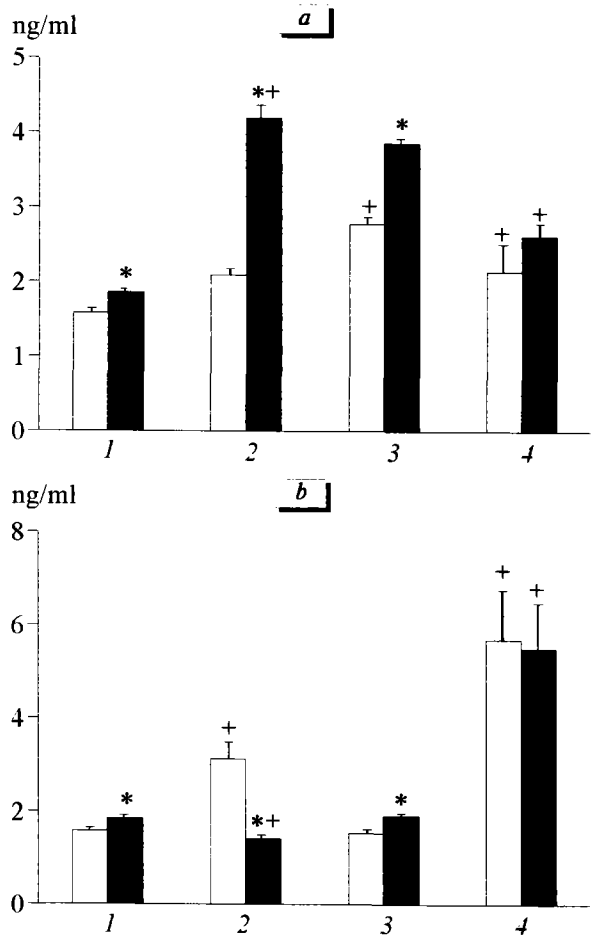

Fig. 1. Diurnal rhythms of plasma thymosin-α_1 in healthy women and patients with acute (*a*) and chronic (*b*) inflammatory gynecologic diseases. Light bars: 8:00; dark bars: 20:00. Donors (*1*) and patients before treatment (*2*), after effective (*3*), and ineffective treatment (*4*). *$p<0.05$ compared to morning indices, +$p<0.05$ compared to donors.

Inverted diurnal variations were observed during relapse of chronic salpingitis with high morning and low evening concentrations of thymosin-α_1.

After complete recovery without relapses, the plasma content of thymosin-α_1 and its diurnal variations returned to normal, with higher levels in the evening and lower in the morning ($p<0.05$). Ineffective treatment nullified diurnal changes and increased plasma levels of thymosin-α_1 both in the morning and in the evening (Fig. 1, *b*), which probably reflected persistent inflammation and deterioration of the immune status [3].

Thus, our findings indicate that impaired endocrine function of the thymus is a possible pathological mechanism underlying transitory immunodefficiency in acute or chronic inflammatory diseases of the uterus and adnexa. Abnormal levels of thymosin-α_1 can result from ovarian hypofunction during inflammation and shifts in the pituitary hormones (prolactin, adrenocorticotropic, and follicle-stimulating hormones) [2, 8,14]. This assumption in confirmed by published data on close interaction between the hypothalamic-pituitaryl-ovarian and hypothalamic-pituitary-thymic endocrine axes [4,11].

Immunodefficiency in gynecologic patients [3] is associated with increased levels of thymosin-α_1. This can be due to disturbed lymphocyte response to thymus-derived regulatory factors [5].

It can be concluded that circadian variations are the marker of favorable prognosis even when plasma content of thymosin-α_1 is changed. In patients with restored diurnal plasma thymosin-α_1 variability (effective treatment), immune reactivity and endocrine parameters also rapidly restored after treatment [3]. This implies that not only the content of thymic hormones but also their normal biorhythmic variations are critical for effective immune regulation.

REFERENCES

1. I. M. Belyakov, A. A. Yarilin, and V. Yu. Arshinov, *Byull. Eksp. Biol. Med.*, **113**, No. 5, 30-33 (1992).
2. I. G. Vorona and A. S. Bergman, *Hormonal Homeostasis in Patients with Nonspecific Salpingo-Oophoritis* [in Russian], Riga (1990).
3. T. I. Dergacheva, *Reactivity in Patients with Nonspecific Inflammatory Diseases of the Uteris*, Abstract of Doct. Med. Sci. Dissertation, Novosibirsk (1996).
4. E. A. Korneva and E. K. Shkhinek, *Hormones and Immune System* [in Russian], Leningrad (1988).
5. V. A. Trufakin, A. V. Shurlygina, T. I. Dergacheva, and G. I. Litvinenko, *Byull. Eksp. Biol. Med.*, **119**, No. 2, 181-183 (1995).
6. J.-F. Bach, M. Dardenne, J. M. Pleau, and J. Rosa, *C. R. Acad. Sci.*, **283**, 1605-1607 (1976).
7. C. A. Baumann, M. Badamchian, and A. L. Goldstein, *Mech. Ageing. Dev.*, No. 1-3, 85-101 (1997).

8. J. S. Berek and Ph. D. Darney, *Obstet. Gyn.*, **54**, No. 4, 490-492 (1989).
9. A. P. Knutsen, J. J. Freeman, K. R. Mueller, *et al.*, *Int. J. Immunopharmacol.*, **21**, No. 1, 15-26 (1999).
10. J. P. McGillis, N. R. Hall, and A. L. Goldstein, *J. Immunol.*, **131**, No. 1, P. 148 (1983).
11. G. Renoux, *Biomed. Pharmacother.*, **37**, No. 9-10, 433-440 (1983).
12. H. Sasaki, Y. Fujii, A. Masaoka, *et al.*, *Eur. J.Cardiothorac. Surg.*, No. 6, 885-910 (1997).
13. S. A. Serrate, R. S. Schulof, and L. Leonardis, *J. Immunol.*, **139**. 2338-2343 (1987).
14. Y. Yoshimura, M. Jinno, T. Oda, *et al.*, *Biol. Reprod.*, No. 6,1223-1230 (1994).
15. M. M. Zatz, J. Oliver, and C. Samuels, *Proc. Natl. Acad. Sci. USA.*, **81**, 2882-2885 (1984).