EXPERIMENTAL BIOLOGY

Circadian and Seasonal Variations in Blood Lymphocyte Dehydrogenase Activities in Women with Secondary Immunodeficiency and Acute Nonspecific Gynecological Inflammations

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

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 124, No. 5, pp. 576-578, May, 1998
Original article submitted July 3, 1997

Development of secondary immunodeficiency in patients with acute nonspecific inflammatory diseases of the uterine appendages is associated with disorders in chronobiological characteristics of energy metabolism in blood lymphocytes. The differences in the enzyme activities in patients and donors are observed in the evening during all seasons of the year; seasonal variations are typical only of the morning enzyme spectrum.

Key Words: *dehydrogenases; lymphocyte; biorhythms; gynecological inflammations*

Functional activity of immunocompetent cells is closely related to metabolic processes in them and, specifically, energy metabolism [3]. Activities of enzymes responsible for the redox reactions is in many cases highly informative for the diagnosis of immunopathology [4]. There are reports on the biorhythms of lymphocyte population and subpopulation structures and their functional and metabolic parameters [1,6,12]. Chronobiological characteristics are known as the first parameters that change in immune dysfunctions [9]. Development of acute nonspecific gynecological inflammations (AGI) involves T cell immunodeficiency and disorders of the redox enzyme reactions in blood lymphocytes in response to hormonal immunomodulators [8]. However, there are no reports about time regularities in changes of energy metabolism of immunocompetent cells in such diseases. We investigated circadian and seasonal fluctuations in the activities of succinate, lactate, and α-glycerophosphate dehydrogenase (SDH, LDH, and GPDH, respectively) in blood lymphocytes of women with acute nonspecific inflammations of the uterine appendages.

Institute of Clinical and Experimental Lymphology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk

MATERIALS AND METHODS

Twenty-seven healthy women aged 25-40 years and 28 patients with acute nonspecific salpingitis and salpingo-oophoritis were examined in winter (January-February), spring (April-May), and autumn (October-November). Blood was collected from the ulnar vein 2 times a day: at 8:00 and 20:00. Blood smears were prepared on slides, fixed in 60% acetone at 4°C, and stained for SDH, LDH, and GPDH as described previously [2] using n-nitroviolet tetrazolium. Formazan granules were counted per 30 lymphocytes in each smear and the mean number of granules per lymphocyte was calculated. Results were statistically processed using Wilcoxon—Mann—Whitney's test. The relationship between time of the day and season and the enzyme activities was assessed using multifactorial analysis of dispersions.

0007-4888/98/0005-0511$20.00

RESULTS

In winter the differences between the morning and evening activities of the studied enzymes were more expressed in patients with AGI (Fig. 1). This may indicate a higher degree of synchronization of circadian biorhythms of lymphocyte energy metabolism in this condition. Presumably, it reflects a certain strain of metabolic processes in immunocompetent cells, which is associated with immunodeficiency [7]. Lymphocyte dehydrogenase activities of patients and donors were different only in the evening. In the patients LDH activity was decreased, while GPDH increased at this time of the day in comparison with donors (Fig. 2). LDH is an anaerobic hydrolysis enzyme, most often representing a compensatory reaction in lymphocytes aimed at production of extra energy equivalents [10]. Therefore, the development of secondary immunodeficiency may involve a decrease in the compensatory potential of immunocompetent cells, which can be a pathogenetic mechanism of their dysfunction.

In spring, the differences in the morning and evening activities of SDH and LDH were observed in 50% of both patients and donors (Fig. 1). The mean activities of the studied enzymes were almost the same in patients and donors during this season. Therefore, in spring the enzyme spectrum of immunocompetent cells of healthy women and AGI patients was the same by its chronobiological characteristics and by the mean activities of dehydrogenases. This may be explained by seasonal desynchronosis of metabolic processes [5,11] leveling the deviations which develop in disease.

In the fall, significant differences between the morning and evening levels of SDH were observed in 25% healthy women and patients. For LDH, there were less shifts in the patients, while for GPDH more shifts in the patients than in donors (Fig. 1). The evening activities of GPDH in the patients were increased in comparison with healthy women (Fig. 2).

Significant seasonal differences in the morning values of metabolism were detected in the patients. LDH and GPDH activities reached the maximum in spring and decreased in autumn and winter (Fig. 3). This may be a mirror reflection of the spring increase in the intensity of compensatory reactions [10] in comparison with other seasons of the year, when a lower activity of LDH may indicate increased strain of intracellular metabolic processes in lymphocytes, associated with seasonal features of an inflammatory process.

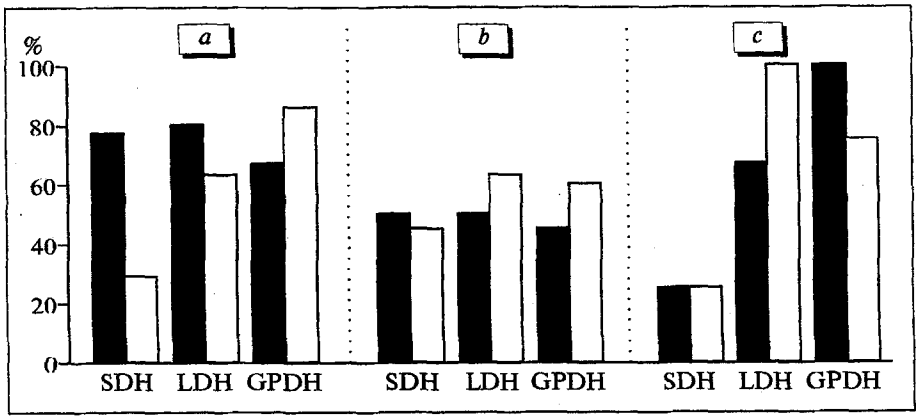

Fig. 1. Percentage of women with significant circadian variations of blood lymphocyte dehydrogenase activities. Here and in Fig. 2: *a*) winter; *b*) spring, *c*) autumn. Dark bars: patients; light bars: donors. Here and in Figs. 2 and 3: SDH) succinate dehydrogenase; LDH) lactate dehydrogenase, GPDH) α-glycerophosphate dehydrogenase.

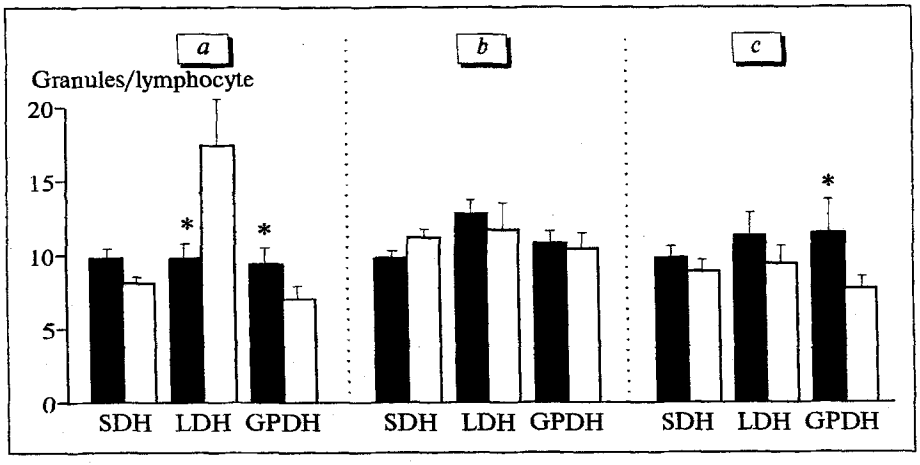

Fig. 2. Evening values of enzyme activities in different seasons of the year in donors and patients with acute nonspecific gynecological inflammations. Here and in Fig. 3: Ordinate: mean number of formazan granules per lymphocyte. *$p<0.05$ *vs.* donors.

Multifactorial analysis of dispersions showed that SDH activity depended on the time of the day both in donors and patients during all seasons at values lower than 0.001: evening activity of the enzyme in AGI (9.82±0.29 granules/lymphocyte) was higher than the morning value (9.47±0.23 granules/lymphocyte). In donors the relationship was opposite: SDH activity was higher in the morning than in the evening during all seasons (9.96±0.29 and 9.16±0.18, respectively).

Thus, chronobiological parameters of redox metabolism in peripheral blood lymphocytes are disordered in patients with AGI associated with T cellular immunodeficiency: circadian variations in the activities of all studied dehydrogenases and inversions in circadian fluctuations of SDH are more frequent. The differences in the studied parameters between donors and patients depend on the season of the year and time of the day. Chronobiological approach to examination of patients is recommended for obtaining more information about the status of energy metabolism in lymphocytes.

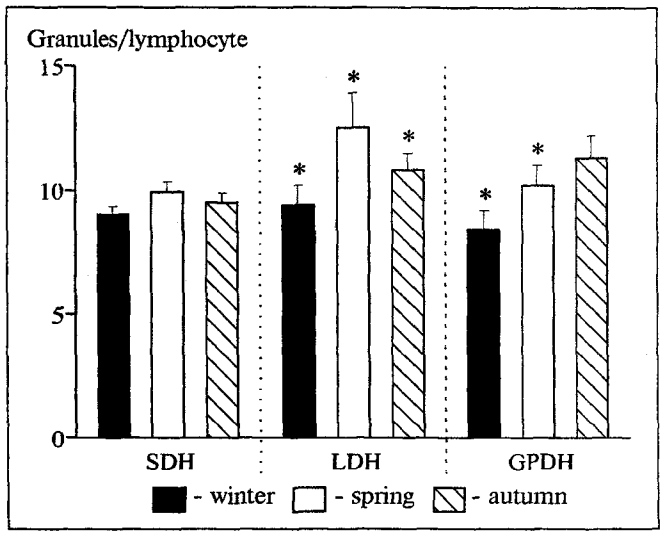

Fig. 3. Morning values of enzyme activities in different seasons of the year in donors and patients with acute nonspecific gynecological inflammations. *$p<0.05$ differences between enzyme activities in different seasons.

REFERENCES

1. N. F. Gamaleya, E. D. Shishko, N. A. Kosinskaya, and A. P. Chernyi, *Immunologiya*, No. 1, 21-22 (1990).
2. R. P. Narcissov, *Arkh. Anat.*, No. 5, 85-91 (1969).
3. A. V. Osipenko and E. B. Makarova, *Byull. Eksp. Biol. Med.*, **120**, No. 9, 310-312 (1995).
4. M. V. Robinson, *Morpology and Cytochemistry of Lymphocytes in Health, Destabilizing Exposures, and Autoimmune Processes and Diseases* [in Russian], Abstr. DSci Thesis, Novosibirsk (1994).
5. I. A. Sapov and V. S. Novikov, in: *Nonspecific Adaptations of Man. Ann. Leningrad Ist Medical Institute, Lenigrad* (1994), pp. 61-81.
6. K. S. Sof'in and K. A. Kuz'mina, in: *The Time Factor in Functional Organization of Live Systems Activity* [in Russian], Leningrad (1980), pp. 98-100.
7. S. I. Stepanova, *Biological Aspects of Adaptation* [in Russian], Moscow (1986).
8. V. A. Trufakin, A. V. Shurlygina, T. I. Dergacheva, and G. I. Litvinenko, *Byull. Eksp. Biol. Med.*, **119**, No. 2, 181-183 (1995).
9. A. V. Shurlygina and V. A. Trufakin, *Vestn. Rossiisk. Akad. Med. Nauk.*, No. 8, 39-42 (1993).
10. V. Geepen, J. J. Legros, P. Franchimont, *et al.*, *Ann. N. Y. Acad. Sci.*, **496**, 55-66 (1987).
11. H. Komada, H. Nakabayachi, T. Voshida, *et al.*, *J. Interdiscip. Cycle Res.*, **20**, No. 2, 107-112 (1989).
12. A. Reinberg, in: *Biological Rhythms and Medicine. Cellular, Metabolic, Physiopathologic, and Pharmacologic Aspects.* Eds. A. Reinberg and M. H. Smolensky, New York (1983), pp. 211-265.