EXPERIMENTAL BIOLOGY

Functional Insufficiency of the System Responsible for Reactive Oxygen Species Generation by Blood Neutrophils

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 132, No. 8, pp. 230-231, August, 2001
Original article submitted June 19, 2001

We studied functional activity of the system responsible for generation of reactive oxygen species by blood neutrophils and involved in pathophysiological mechanisms of bronchopulmonary diseases. Insufficiency of this system can be classified as relative, latent (type I and II), and severe.

Key Words: *reactive oxygen species; neutrophils*

Our previous studies revealed changes in the basal and zymosan-induced luminol-dependent chemiluminescence (LCL) in individuals occupationally exposed to ozone. These changes attested to functional disturbances in the system responsible for generation reactive oxygen species (ROS) by blood neutrophils [1]. Here we studied functional insufficiency of this system in patients with chronic bronchitis (CB) exposed or not exposed to ozone, a modulator of free radical oxidation.

MATERIALS AND METHODS

We examined 196 patients with CB (during remission) employed in plastic industry and occupationally exposed to ozone in a concentration of 0.10-0.23 mg/m^3. Prebronchitis (PB), chronic nonobstructive bronchitis (CNB), and chronic obstructive bronchitis (COB) were found in 48, 82, and 66 workers, respectively. The duration of service was more than 2-10 years. Seventy-five patients with PB (n=26), CNB (n=26), and COB (n=23) not exposed to ozone comprised the control group.

Generation of ROS by neutrophils was evaluated by the intensity of LCL. To this end, luminol in a final concentration of 10^{-5} M was added to the whole blood (0.1 ml) stabilized with 20 U/ml heparin, and the volume was adjusted to 1 ml with Hanks solution. LCL induced by 2 mg/ml zymosan was measured on a KhL-003 chemiluminometer [3]. The leukocyte activation coefficient (AC) was calculated as the ratio between zymosan-induced and spontaneous LCL [2]. The results were processed using Student—Fisher reliability test. The differences were considered reliable at $p<0.05$.

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RESULTS

We proposed the following classification of disturbances in the system of ROS generation by blood neutrophils: relative, type I and II latent, and severe functional insufficiency (Table 1).

In workers with PB spontaneous LCL increased by 67%, zymosan-induced LCL did not differ from normal, and leukocyte AC decreased 1.8-fold (relative ROS insufficiency). In patients with PB not exposed to ozone spontaneous LCL slightly increased, zymosan-induced LCL did not differ from normal, and AC decreased by 1.2 times. Therefore, these patients also had relative ROS insufficiency. These results attest to nonspecific functional disturbances in the system of ROS generation in patients with PB exposed and not exposed to ozone.

In workers with CNB spontaneous LCL did not differ from the control, while zymosan-induced LCL and leukocyte AC decreased by 54% and 2.8 times, respectively. Changes in the spontaneous and zymo-

0007-4888/01/1322-0809$25.00

TABLE 1. Types of Functional Disturbances in the System of ROS Generation in Blood Neutrophils

Type of ROS insufficiency	LCL intensity		Leukocyte AC
	spontaneous	zymosan-induced	
Relative	Above normal	Above normal or normal	Below normal
Latent			
type I	«	Below normal	«
type II	Normal	«	«
Severe	Below normal	«	«

san-induced LCL depended on the duration of service. Spontaneous LCL increased by 70-260% over the first 5 years of exposure to ozone, did not differ from the control after 6 years, but decreased by 34-80% in individuals employed for 7 years. The intensity of zymosan-induced LCL progressively decreased with an increase in the duration of service (by 48 and 94-95% after ozone exposure for 3 and more than 8 years, respectively). In individuals employed for 3-4 and 4-5 years leukocyte AC decreased by 3.1-3.2 and 6.0-7.8 times, respectively. Thus, individuals employed for 3-5 and 7-10 years were characterized by type I latent and severe ROS insufficiencies, respectively. In patients with CNB spontaneous LCL increased by 126%, zymosan-induced LCL did not differ from normal, and leukocyte AC decreased by 2 times. Thus, these patients were characterized by relative ROS insufficiency. In workers with CNB spontaneous LCL decreased by 25-82% independently on the duration of employment. These changes were most pronounced 8 years or more after entering employment. In these workers zymosan-induced LCL and leukocyte AC decreased by 90-97% and 6.7 times, respectively. Therefore, they were characterized by severe ROS insufficiency.

In patients with COB spontaneous LCL increased by 219%, while zymosan-induced LCL and leukocyte AC decreased by 42% and 5.6 times, respectively (relative ROS insufficiency). Therefore, individuals with COB exposed and not exposed to ozone are characterized by specific changes in the system of ROS generation. Our results indicate the development of functional disturbances in the system of ROS generation in workers with CB. The degree of ROS insufficiency in employers increased with increasing in the severity of CB. The type of ROS insufficiency depended on the duration of ozone exposure. It should be emphasized that functional disturbances in the system of ROS generation in employers were more pronounced than in patients not exposed to ozone. These results indicate that CB in workers exposed to ozone should be considered as an occupational lung disease.

This classification of ROS insufficiency reflects functional activity of the system responsible for ROS generation by blood neutrophils and involved in the pathogenesis of various diseases.

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