THE FEATURES OF DEXAMETHASONE-INDUCED LYMPHOCYTE APOPTOSIS IN PATIENTS WITH DIFFERENT CONTROLLABILITY OF BRONCHIAL ASTHMA

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Abstract. The *aim* of this study was to investigate the characteristics of peripheral blood- lymphocyte (Lph) apoptosis induced by dexamethasone in patients with controlled and uncontrolled course of bronchial asthma (BA). *Materials and research methods.* 54 BA patients were examined, including 22 with controlled BA and 32 patients with uncontrolled BA. The control group was formed of 11 volunteers — individuals without clinical signs of infectious and somatic pathology (conditionally healthy). The determination of Lph apoptosis induced by dexamethasone was carried out by 48-hour incubation of heparinized blood in RPMI medium with L-glutamine, HEPES (GIBCO) and gentamicin in the presence of 0.4 μg / ml and 4.0 μg / ml of dexamethasone and T-cell mitogen – phytohemagglutinin, which was used to activate Lph. Apoptotic Lph were detected by their staining with Anexin-5 conjugated with fluorescein isothiocyanate and 7-amino-Actinomycin-D with sample cytometry followed. The percentage of lymphocytes with early, with early and late and late signs of apoptosis, the total indicators of early and late apoptosis, and the integral indicator of lymphocyte apoptosis were determined. Also, the frequency and severity of these indicators changes (increase / decrease) were calculated. In order to study the dependence of Lph apoptosis on the dose of dexamethasone, the ratio of Lph apoptosis induced by 4.0 μg / ml and 0.4 μg / ml of dexamethasone was evaluated, and if this ratio was > 1.0 the increase of Lph apoptosis induction by elevated dexamethasone dose was determined and if this ratio was > 1 0, the absence / attenuation of higher then therapeutic dose of dexamethasone Lph apoptosis induction was determined. *Results.* A 2.8-fold increase of the average value of the integral indicator of Lph dexamethasone-induced apoptosis in the group of patients with controlled asthma was revealed mainly due to its early stages and the absence of these changes in the group of patients with an uncontrolled course of the disease was shown. It was demonstrated that the adaptive enhancement of Lph apoptosis induced by a therapeutic dose of dexamethasone (0.4μg/ml) was occurred in 54.5 % of patients with controlled BA by an average of 151.9 %, whereas in uncontrolled BA it occurred only in 31.3 % of patients, and its severity was in 2.6 times less (58.8 %). It was established that the absence of increased Lph apoptosis induced by this dexamethasone dose was found in 45.5 % patients with controlled asthma and in 69.7 % of patients with its uncontrolled course, which may indicate that they have steroid resistance. It was detected that a 10-fold increasing of the therapeutic dexamethasone dose in 72.7 % patients with controlled asthma is not accompanied by increasing of Lph apoptosis which suggests that they receive the most effective doses of glucocorticosteroids (GCS), and therefore their further increase is not advisable. At the same time, near 2/3 of patient with uncontrolled BA demonstrate Lph apoptosis increasing with higher doses of GCS for its induction, which is typical for steroid-sensitive and steroid-dependent patients. *Conclusions.* In every third patient with an uncontrolled BA the increase of GCS dose does not lead to increasing of Lph apoptosis that can testify to steroid resistance and be considered such an indication for the targeted drugs appointment.
Key words: bronchial asthma, controllability, dexamethasone-induced lymphocyte apoptosis.

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