BRONCHIAL ASTHMA AND ENDORPHINS

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Endorphins are neuropeptides which act on opiate receptors. Besides β-endorphin, α- and γ-endorphins, which are fragments 1-16 and 1-17 of β-endorphin, are formed from pro-opiomelanocortin [2, 3, 6, 8].

Dexamethasone inhibits formation of the mRNA which codes pro-opiomelanocortin [4]. It has shown that expression of the pro-opiomelanocortin gene and, consequently, secretion of endorphins are inhibited by corticosteroid hormones of the adrenals [4, 5]. Meanwhile the high therapeutic effect of corticosteroids in terminating severe attacks of asthma is well known. Attacks of bronchial asthma are a stress reaction, and it can be postulated that this state may be reflected in body endorphin levels.

The aim of this investigation was to study plasma concentrations of α-, β-, and γ-endorphins in patients with bronchial asthma and their dependences on clinical manifestations and the severity of the disease, and also to study the effect of dexamethasone on blood levels of these peptides.

EXPERIMENTAL METHOD

Twenty patients with bronchial asthma (10 women and 10 men) underwent general clinical and allergologic investigations and function testing at the Clinical Department of the Institute of Immunology, Ministry of Health of the USSR. The patients' ages ranged from 14 to 54 years. The control group consisted of healthy subjects (12 men and 6 women) aged from 18 to 37 years.

Blood samples (10 ml) were taken from the cubital vein into a test tube containing 0.2 ml of 0.5M EDTA and centrifuged at 1500 rpm and 0°C. The plasma was treated with 2-mercaptoethanol up to a final concentration of 0.1% and kept at −70°C.

Concentrations of α- and γ-endorphins in the plasma were determined by radioimmunoassay [1]. The β-endorphin concentration was determined by means of kits from the firm DRg.

EXPERIMENTAL RESULTS

On the basis of the results of the general clincial and allergologic investigations and function tests, a noninfectious-allergic form of bronchial asthma was diagnosed in 7 patients, an infectious-allergic form in 9, and a mixed form in 4 patients; six patients were in a phase of remission, 7 in a phase of moderately severe clincial manifestations, and 7 in a phase of exacerbation of the disease. Blood for assay of α-, β-, and γ- endorphins was taken from 6 patients between attacks, from 7 patients during a mild attack, from 4 during a moderately severe attack, 2 patients after a severe attack had been termined by corticosteroids, and one patient at the height of a severe attack.

In the infectious-allergic form of bronchial asthma during a remission, no significant change in the α-endorphin concentration was found compared with the control. In the atopic

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TABLE 1. Concentration of Endorphins (in pmoles) in Patients with Infectious-Allergic and Atopic Forms of Bronchial Asthma

Form of bronchial asthma	Type of endorphin	Normal	Remission	Clinical manifestations			
				Mild	Moderately severe	At height of attack	After administration of corticosteroids
Infectious-allergic	α	224±32 (n=18)	234±17 (n=2)	300±24 (n=4)	356±14 (n=2)	571 (n=1)	37±8 (n=2)
	γ	11±1	27,1±13	15±4,3	10,4±2	34	7,4±0,5
	β	6	2 (n=1)	4,5±1 (n=4)	5 (n=1)	7 (n=1)	1±1 (n=2)
Atopic	α	224±32 (n=18)	139±39 (n=4)	274±19 (n=3)	471±14 (n=2)	—	—
	γ	11±1	12,4±3	16,9±3	14,3±9	—	—
	β	6 (n=18)	0,5±0,3 (n=2)	8,3±3,9 (n=3)	9,5±4 (n=2)	—	—

form of bronchial asthma the α-endorphin concentration was a little lower than in the control. For instance, during a remission it was 139 ± 37 pmoles (224 ± 32 pmoles in the control). In the infectious-allergic form of bronchial asthma during a remission the γ-endorphin concentration was 27 ± 13 pmoles (11 ± 1.1 pmoles in the control). The relatively low β-endorphin concentration will be noted during a remission in patients with infectious-allergic (2 pmoles) and atopic (0.50 ± 0.3 pmole) forms of the disease.

In patients with mild clinical manifestations of bronchial asthma of the infectious-allergic and atopic forms a tendency was observed for α- and β-endorphin concentrations to rise. The α-endorphin concentration rose in the infectious-allergic form from 234 ± 17 to 300 ± 24 pmoles and in the atopic form from 139 ± 37 to 274 ± 19.6 pmoles. Concentrations of β-endorphin in patients with the infectious-allergic form of bronchial asthma and with mild clinical manifestations rose from 2 to 4.5 pmoles, and in patients with the atopic form from 0.5 to 8.3 pmoles. The tendency for the α-endorphin concentration to rise during exacerbation of the disease was evident. For instance, its concentration in patients with the infectious-allergic form of the disease, with moderately severe clinical manifestations, rose to 356 pmoles, and in one patient at the height of an attack it reached 571 pmoles. In patients with the atopic form of the disease and with moderately severe clinical manifestations the α-endorphin level reached 471 pmoles. The γ-endorphin concentration at the height of an attack in a patient with the infectious-allergic form of bronchial asthma was 34.4 pmoles (11.1 ± 1.1 pmoles in the control). A general tendency also was observed for the β-endorphin concentration to rise. Whereas in the period of remission in the infectious-allergic form of bronchial asthma it was 2 pmoles, and in the atopic form 0.5 pmole, when mild clinical manifestiations were present its level rose to 4.5 and 8.3 pmoles respectively. An increase in the β-endorphin concentration also was observed in patients with moderately severe clincial manifestations: up to 5 pmoles in patients with the infectious-allergic form and up to 9.5 pmoles in patients with the atopic form.

It is very characteristic that in the infectious-allergic form of the disease, after termination of attacks with dexamethasone the concentrations of all three types of endorphins fell sharply: the α-endorphin level from 224 ± 32 to 37 pmoles, β-endorphin from 6 to 1 pmole, γ-endorphin from 11 to 7.4 pmoles ($P < 0.01$; Table 1).

An increase in the concentrations of α- and β-endorphins, proportional to the severity of the clinical manifestiations, is thus observed in patients with bronchial asthma of the infectious-allergic and atopic forms. In the atopic form of the disease the concentrations of α- and β-endorphins during a remission was a little lower than in the control. No such pattern could be observed in the case of γ-endorphin.

Endorphins of all three types showed a sharp fall below the control level after termination of attacks by dexamethasone. This fall was evidently due to the fact that dexamethasone inhibits synthesis and subsequent secretion of endorphins into the blood stream [4, 5]. The possibility cannot be ruled out that after injections of dexamethasone, synthesis and secretion of endorphins are inhibited not only in the pituitary, but also in the lungs. Very probably termination of an attack of bronchial asthma by dexamethasone is directly or indirectly connected with inhibition of biosynthesis and secretion of endorphins by the lung tissues, but this is a problem for further study.

In our opinion, the fact that the endorphin concentrations are directly proportional to the severity of the clinical manifestations of bronchial asthma, together with the sharp fall of the endorphin levels as the result of corticosteroid therapy are evidence that the system for synthesis and secretion of these compounds is involved in the pathogenesis of the disease.

However, on the basis of the results so far obtained, the possibility cannot be completely ruled out that the changes observed are a secondary effect, due to a stress reaction of the patient to the asthmatic attack [7, 9].

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FORMATION OF ANTIGEN-DEPENDENT NONSPECIFIC IMMUNOGLOBULIN PRODUCING CELLS IN MICE IMMUNIZED WITH TWO T-INDEPENDENT ANTIGENS

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Injection of an antigen into an animal, besides inducing antibody formation, at the same time casues a sharp increase in synthesis of antigen-dependent nonspecific immunoglobulins (NIG) and an increase in the number of cells forming them (NIGFC) [1, 3, 4]. It was shown previously that on injection of two T-dependent [6] or one T-dependent and another T-independent [1] antigen, the number of NIGFC formed in the mouse spleen is about equal to the total number of cells arising in response to the action of each antigen separately.

The aim of this investigation was to study how the number of NIGFC changes during simultaneous administration of two T-independent antigens.

EXPERIMENTAL METHOD

Experiments were carried out on female BALB/c and C3H/A mice weighing 12-14 g. Salmonella Vi antigen [2] and polyvinylpyrrolidone (PVP) with a molecular weight of 350 kilodaltons (kD/ PVP_{350}) [5] were used as the T-independent antigens. The Vi-antigen and PVP_{350} were injected intravenously into mice in doses of 1 and 0.25-1 μg per mouse respectively. The number of antibody-forming cells (AFC) [7] and the number of immunoglobulin-forming cells (IGFC) [9] in the animals' spleens were determined on the 4th day. The number of NIGFC was calculated as the difference between the number of IGFC and the number of AFC per 10^6 living cells. The results were expressed in the form (M ± m).

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