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CHANGE IN ADRENAL FUNCTION IN DOGS WITH EXPERIMENTAL BRONCHOSPASM

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UDC 616.248-039.31-092.9-07: 616.154.453-074

KEY WORDS: adrenal glands; dogs; bronchospasm; catecholamines; glucocorticoids

A tendency is observed nowadays for the prevalence of bronchial asthma (BA) to continue to rise, and it is reported to be 3.5% among children [7] and 3-8% among adults [6]. The role of glucocorticoids in the pathogenesis of BA has not been adequately studied.

The aim of this investigation was to study changes in blood levels of adrenocortical and adrenomedullary hormones during an attack of experimental bronchospasm in dogs.

EXPERIMENTAL METHOD

Experiments were carried out on 7 male mongrel dogs weighing 20-25 μg, sensitized with ovalbumin for 8 weeks in gradually increasing concentrations (50, 250, 500, and 1000 μg subcutaneously). As adjuvant, 30 mg of aluminum hydroxide was used [4]. For bronchial provocation, the dogs were anesthetized by intravenous injection of 1% thiopental sodium solution, incubated, and the endotracheal tube connection to an inhaler and pneumotachograph.

Physiological saline (5 ml) and the solution of ovalbumin (100, 500, and 1000 μg in 5 ml of physiological saline) were inhaled for 15 min (each solution). The depth of anesthesia was monitored by testing the corneal reflex and was maintained at a constant level by repeated injections of thiopental sodium after inhalation of ovalbumin. The parameters of ventilation were recorded on a "Godart" pneumotachograph and the volume velocity of expiration (V) calculated. The presence of bronchospasm was judged from a fall of 25% or more in the value of V during 1 sec compared with its value before inhalation of physiological saline. The measurements were made at the 15th minute of inhalation. Concentrations of 11-hydroxycorticosteroids (11-HCS), adrenalin, noradrenalin, dopamine, and histamine were determined by fluorometric methods in blood samples taken from a peripheral vein before inhalation, at the 15th minute of inhalation, and 2 h after its end [1, 2, 8].

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TABLE 1. Fall of V (in percent) after Inhalation of Physiological Saline and Ovalbumin

Expt. No.	Inhalation of physiological saline	Inhalation of ovalbumin, μg		
		100	500	1000
1	0	0	24	59
2	33	46	52	60
3	21	38	34	31
4	54	46	65	69
5	36	42	50	80
6	50	68	61	53
7	10	69	56	52
$M \pm m$	29,0±8,2	44,0±10,4	49,0±6,2*	58,0±7,4*

Legend. Here and in Table 2: $*p < 0.05$.

TABLE 2. Changes in Plasma Levels of 11-HCS and Some Biologically Active Substances in Sensitized Dogs after Inhalation of Ovalbumin ($M \pm m$)

Period of investigation	11-HCS	Adrenalin	Noradrenalin nmoles/liter	Dopamine	Histamine
Before inhalation of physiological saline	306,6±12,1	27,1±2,3	39,1±3,7	35,5±4,4	208,6±29,6
After inhalation of 1000 μg ovalbumin	256,6±16,6*	6,0±1,7*	8,2±1,8*	19,0±2,5*	269,4±27,3
2 h after inhalation of ovalbumin	320,0±38,0	43,5±11,2	26,6±10,1	29,5±8,4	345,7±79,0

The control group consisted of two intact (unsensitized) dogs on which the provocation test with physiological saline and ovalbumin were carried out by the method described above.

EXPERIMENTAL RESULTS

None of the sensitized dogs showed changes in the volume velocity of the expiratory flow after inhalation of physiological saline compared with the initial level. In the remaining animals inhalation of physiological saline led to a decrease in V. Inhalation of ovalbumin was accompanied by more marked obstruction of the bronchi and a decrease in V (Table 1). The presence of individual differences in the development of the syndrome of bronchial obstructions in different dogs and the different degrees of disturbance of bronchial patency will be noted, and can evidently be explained by individual differences in the sensitivity of the animals to ovalbumin and to activity of the defensive systems of the body. Auscultation of the chest of many of the animals during inhalation of ovalbumin revealed a lengthened expiration and the presence of dry, scattered crepitations, evidence of marked bronchospasm.

Inhalation of physiological saline and ovalbumin by the two control (unsensitized) dogs did not lead to any significant changes in bronchial patency: V fell by 15% after inhalation of ovalbumin, and there was no reaction after inhalation of physiological saline.

Changes in blood plasma levels of glucocorticoids, adrenalin, noradrenalin, dopamine, and histamine in the sensitized dogs are given in Table 2. The level of total plasma 11-HCS fell significantly after inhalation of 1000 μg ovalbumin and rose to the initial level 2 h after the end of bronchial provocation. A similar trend also was observed in concentrations of catecholamines (adrenalin, noradrenalin, dopamine), but a tendency was observed for the plasma histamine concentration to rise. The marked decrease in the plasma adrenalin and noradrenalin concentrations after inhalation of 1000 μg ovalbumin and the smaller fall of the 11-HCS level will be noted. The results are evidence of different degrees of intensity of the response of the adrenal cortex and medulla to stress (bronchial provocation), and also differences in the role of these compounds in the regulation of reflex bronchospasm. The most significant changes at the height of bronchial provocation (after inhalation of 1000 μg of ovalbumin) were observed in the adrenal medullar a sharp fall of the catecholamine level. The secretion of catecholamines by cells of the adrenal medulla was evidently disturbed. It has been shown that dopamine and noradrenalin do not participate in the regulation of bronchial tone either in normal subjects or in patients with BA, whereas adrenalin, in physiological concentrations, stimulates the β_2-receptors of the bronchi and induces bronchial dilatation in normal subjects and patients with BA [5], and it also acts on the β_2-receptor apparatus of the mast cell, preventing the release of bronchoconstrictor substances [3]. It can therefore be postulated that, on the one hand, lowering of the plasma adrenalin concentration during bronchospasm is a protective reaction

of the body to bronchial provocation induced by antigen, and on the other hand, a low adrenalin level may not have a bronchodilator action on the bronchial smooth musculature, and this may favour bronchoconstriction [5].

The plasma 11-HCS level in the dogs was significantly lowered at the height of bronchospasm, although not so much as in the case of adrenalin. The fall in the glucocorticoid level which we found experimentally may evidently promote the development of a bronchospastic reaction. Similar results were obtained by other workers [9] studying patients with BA.

An important role in the development of reflex bronchospasm is thus played not only by the formation and secretion of bronchoconstrictor agents, but also by the activity of biologically active substances regulating bronchial tone, which may include adrenomedullary and adrenocortical hormones. Differential treatment of patients with atopic BA in the early (histamine) phase of the bronchospastic response by β_2-stimulators and by administration of glucocorticoid preparations, with the aim of preventing the development of the late (inflammatory) phase of the bronchospastic reaction will lead to more effective methods of terminating an exacerbation of the disease.

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