

BIOCHEMISTRY AND BIOPHYSICS

THE EFFECT OF ACTH ON THE PLASMA LEVEL OF NON-ESTERIFIED FATTY ACIDS IN HEALTHY SUBJECTS AND IN DIABETIC PATIENTS

(UDC 616.379-008.64-085.361.814.3-07:616.153.915+612.123-06:615.361.814.3)

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Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 59, No. 5,
pp. 48-51, May, 1965

Original article submitted October 9, 1963

In distinction from the manifest fat-mobilizing effect in vitro, the action of ACTH on fat metabolism in vivo is less pronounced [11, 14] and the literature yields no unified opinion about the nature of this effect. It is reported, for example, that injection of ACTH into rabbits produces a significant rise in the plasma level of non-esterified fatty acids (NEFA) already at 30 min after the injection [7]. In man and in the dog, ACTH injection does not appear to have a noticeable effect [12]. The problem of the mechanism of ACTH action on fat metabolism in man is also poorly explored.

This article presents the results of our observations which indicate a biphasic character of the ACTH effect of plasma NEFA levels in man and suggest an extra-adrenal mechanism for this action.

METHODS

Fourteen clinically healthy subjects and 13 diabetic patients without manifestations of ketosis were examined while fasting at 12 h after last receiving food. All subjects were given 40 units of ACTH intramuscularly; directly prior to the ACTH injection, and at 30, 60, and 180 min after it, blood was taken from the brachial vein and the

TABLE 1. Concentration of Non-esterified Fatty Acids (in μ eq) and Free 11-Hydroxycorticosteroids (in μ g per 100 ml of Plasma) in the Plasma of Healthy Subjects after Injection of ACTH and Control Observations. The arithmetic means of the corresponding values and the confidence limits ($P < 0.05$) are presented

Index studied	Time (in min)			
	0	30	60	180
Concent of non-esterified fatty acids after administration of ACTH	553 \pm 42	524 \pm 33	584 \pm 58	720 \pm 108
Content of non-esterified fatty acids in control observations	510 \pm 34	531 \pm 46	551 \pm 53	579 \pm 62
Content of 11-hydroxycorticosteroids after ACTH administration	16,4 \pm 3,9	33,4 \pm 7,4	36,9 \pm 4,8	28,2 \pm 6,4
Content of 11 hydroxycorticosteroids in control observations	14,5 \pm 4,2	13,0 \pm 3,8	11,0 \pm 3,8	8,2 \pm 2,4

TABLE 2. Concentration of Non-esterified Fatty Acids (in μeq) and Free 11-Hydroxycorticosteroids (in $\mu\text{g}/100\text{ ml}$ of Plasma) in the Plasma of Diabetic Patients after Administration of ACTH and in Control Observations. The arithmetic means of corresponding values and confidence limits ($P < 0.05$) are given

Index studied	Time (in min)			
	0	30	60	180
Concent of non-esterified fatty acids after administration of ACTH	763 ± 129	768 ± 118	753 ± 117	895 ± 94
Content of non-esterified fatty acids in control observations	710 ± 129	774 ± 159	784 ± 155	859 ± 127
Content of 11-hydroxycorticosteroids after ACTH administration	$17,8 \pm 3,4$	$32,8 \pm 6,5$	$35,0 \pm 4,8$	$23,7 \pm 5,5$
Content of 11-hydroxycorticosteroids in control observations	$15,8 \pm 2,9$	$15,3 \pm 3,5$	$14,6 \pm 3,6$	$11,0 \pm 2,9$

quantity of plasma NEFA [5] and free 11-hydroxycorticosteroids [2] was measured. After 4-5 days control observations were made on the same subjects without injection of ACTH.

RESULTS

The arithmetic means of the parameters measured within limits of confidence ($P < 0.05$) in the respective groups are presented in Tables 1 and 2. The displacement of the indices measured was checked by the method of paired comparison with the corresponding indices in control observations [3].

A statistical analysis of the results obtained shows that the plasma concentration of NEFA after ACTH injection in the group of healthy subjects is lower, on the average, by $5\ \mu\text{eq}$ than the initial level ($P < 0.01$) and in the diabetic group by $109\ \mu\text{eq}$ ($P < 0.05$). The maximum decrease in plasma NEFA concentration after ACTH injection into healthy subjects came after 30 min, and in the diabetic group, after 60 min. A more marked drop in plasma NEFA following ACTH administration is observed when the original level is higher, although no regular quantitative relationship is found, according to our data (Table 3). At 180 min after ACTH injection the plasma NEFA is seen to rise in healthy subjects as compared to control observations without hormone administration ($P < 0.05$). The level of 11-hydroxycorticosteroids in the plasma is already elevated above the initial level at 30 min and attains a maximum at 60 min after ACTH injection. In this connection, the differences between the groups is statistically invalid. During the control period of observation (no hormone given) a gradual, uniform rise in NEFA concentration and fall in plasma 11-hydroxycorticosteroid level is observed. We could not establish a regular, quantitative relationship between the increase in amount of free 11-hydroxycorticosteroids and the decrease in plasma NEFA concentrations following ACTH administration.

The decrease in plasma NEFA concentration after ACTH injection, which later changes into a rise in NEFA level (in healthy subjects) indicates the biphasic action of ACTH. The primary decrease in plasma NEFA level after ACTH injection in instances with a higher starting level, and the lack of an increase phase in the diabetic patients (in the observation conditions) indicates that the effect of ACTH administration may vary, depending on the initial status of the organism. This is a particular manifestation of the adaptational-compensatory action of ACTH on a number of metabolic indices [1]. It is possible that the lack of unified opinion in the literature concerning the fat-mobilizing action of ACTH in vivo is explained not only by the evident peculiarities of the objects observed but also by the failure to study these factors, i.e., the biphasic nature of the effect and its dependence on the initial state of the organism.

TABLE 3. Mean Decrease in Non-Esterified Fatty Acid Level in the Plasma After Administration of ACTH as a Function of Its Initial Level

Initial level of non-esterified fatty acids in plasma (in μeq)	450—599	600—749	750—899	900—1149
Mean decrease in level of non-esterified fatty acids after administration of ACTH (in μeq)	38	70		300

Some authors explain the phase of decreased plasma NEFA level after ACTH administration by an increase in glycolysis and in blood glucose concentration [6]; our preliminary studies did not confirm a correlation between the displacement of glucose level and the NEFA level after ACTH [14].

The lack of a quantitative relation between the decrease in NEFA concentration and the increase in free 11-hydroxycorticosteroids in the plasma after ACTH administration argues in favor of the hypothesis that the effect of ACTH on the plasma concentration of NEFA is a direct, extra-adrenal one. The results of experiments on animals are also in accord with this hypothesis [10, 13]. It has been proved that the lipolytic effect of ACTH is mediated by the indirect action of this hormone on the lipase of fat tissue and, consequently, is extra-adrenal; this lipase is distinguished by a number of characteristics (optimal hydrogen ion concentration, effect of inhibitors, alimentary factors) from lipoprotein lipase [10].

The gradual increase in plasma NEFA concentration detected in our control experiments is conditioned evidently by abstinence from food [8] and the gradual decrease in plasma 11-hydroxycorticosteroids is possibly a reflection of the daily production rhythm of this hormone [9].

SUMMARY

Following an intramuscular injection of ACTH to a group of healthy subjects a decrease was observed in the level of non-esterified fatty acids of the plasma, replaced by an increase in their concentration, whereas in a group of diabetes patients only a stage of decrease was observed under identical conditions. The most marked decrease in the concentration of non-esterified fatty acids in the plasma was noted in cases with a higher initial level. No quantitative relationship could be established between the decrease in the concentration of non-esterified fatty acids in the plasma was noted in cases with a higher initial level. No quantitative relationship could be established between the decrease in the concentration of non-esterified fatty acids and the increase in the amount of free 11-hydroxycorticosteroids of the plasma following an ACTH injection. The results of observations evidence the dependence of the ACTH administration effect on the initial condition of the organism, and agree with the hypothesis of a direct, extra-adrenal mechanism of ACTH action on the level of non-esterified fatty acids of the plasma.

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