THE EFFECT OF THE SOMATOTROPIC HORMONE AND CORTISONE ON THE LIVER INSULINASE ACTIVITY IN INFANTILE AND SEXUALLY MATURE RATS

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In our previous work [2] we demonstrated that the activity of liver insulinase in infantile rats (21-30 days old, weighing 30-50 gm) is reduced in comparison to the insulinase activity of sexually mature rats (1-2 years old, weighing over 170 gm). Administration of chorionic gonadotropine (25 mg twice daily) to sexually immature male and female rats, of estradiole-dipropionate (100 m. u.) to female and testosterone-propionate (0.4 mg) to male for a period of five days increases the activity of their liver insulinase, whereas administration of testosterone-propionate (two mg daily, for five days) to sexually mature rats does not affect the activity of liver insulinase. These data attest to the fact that sexual hormones do not directly activate insulinase, but merely contribute to the formation of this function during ontogenesis.

In view of the fact that the insulin activating system of the liver (insulinase) represents one of the factors of the extra-pancreatic inactivation of insulin, and that the enhancement of its activity may play a definite part in the pathogenesis of certain forms of diabetes mellitus, it seemed to us essential to elucidate the manner in which other hormones affect this system, in the first place, those which may contribute to the development of diabetes mellitus. A solution of this problem would enable us to elicit the role of the insulin activating system of the liver within the mechanism of the diabetogenic action of these hormones.

In the present work we set ourselves the task of investigating the effect of the somatotropic hormone of the hypophysis and cortisone, which as is known may play a definite part in the pathogenesis of certain forms of diabetes mellitus [3], on the activity of the liver insulinase of sexually mature and infantile rats.

METHOD OF EXPERIMENTS

Experiments were staged on infantile rats (aged 21-30 days, weighing 30-50 gm) and sexually mature rats (aged one to two years, weight 190-270 gm). The somatotropic hormone* was administered for five days, twice daily to infantile rats at 0.5 mg and to sexually mature rats at 1.5 mg. Cortisone was administered to infantile and mature rats at 1.0 mg per 100 gm body weight daily, for five days. Determination of insulinase activity was carried out by Mirskii method [4] with I^{131} labeled insulin as follows: the rats were decapitated, their liver removed and immediately homogenized on cold with a quadruple volume of 0.067 M phosphate buffer. The homogenate was centrifuged for 20 minutes in a refrigeration centrifuge at 1-5° and 10,000 revolutions per minute.

* In our work we used the somatotropic hormone obtained in a manufacturing laboratory and tested by means of the tibial test at the Department of Biology of the All-Union Institute of Experimental Endocrinology.

After centrifugation, the fluid over the precipitate was filtered off through gauze. One ml of this fluid and one ml of 0.067 M phosphate buffer with pH 7.5 containing 0.25 mg of I^{131} labeled insulin were put into the centrifuge test tube. One ml of this mixture was placed on the target for the determination of total radioactivity, and 0.2 ml into a centrifuge test tube containing 0.8 ml of 0.067 M phosphate buffer for determination of the free radioactivity of insulin with I^{131} not incorporated in the molecule. For this purpose, several ml of soluble protein and one ml of a 10% solution of trichloracetic acid were added so as to precipitate the insulin bound I^{131}. The mixture was centrifuged, the fluid over the precipitate poured off into a centrifuge tube, and 0.2 ml from this tube were placed on the target for the determination of radioactivity of the non-precipitated I^{131}. After determining the total and free radioactivity, the mixture was kept for 30 minutes in a thermostat at 37° and the free radioactivity was again determined. The insulinase activity was expressed in percentages of I^{131} which had been split off, as the result of enzymic fission of insulin; the latter was determined according to the extent of the increase of free I^{131} radioactivity during the 30 minutes incubation period. All calculations were made on one ml of incubation mixture. In order to determine the possible spontaneous splitting off of I^{131} we conducted simultaneously a control test in which the homogenate was substituted with one ml of 0.067 M phosphate buffer.

RESULTS OF EXPERIMENTS

As seen in Fig. 1, a 5-day administration of the somatotropic hormone to sexually mature rats causes an increase of liver insulinase activity in them. Whereas in the control group the insulinase activity prior to I^{131} splitting off equalled 26.1% on the average, in the tested group it proved to be 34.4%, i.e., increased by 20.3%. Administration of the somatotropic hormone to infantile rats revealed a more considerable increase of insulinase activity. Whereas in the control group the insulinase activity in infantile rats was 14.6% after the I^{131} split off, in the tested group after a five day administration of the somatotropic hormone it was 32.4%, i.e., two-fold higher, than the activity in the control group.

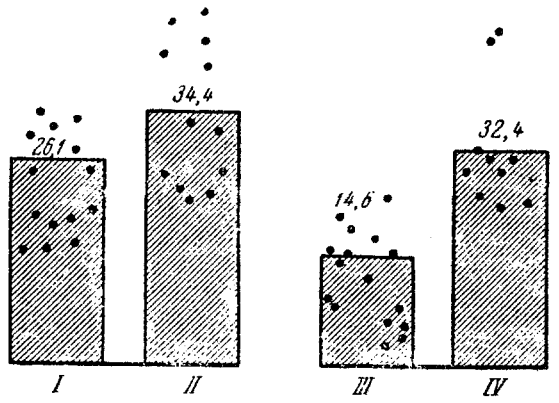

Fig. 1. Effect of administration of the somatotropic hormone on the activity of the liver insulinase of mature and infantile rats. Sexually mature rats: I) Norm; II) subcutaneous injection of the somatotropic hormone, 1.5 mg daily for five days; infantile rats: III) norm; IV) subcutaneous injection of the somatotropic hormone, 0.5 mg daily for five days.

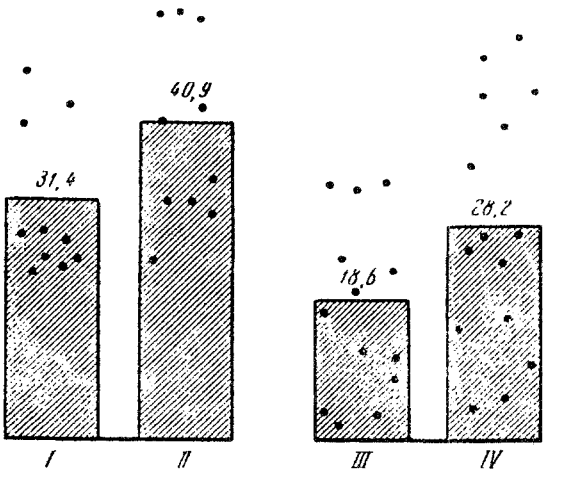

Fig. 2. Effect of cortisone administration on liver insulinase activity in sexually mature and infantile rats. Mature rats: I) Norm; II) administration of one mg/100 gm of cortisone, daily for five days; infantile rats: III) norm; IV) administration of one mg/100 gm cortisone, daily for five days.

We demonstrated in our previous work [1]that antidiabetic sulfonamide preparations (nadisan) reduce the activity of liver insulinase. Recently, Mirskii and his co-workers [5] have found that administration of tolbutamide to dogs protects them from developing diabetes resulting from the injection of the somatotropic hormone. This is, presumably, connected with the inhibiting effect of tolbutamide on the insulinase activity of the liver.

An action analogous to somatotropic hormone, i.e., an increase of insulinase activity, was elicited also upon injection of cortisone to sexually mature and infantile rats (Fig. 2). In mature rats, the insulinase activity in the control group comprised 31.4%, in the tested group – 40.9%, or an increase of 30.2%. In infantile rats, the

indices were 18.6% and 28.2%, respectively, i.e., under the effect of cortisone the insulinase activity increased over 1½ times.

Thus, administration of the somatotropic hormone and cortisone increases liver insulinase activity in mature and infantile rats, and it is somewhat more pronounced in the latter. The obtained data permit us to assume that in the mechanism of the diabetogenic effect of these hormones a definite role may be played by their stimulating effect on insulinase activity.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
