EFFECT OF ADRENALECTOMY ON ENZYME ACTIVITY IN THE MUCOUS MEMBRANE OF THE RAT SMALL INTESTINE

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Bilateral adrenalectomy leads to a decrease in the invertase, pepidase, and alkaline phosphatase activity in the mucous membrane of the rat small intestine. Monoglyceride-lipase activity is increased under the circumstances in the great majority of cases. The character of the change in activity of the various enzymes also depends on the time elapsing after adrenalectomy. Compensation of the mineralocorticoid or glucocorticoid deficiency by administration of sodium chloride to the adrenalectomized rats or by injection of hydrocortisone abolished the observed effects only partially.

KEY WORDS: adrenalectomy in rats; small intestine; enzymes of the mucous membrane; hydrocortisone.

According to the available evidence, after total adrenalectomy the activity of alkaline phosphatase, invertase [12], maltase, and peptidase [11] is reduced in homogenates of the mucous membrane of the rat small intestine. Injection of corticosteroid hormones has no significant effect on the enzyme activity of the mucous membrane of the small intestine in adult rats, but it induces activity of the intestinal enzymes in growing animals [3, 7, 8, 10]. Prolonged injection of large doses of hydrocortisone, leading to atrophy of the adrenals, causes a decrease in the amylolytic activity of the blood and a simultaneous increase in the amylolytic activity in the pancreas and small intestine [2]. It can be concluded from these findings that adrenocortical hormones play an important role in the regulation of intestinal digestion. However, difficulties arise during the examination of results obtained with different animals and by means of different methods. In addition, many contradictory factors are still to be found in this problem. Some workers state that correction of the disturbances of water and salt metabolism following adrenalectomy by administration of NaCl to the animals prevents the enzymic changes in the small intestine [1, 11], whereas others deny any such effect [12].

In this investigation an attempt was made to determine the activity of several intestinal enzymes in the mucous membrane of the rat small intestine simultaneously at various times after adrenalectomy, and also in adrenalectomized animals after receiving NaCl solution or injections of hydrocortisone.

EXPERIMENTAL METHOD

Experiments were carried out on 160 male albino rats weighing about 150 g. Simultaneous bilateral adrenalectomy was performed on some (120) of the animals. The other animals (40 rats) underwent a mock operation and were used as the control. The adrenalectomized rats in turn were divided into three groups: group 1 received ordinary tap water for drinking, group 2 received 1% NaCl solution, whereas group 3 received daily injections of hydrocortisone in a dose of 4 mg/100 g body weight. The animals' diet was kept constant for all groups throughout the experiment (20 days). On the 2nd, 4th, 8th, 15th, and 20th days after the operation 8 animals were decapitated from each group after starvation for 16-18 h and the enzyme activity was determined in homogenates of the mucous membrane of the small intestine made up in

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Ringer's solution (pH 7.4): invertase by the modified Nelson's method [4], glycl-l-leucine dipeptidase from the increase in glycine [5], monoglyceridelipase from the increase in glycerol [6], and alkaline phosphatase from the increase in inorganic phosphorus [9]. The activity of the enzymes in all cases was expressed in micromoles of the hydrolysis products formed in 1 min per gram wet weight of mucous membrane.

EXPERIMENTAL RESULTS AND DISCUSSION

In the adrenalectomized rats receiving ordinary tapwater, by the second day after the operation a significant increase in vertase activity of the mucous membrane of the small intestine was observed by comparison with the control group (mock operation) of animals (from 7.3 ± 0.7 to $5.3 \pm 0.6 = \mu$mole/min), and this decrease persisted on the 4th, 8th, 15th, and 20th days of the experiments (5.8 ± 0.4 compared with 7.9 ± 0.6, 4.8 ± 0.2 compared with 6.7 ± 0.5, 5.2 ± 0.3 compared with 6.6 ± 0.4, and 5.5 ± 0.3 compared with 6.5 ± 0.4 μmoles/min, respectively). The dipeptidase activity in this series of experiments also showed a marked decrease except on the 15th day after the operation, when it was a little higher than the control (17.5 ± 0.4 compared with 16.2 ± 0.4 μmoles/min). The changes in the monoglyceride-lipase activity were cyclic; on the second day after the operation it was higher in the adrenalectomized rats than in animals undergoing the mock operation (5.2 ± 0.2 compared with 4.2 ± 0.2 μmoles/min; $P < 0.002$), by the 4th day it had fallen virtually to the control level, on the 8th day it fell sharply (3.4 ± 0.4 compared with 6.4 ± 0.2 μmoles/min; $P < 0.001$), and on the 15th and 20th days it was again increased (6.7 ± 0.3 compared with 4.1 ± 0.2 μmoles/min; $P < 0.001$, and 6.0 ± 0.4 compared with 4.5 ± 0.2 μmoles/min; $P < 0.001$, respectively). As regards the alkaline phosphatase activity its level was virtually indistinguishable from the control on the 2nd and 4th days after the operation, but later it fell considerably.

Experiments with compensation of the mineralocorticoid function by administration of NaCl solution to the adrenalectomized rats gave the following results. The invertase activity was not significantly altered until the 15th day of the experiment, and the decrease became significant only on the 20th day (5.2 ± 0.3 compared with 6.5 ± 0.4 μmoles/min; $P < 0.05$). The dipeptidase activity was increased on the 2nd and 4th days of the experiment, it fell slightly by the 8th day (from 18.9 ± 0.2 to 15.5 ± 0.4 μmoles/min; $P < 0.001$), reached the control level on the 15th day, and then fell again by the 20th day (from 18.0 ± 8.3 to 14.0 ± 0.3 μmoles/min; $P < 0.001$). The monoglyceride lipase activity was lowered only on the 2nd day after adrenalectomy (3.3 ± 0.1 compared with 4.2 ± 0.2 μmoles/min; $P < 0.001$). At the other times it was considerably higher than in the control. A characteristic feature of alkaline phosphatase was a decrease in its activity on the 2nd, 4th, and 8th days after the operation and a significant increase on the 15th day, followed by a return to the initial level by the end of the experimental period (20th day).

In the animals which received hydrocortisone after adrenalectomy, the invertase activity was not significantly changed throughout the experimental period compared with the control (in every case $P > 0.05$). The dipeptidase activity of these rats was significantly higher than in the control only on the 2nd day after adrenalectomy (19.3 ± 0.7 compared with 14.6 ± 0.4 μmoles/min; $P < 0.001$), and at the other times it remained practically at the control level. The monoglyceride lipase activity was a little higher than in the control on the second day after the operation (5.3 ± 0.2 compared with 4.2 ± 0.2 μmoles/min; $P < 0.002$), it returned to its initial level by the 4th and 8th days, and increased again by the 15th and 20th days (5.2 ± 0.1 compared with 4.1 ± 0.2 μmoles/min; $P < 0.001$, and 5.8 ± 0.2 compared with 4.5 ± 0.2 μmoles/min respectively; $P < 0.001$). The alkaline phosphatase activity showed a small decrease on the second day of the experiment (from 4.7 ± 0.1 to 4.1 ± 0.2 μmoles/min; $P < 0.001$), on the 4th and 8th days it returned to its original level, but later it fell again (from 4.8 ± 0.2 to 4.0 ± 0.2 μmoles/min on the 15th day and from 5.0 ± 0.2 to 3.5 ± 0.1 μmoles/min on the 20th day).

These results thus show that after adrenalectomy significant changes take place in the activity of enzymes participating in membrane hydrolysis of the principal components of the diet. First, the changes in activity of the various enzymes may take place in different directions, leading to definite changes in the spectrum of enzyme activity of the intestinal mucous membrane, and second, the character of the changes in the activity of the various enzymes varies depending on the time after adrenalectomy. This fact must evidently be taken into account when problems connected with the role of the adrenals in the regulation of intestinal digestion are considered.

Comparison of the results of the various series of experiments suggests that changes in enzyme activity of the mucous membrane of the small intestine during adrenal hypofunction are probably not only due to disturbances taking place at the level of water–electrolyte and carbohydrate metabolism, but are also connected with other functional transformations in the body. This is shown by the fact that compensation

of mineralocorticoid deficiency by administration of NaCl to the rats abolishes to some degree the effect of adrenalectomy for invertase only. Changes in the activity of the other enzymes studied were ill defined under these circumstances. Compensation of the glucocorticoid deficiency by injections of hydrocortisone prevented the effect of adrenalectomy in the case of invertase and peptase, but in most cases it did not have the characteristic effect on the change in monoglyceride lipase and phosphatase activities.

LITERATURE CITED

1. G. A. Bulbuk, Fiziol. Zh. SSSR, No. 5, 607 (1968).
2. Yu. N. Kolesnikov, in: Problems in Medical Theory, Clinical Practice, and Balneotherapy [in Russian], No. 4, Simferopol' (1971), p. 80.
3. A. M. Ugolev, Contact Digestion, Semisubstrate Processes, Organization and Regulation [in Russian], Leningrad (1972).
4. A. M. Ugolev and N. N. Iezuitova, in: Investigations of the Digestive Apparatus in Man [in Russian], Leningrad (1969), p. 192.
5. A. M. Ugolev and N. N. Timofeeva, in: Investigations of the Digestive Apparatus in Man [in Russian], Leningrad (1969), p. 178.
6. A. M. Ugolev and M. Yu. Chernyakhovskaya, in: Investigations of the Digestive Apparatus in Man [in Russian], Leningrad (1969), p. 183.
7. J. J. Deren, in: Handbook of Physiology, Sec. 6, Vol. 3, Washington (1968), p. 262.
8. R. G. Doell and N. Kretchmer, Science, 143, 42 (1964).
9. C. H. Fiske and G. Subbarow, J. Biol. Chem., 66, 375 (1925).
10. O. Koldovsky, Development of the Function of the Small Intestine in Mammals and Man [in Russian], Vol. 11, Basel (1969).
11. R. J. Levin, H. Newey, and D. H. Smyth, J. Physiol. (London), 177, 58 (1965).
12. W. C. Watson, E. S. Murray, and M. D. Gardener, J. Clin. Path., 20, 185 (1967).