THE MECHANISM OF DISORDERS IN MOTOR AND SECRETORY FUNCTION OF THE SMALL INTESTINE IN ACUTE RADIATION SICKNESS

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Extensive reports concerning various functional changes in the small intestine in case of radiation sickness can be found in the Russian and foreign literature. Both disorders of the secretory process [5, 7, 9, 10] and motor disorders in the small intestine have been studied [3, 8, 11, 15, 16, 18]. The results obtained suggest the presence of severe disorders. There are, however, no adequate experimental data revealing the mechanism of the pathological changes mentioned above.

Conard [15] studied the influence of acetylcholine upon the motor function of the small intestine in rats and voiced the assumption that under the influence of ionizing radiation the quantity of acetylcholine present in the animal body possibly increases. Later, numerous authors established an increase in the acetylcholine content and a decrease in the cholinesterase activity in the peripheral blood and in tissues from various organs at certain stages of the development of radiation sickness [4, 6, 14, 16, 19].

In the present paper we made an attempt to discover certain factors which – in acute radiation sickness – cause functional changes in the small intestine.

In view of the importance of acetylcholine in the regulation of the functional activity of the small intestine, we studied – on one and the same animal – the secretory and motor function of the small intestine, and also investigated the acetylcholine content and the cholinesterase activity of the arterial blood as well as of the blood leaving the intestine (in the portal vein).

EXPERIMENTAL METHOD

The experiments were carried out on three dogs, operated upon by the Thiry-Vella method. Simultaneously, angiostomy was carried out on the same animals; an isolated loop of the small intestine was used as cannula.

The investigation was carried out on the day following surgery and lasted four hours. During that time, intestinal juice was collected from the dogs and the enterokinase and alkaline phosphatase activity was determined in the juice; the motor activity of the isolated intestinal loop was recorded [10, 11]. In addition, the enterokinase and alkaline phosphatase activity of the stools was determined two to three times a week.

Immediately after the animal had been taken down from the stand, blood was taken from the portal vein and the femoral artery by means of a syringe, and the cholinesterase activity as well as the content of acetylcholine in the blood were estimated.

The cholinesterase activity was estimated by the method of S. R. Zubkova and T. V. Pravdich-Neminskaya [1], which is based on the titration of acetic acid formed by the breakdown of acetylcholine; the cholinesterase activity was expressed in mg of acetylcholine destroyed by 1 ml serum within one hour.

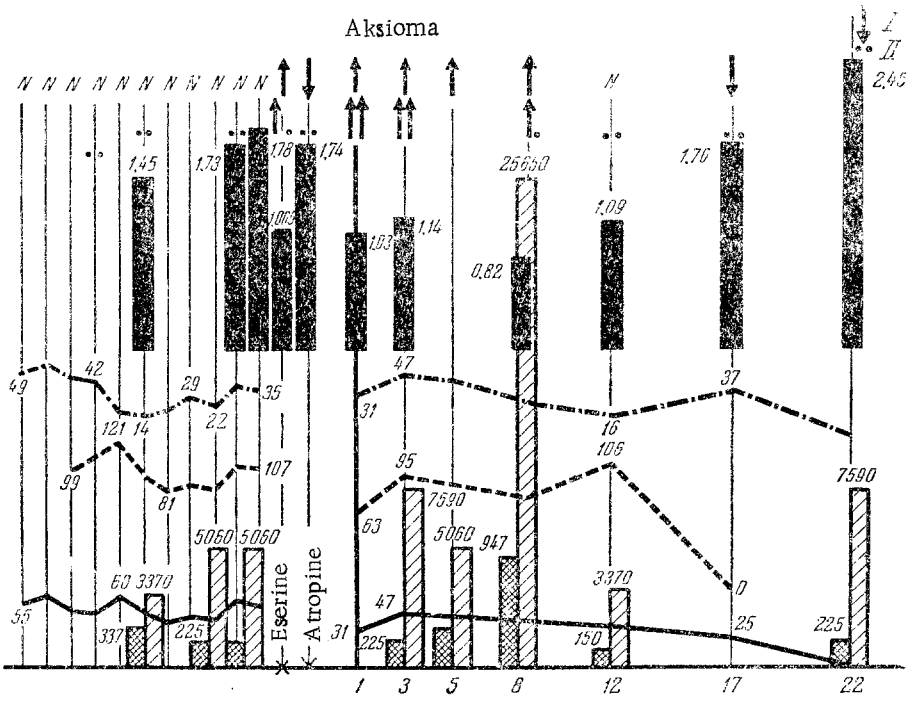

Fig. 1. I) Changes in the motor and secretory function of the small intestine in acute radiation sickness in the dog Aksioma; N) the motor function under normal conditions; ↑) intensified motor function; ↓) depression of the motor function; II) key to signs relating to the acetylcholine content of the blood: . .) traces of acetylcholine; ↑) increased content of acetylcholine in the blood; black columns) cholinesterase activity in the serum from portal blood. —.—.) phosphatase activity, — —) enterokinase activity, — — —) quantity; of the intestinal juice; crosshatched columns) enterokinase content in the stool; hatched columns) phosphatase content in the stool; X) moment of eserine administration; ↓) moment of atropine administration. Vertical lines: day of exposure to x-rays; left part of the figure : normal conditions; right part of the figure : after exposure to radiation: abscissas : days before and after exposure to radiation.

The acetylcholine content in the blood serum was estimated on a biological test object: the dorsal muscles of the leech.

Acute radiation sickness was produced in the dogs by total body radiation in a dose of 400 r under the following conditions: potential 180 kv; current strength 20 ma; capacity of dose 16.2-16.7 r/min; focus distance 90 cm, filters 0.5 mm Cu and 1 mm Al.

EXPERIMENTAL RESULTS

To increase the motor activity of the isolated intestinal loop, eserine (a cholinesterase inactivator) was injected subcutaneously in a dose of 0.1 mg per kg weight. Figures 1-3 show that this caused a considerable intensification in the motor function of the isolated intestinal loop. At the peak of the increased motor activity blood was taken from the portal vein and the femoral artery. This procedure was followed by a marked decrease in the cholinesterase activity in the sera from both blood samples. In the dog Vazhnyi the activity decreased in the portal blood from 0.60-0.69 to 0.37, in the dog Aksioma the activity decreased from 1.45-1.89 to 1.005, and in the dog Bezdomnyi, from 0.80-0.88 to 0.69. At the same time, the appearance of acetylcholine in the portal blood could be observed in all three animals (normally this substance can hardly be found in the portal blood).

Administration of atropine diluted 1:1000, in a dose of 1 ml, blocked the action of acetylcholine and caused a decrease in the motor function of the isolated intestinal loop. Under these conditions the cholinesterase

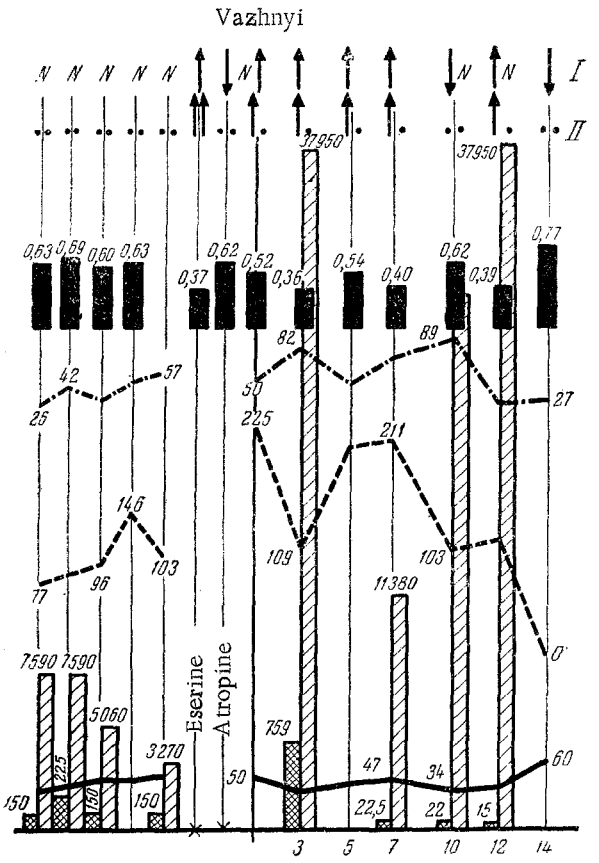

Fig. 2. Changes in the motor and secretory function of the small intestine in acute radiation sickness in the dog Vazhnyi. Designations and symbols same as in Fig. 1.

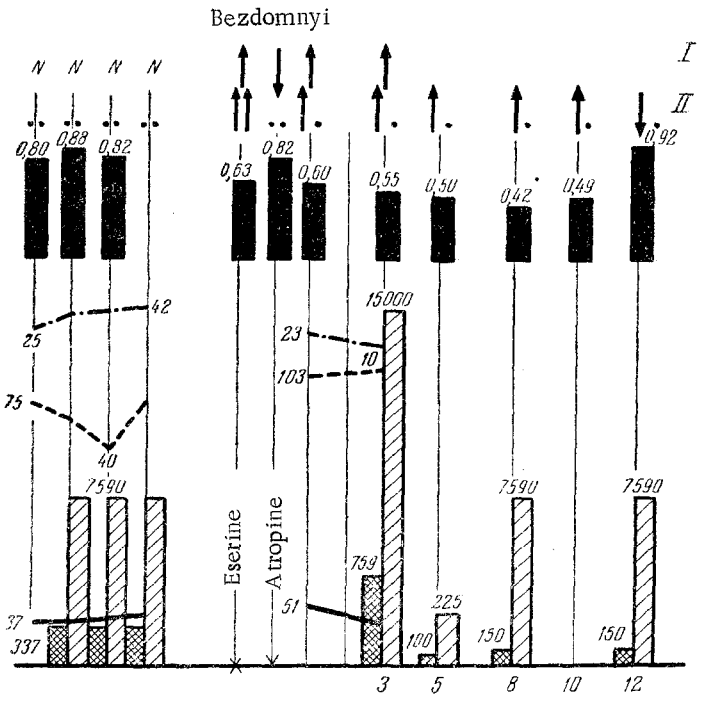

Fig. 3. Changes in the motor and secretory function of the small intestine in acute radiation sickness in the dog Bezdomnyi. Designations and symbols same as in Fig. 1.

activity of the serum in the portal blood and the arterial blood fell within the normal range and no acetylcholine was found.

After exposure of the dogs to x-rays in a dose of 400 r, suppression of the cholinesterase activity in the portal blood and the arterial blood could be observed from the first day up to the 10th-12th days. At the same time, acetylcholine appeared in the blood of the portal vein, and could be found here up to the 8th-12th days (see Fig. 1). Simultaneously, i.e., from the first day and until the 10th-12th days after exposure to radiation, the motor activity of the isolated intestinal loop was intensified in all dogs.

This period was later followed by an increase in the cholinesterase activity of the portal blood and the arterial blood to a level considerably exceeding the normal. The maximal cholinesterase activity in the dog Vazhnyi was observed on the 14th day after radiation (0.77 compared with 0.60-0.69 under normal conditions), in the dog Aksioma on the 22nd day (2.45 compared with 1.45-1.80) and in the dog Bezdomnyi on the 12th day (0.92 compared with 0.80-0.88). This was accompanied by a decrease in the acetylcholine content of the blood up to the complete disappearance of that substance. Simultaneously, an inhibition of the motor function of the isolated intestinal loop could be observed. This period usually coincided with the terminal period, after which the animal perished.

The data quoted above show that variations in the motor function of the small intestine in acute radiation sickness can be related to the state of the acetylcholine-cholinesterase system. After exposure to radiation, the cholinesterase activity of the blood is suppressed; simultaneously the blood leaving the intestine contains acetylcholine, which normally cannot be found in fasting dogs; at the same time the motor activity of the isolated intestinal loop becomes more intensive. And, on the contrary, if the serum cholinesterase activity increases acetylcholine disappears from the portal blood and the motor function of the isolated intestinal loop becomes inhibited.

The changes in the acetylcholine-cholinesterase system, however, exert – according to our findings [10, 11] – no appreciable influence upon the enterokinase and alkaline phosphatase activity in the small intestine. It seems that the disorders in the secretory function of the small intestine established by us after exposure to ionizing radiation depend on other mechanisms as well.

The discharge of intestinal enzymes with the stools in the terminal period is connected with the motor activity of the intestine. As a rule, increased motor activity of the intestine led to an increase in the quantity of enzymes discharged with the stools. In the dog Vazhnyi the enterokinase activity in the stools increased on the third day after exposure to radiation from the 150-225 units found under normal conditions to 759 units, and the alkaline phosphatase activity increased from 5060-7590 to 37950 units. When the motor function of the intestine became less intensive, smaller quantities of intestinal enzymes entered the stool.

In the terminal period of radiation sickness, however, the excretion of enzymes with the stools was always increased, notwithstanding the fact that the motor function of the intestine was strongly inhibited. This fact is at present difficult to explain. We can only voice the assumption that in this period of radiation sickness either some processes normally participating in the partial breakdown of intestinal enzymes are disrupted or extensive desquamation of the intestinal epithelium takes place.

SUMMARY

Thiry-Vella operation and angiostromy of the portal vein were performed in 3 dogs. The secretory and motor functions of the small intestine were studied in these animals; the content and the activity of cholinesterase in the arterial blood and the blood of the portal vein were investigated as well. After x-ray irradiation of dogs in a dose of 400 r the portal vein showed the presence of acetylcholine which is absent in a fasting normal animal. The activity of cholinesterase in these conditions has considerably diminished, whereas the motor activity increased. Later, with the rise of the cholinesterase activity, acetylcholine was seen to disappear, and the motor intestinal function depressed. These facts point to the relationship between disturbed intestinal motor function and the changes in the acetylcholine-cholinesterase system.

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