THE ACTION OF PITUITRIN ON THE WORK OF THE GASTRIC GLANDS

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Preparations of the posterior lobe of the hypophysis and, in particular, pituitrin, are widely used in clinical practice. Pituitrin is indicated in uterine inertia during labor, postoperative and postpartum retention of urine, uterine hemorrhage, diabetes insipidus, paralytic ileus, lowered blood pressure, and so on. In this connection the problem arises of the action of pituitrin on the body as a whole and, in particular, on the digestion in the stomach, as one of practical as well as theoretical interest.

The action of preparations of the posterior lobe of the pituitary on the secretory function of the stomach has been studied by many authors, but their findings are very contradictory. Several workers, for instance [16, 17, 19, 20], after injection of preparations of the posterior lobe of the hypophysis, observed an increase in the volume of gastirc juice and also in the free and total acidity. The majority of authors [1,2,4,5,6,7,8,10,14,18, and others], however, have observed inhibition of gastric secretion after the action of preparations of the posterior lobe of the hypophysis, and also a decrease in the acidity and digestive power of the juice. Certain authors [9 and others] were unable to detect any changes in the gastric secretion as a result of the action of preparations of the posterior lobe of the hypophysis.

Bearing in mind that in the majority of these investigations, particular attention was directed towards the changes in the volume of the gastric juice, and that changes in the composition of the gastric juice may be of no less importance in the pathology of digestion, we deci ded to study the qualitative changes arising in the gastric juice under the influence of pituitrin.

METHOD

Experiments were carried out on dogs. Of the 3 animals taking part in the experiments, two had isolated gastric pouches of the Heidenhain type (the dogs Rex and Raketa) and one, a Pavlov pouch as modified by G. M. Shpug (the dog Lyutik). The experiments were all performed in the same room. The dogs were kept on roughly identical conditions of diet.

Pituitrin P (produced at the Moscow factory for endocrine preparations, activity 3 i.u./ml) was injected subcutaneously and intravenously in a dose of 0.1 ml/kg body weight. In the majority of experiments the pituitrin was injected immediately after feeding the dog on meat (in the latent period of secretion), and in 2 experiments, on the dog Raket, pituitrin was injected intravenously one hour after a meal, i.e. at the height of secretion.

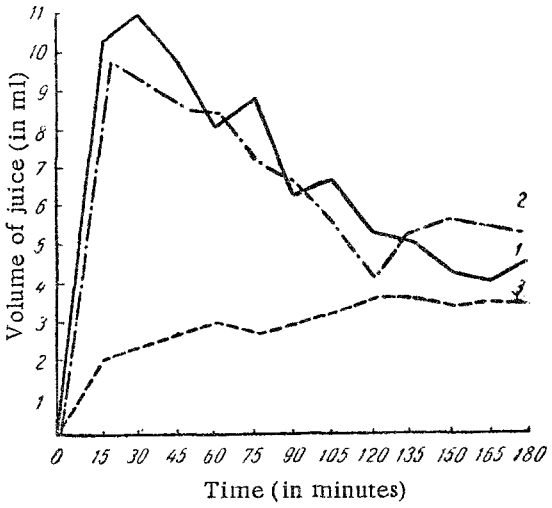

Fig. 1. Changes in the volume of gastric juice after the subcutaneous and intravenous (during the latent period) injection of pituitrin. 1) Control experiment; 2) subcutaneous injection of pituitrin; 3) intravenous injection of pituitrin.

Excitation of the gastric glands was caused by feeding 200 g of raw meat in the course of 5 minutes. Observations were made on the secretion of juice for 3 hours. In each hourly sample of juice we determined the protease and lipase activity, the free, combined and total hydrochloric acid contents, the total acidity, the specific gravity, and the content of dry residue, organic and inorganic substances.

The protease activity was determined by Mett's method. Ths lipase activity was estimated by the vol-

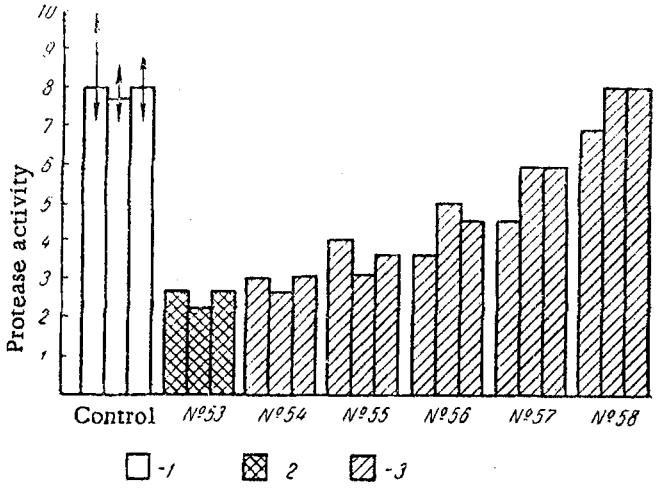

Fig. 2. Changes in the protease activity (in mm, by Mett's method) in the dog Rex after intravenous injection of pituitrin (during the latent period). 1) Mean results of control experiments; 2) protease activity on the day of injection of pituitrin; 3) protease activity on the days after injection.

ume of N/10 alkali used in the titration of the fatty acids formed in milk under the action of the lipase of the gastric juice. The free, combined and total hydrochloric acid contents and the total acidity were determined in the same sample by the generally accepted methods. In all, 92 experiments were performed on the three dogs.

RESULTS

After the subcutaneous and intravenous injection of pituitrin, the latent period of secretion was lengthened. Whereas in the dog Lyutik, for instance, this period normally lasted 10-18 minutes, after the subcutaneous injection of pituitrin it was extended to 35 minutes, and after intravenous injection—to 45-55 minutes. Lengthening of the latent period of secretion evidently suggests that pituitrin has a depressing action of the level of excitation of the gastric glands.

After the subcutaneous injection of pituitrin, the volume of gastric juice decreased slightly in all the experiments (Fig. 1), and corresponded to the lower limit of the variations in the control experiments. No more appreciable fall in gastric secretion could be observed. After the intravenous injection of pituitrin, however, during the latent period of secretion, we always observed a considerable decrease in the volume of gastric juice (to 1/2 or 1/4). If the pituitrin was injected at the height of secretion, then in the hour following injection, the volume of gastric juice fell sharply and amounted to 30-35% of the mean values in the control experiments. A fall in the volume of gastric juice, caused by the action of pituitrin, was also observed in the 1-2 days following its intravenous injection.

When we studied the changes in the enzymic activity of the gastric juice under the influence of pituitrin, in all the experiments we found a significant fall in the protease activity of the gastric juice, after both the subcutaneous and intravenous injection of pituitrin, regardless of the time of injection. Whereas after the subcutaneous injection of pituitrin, the protease activity fell on the average by 35-40%, however, after intravenous injection the preparation caused an even greater decrease in the protease activity, which amounted to only 20-25% of the average values of the control experiments. The intravenous injection of pituitrin resulted not only in a sharper but also in a more prolonged fall in the protease activity than after subcutaneous injection (Fig. 2). Whereas pituitrin, when injected subcutaneously, caused a decrease in the protease activity for 2-3 days, when injected intravenously in the same dose, it had the effect of depressing the protease activity for 5-6 days.

Pituitrin had a somewhat different effect on the lipase activity of the gastric juice (Fig. 3). The subcutaneous injection of this preparation caused hardly any changes in the activity of the lipase, if the fact that on

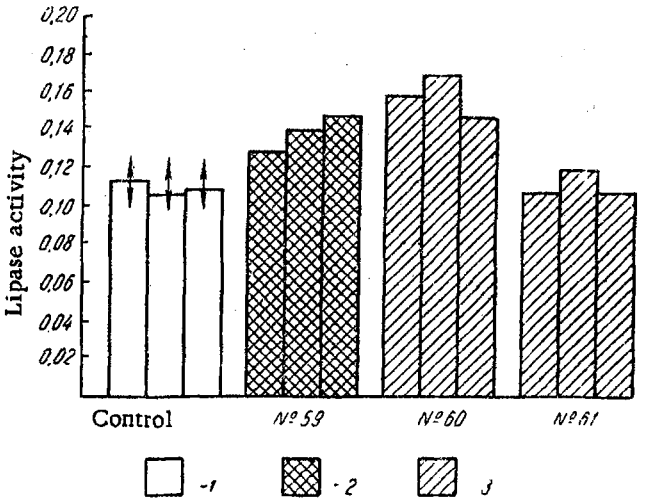

Fig. 3. Changes in the lipase activity (in ml 0.1/N NaOH) after the intravenous injection of pituitrin (during the latent period). 1) Mean results of control experiments; 2) lipase activity on the day of injection of pituitrin; 3) lipase activity on the days after the injection.

the day after injection the lipase activity rose (by 15-25%) is disregarded. After injection of pituitrin intravenously during the latent period of secretion the lipase activity on the day of the injection was either unchanged or slightly increased. On the next day we always observed a considerable increase in the activity of the lipase (by 40-60%), and in 2 experiments only, on the 3rd day, the lipase activity exceeded the upper limit of the variations of the control results; in the remaining experiments, on the 3rd day after injection of pituitrin no increase in the lipase activity was observed. The intravenous injection of pituitrin at the height of secretion produced a sharp increase (2-2 1/2 times) in the lipase activity in the 2nd hour of the experiment; the same was observed on the following 2-3 days.

During the investigation of the changes in acidity we found that the subcutaneous injection of pituitrin led to an insignificant decrease in the free hydrochloric acid content (by 8-12%) and an increase of roughly the same magnitude in the content of combined hydrochloric acid. We observed the same changes after the intravenous injection of pituitrin (irrespectively of the time of injection), but in a more pronounced form. The changes in the total hydrochloric acid content and the total acidity, irrespectively of the mode of injection, did not extend beyond the limits of variation in the control experiments. In view of these findings, it may be assumed that the content of combined hydrochloric acid increased at the expense of a decrease in the content of free hydrochloric acid. Irrespective of the mode of injection of pituitrin, no changes in the acidity could be detected on the day after injection of the preparation.

After the subcutaneous and, especially, the intravenous injection of pituitrin, the specific gravity of the gastric juice showed an increase. Whereas normally its value was 1.009-1.012, after injection of pituitrin it rose to 1.018-1.030. A very slight increase in the specific gravity was also observed on the next day.

Because of the increase in the specific gravity, we investigated the action of pituitrin on the content of dry residue. It was found that the content of dry residue increased irrespectively of the mode of injection of the pituitrin, but after intravenous injection the increase was more sharply expressed. The increase in the dry residue, like that in the specific gravity, was observed also on the following 2-4 days.

When the content of organic and inorganic substances in the dry residue was studied, it was found that the increase in the total dry residue took place mainly at the expense of organic substances, for the content of inorganic substances increased only very slightly.

It must be mentioned that pituitrin, when injected intravenously, caused sharper and more prolonged changes in the quantity and quality of the gastric juice than when injected in the same dose, but subcutaneously. This was evidently because absorption of pituitrin from the subcutaneous cellular tissue into the blood stream takes place gradually; as a result of this, its concentration in the blood does not reach high values, the more so because when the pituitrin does enter the blood it is partially destroyed. After intravenous injection, the concentration of pituitrin in the blood at once reaches a high level, which leads to the stronger effect of the action of the preparation.

Among the extensive literature reports there is no unanimity about the mechanism of action of pituitrin on the gastric glands. An attempt has been made [14] to explain the diminished secretion resulting frm the action of hypophysin by constriction of the blood vessels in the abdominal cavity and to a reduction in the blood supply of the stomach. In another paper [15], the same author considers that hypophysin acts on the secreto-depressor fibers of the splanchnic nerve.

Several authors [3,11,12,13] account for all the changes in the gastric secretion by an anemia of the stomach arising from the action of vasopressin. The opinion has also been expressed [7] that the action of hypophyseal preparations in depressing secretion "depends on the direct influence of the hypophyseal hormone on the gland cell or on its nerve endings".

It may be postulated that in the mechanism of action of pituitrin a part is played both by its influence on the vessels of the gastric mucosa, causing anemia, and by changes in the trophism of the glandular apparatus. Our hypothesis is supported by the fact that in all the experiments the changes in the qualitative composition of the juice were more prolonged than the quantitative changes.

These findings clearly show that pituitrin causes considerable and lasting changes in the working of the glandular apparatus of the stomach.

From the results obtained, the suggestion can be made to clinicians that patients suffereing from hypochlorhydric and achlorhydric gastritis, and also patients with dyspeptic disorders and other chronic diseases of the stomach, should be given pituitrin with great care, and in general its use in these patients should be avoided, for it should be replaced by drugs with a similar action, but which do not interfere with the working of the gastric glands.

SUMMARY

This work dealt with the study of the effect of pituitrin on the activity of gastric glands in Pavlov and Heidenhain stomach pouches. The volume of juice is decreased with administration of pituitrin. The latter also reduced the protease activity and increased the lipase activity of the gastric juice: The amount of free hydrochloric acid is diminished and that of the combined hydrochloric acid rises; however, the total hydrochloric acid content and the total acidity remain unchanged. Both specific gravity and dry residue are increased, the latter on account of organic substances.

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