PARTICIPATION OF THE NERVOUS SYSTEM IN THE ACTION OF SECRETIN

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Bayliss and Starling (1902) denied participation of the nervous system in the secretion-inducing action on the pancreas of both secretin and of hydrochloric acid. However, this topic remained debatable owing to the existence of contradictory data.

Much factual material has accumulated over recent years concerning the mechanism of hydrochloric acid action on the pancreas; these data indicate that hydrochloric acid solutions, on the one hand, stimulate the formation of secretin in the small intestine and, on the other hand, affect reflexly the secretory function of the pancreas. A. V. Solov'ev [6], for example, observed considerable reduction in volume of acid-induced pancreatic secretion associated with subcutaneous injection of ergotoxin. Facts pertaining to participation of the nervous system in the acid-induced pancreatic secretion have also been obtained by T. V. Serbeniuk [5], Z. V. Kobakhidze [3] and V. E. Robinson [7]. Nevertheless, up to the present some questions concerning the mechanism of secretion-inducing action of secretin on the pancreas still remain unclear. In particular, it is not clear whether secretin acts directly on the secretory tissue of the gland or affects it by a reflex mechanism.

The aim of the present work, suggested by Professor E. S. Airapet'iants was to probe the reflex component of secretin action. An attempt was made to elucidate the distinctive features of direct action of secretin on the receptors of a humorally-isolated area of the intestine connected with the organism by nervous connections only.

A brief report of the results of our first investigations was made at the Conference on Problems of Physiology and Pathology of Digestion [1].

EXPERIMENTAL METHODS

Short-term experiments were performed on cats under urethane anesthesia, using the well-known perfusion techique. The following functions were recorded during the experiments: blood pressure in the carotid artery, respiration by way of a tracheotomy tube, and volume of pancreatic secretion by means of a drop-recorder. Secretin prepared by the Bayliss and Starling method was used in most of the experiments. In control experiments secretin obtained by the method of Weaver [10] was used, as well as the crystalline secretin preparation (Eli Lilly and Company, Indianapolis).

EXPERIMENTAL RESULTS

The results of 30 experiments showed that introduction of 1-5 ml secretin into the stream of perfusion fluid gave rise to changes both in blood pressure and (in half the experiments) in respiration (Fig. 1). The area of intestine stimulated by secretin was connected with the organism by nervous connections only, so that changes in cardiovascular and respiratory activity could only be induced by reflex action of secretin. However, no pancreatic secretion could be observed even when large doses of secretin were introduced into the perfusing fluid. Nor could any appreciable differences be detected in the reflex action of secretin on using it to stimulate the

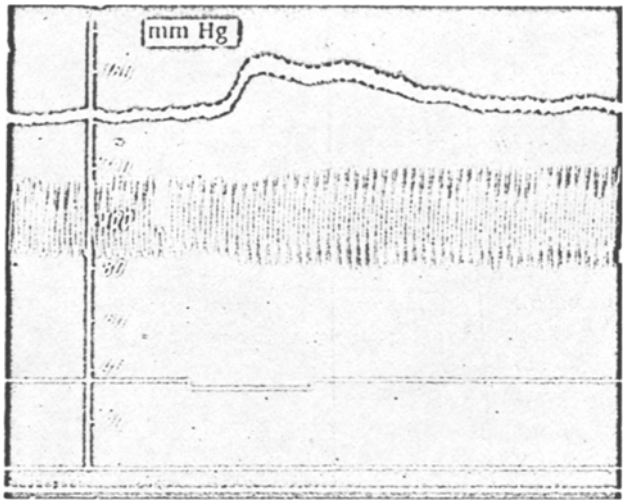

Fig. 1. Changes in blood pressure level and character of respiratory movements on introduction of 2 ml secretin (prepared by the Bayliss and Starling method) into the blood vessels of a perfused area of intestine.
Experiment No. 28, July 31, 1952. Records from above down: blood pressure, respiration, stimulus marker, base line, time marker (1 second).

receptors in different parts of the small intestine. The magnitude of changes in the blood pressure and respiration depended on the amount of secretin introduced. Thus, for example, in Experiment No. 27 (June 26, 1952) addition of 1 ml secretin to the perfusate caused a rise of 8 mm Hg in the blood pressure, and addition of 5 ml secretin increased the blood pressure by 24 mm Hg.

No changes were ever noted in the activity of the cardiovascular and respiratory systems when Tyrode solution in amounts similar to those of secretin was introduced into the perfusate; the same techniques were employed throughout. A similarly negative result was obtained when the chemical medium used for the preparation of secretin was tested (0.5% solution HCl and 10% solution NaOH at pH 6.65).

Secretin obtained by the method of Bayliss and Starling possesses vasodilator properties and special control experiments were therefore staged in which secretin free of vasodilator properties, prepared by the method of Weaver, was used. Changes in cardiovascular activity were noted in this case also. However, this considerably more highly purified secretin extract (as the mucosal extract of Bayliss and Starling) contains a series of other substances (pancreazymin, cholecystokinin) which may have, in some way, exerted a reflex influence resulting in the observed phenomena. To resolve these doubts, we resorted to Bayliss' and Starling's reference to the fact that secretin was absent in the lower part of the small intestine. It seemed to us that introduction into the perfusate of the extract of mucosa from the lower portion of the small intestine, containing all the same substances as the extract from the upper portion of the small intestine (excepting secretin) could, under the given experimental conditions, give valuable control results. The experiments, however, showed that in this case also changes occurred in respiration and blood pressure.

Subsequent experiments showed that intravenous injection of extract from the mucosa of the lower portion of the small intestine also induced pancreatic secretion. Eleven supplementary experiments were performed in order to determine the distinctive features of the secretory action of this extract; these experiments revealed that the latter's activity was one-quarter to one-fifth, on the average, of that exhibited by the extract prepared from the upper portion of the small intestine (Fig. 2). On the basis of literature data [8, 9] as well as of our experiments, it may be supposed that the mucosa of all parts of the small intestine contains

secretin, whose secretion-inducing action diminishes with distance from the duodenum. Therefore the extract from the lower portion of the small intestine could not be used in our experiments as control with respect to the observed fact of reflex influence of secretin. It was only possible to resolve doubts as to the ability of secretin to be a stimulus for receptor endings of the small intestine by performing experiments with a chemically pure, standard preparation of secretin. The results of these experiments demonstrated that a dose of 10-20 clinical units of secretin was quite sufficient to induce a rise of blood pressure when introduced into the vessels of the perfused area of the intestine (Fig. 3).

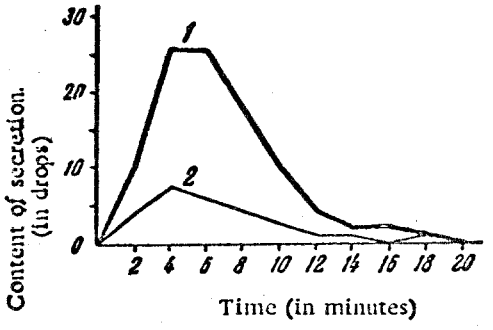

Fig. 2. Comparison of activity of secretin obtained by the Bayliss and Starling method from the mucosa of the upper portion of the small intestine (1) with the action of secretin obtained by the same method but from the lower portion of the small intestine (2). In both cases 5 ml secretin was injected intravenously. Experiment No. 35, August 8, 1952.

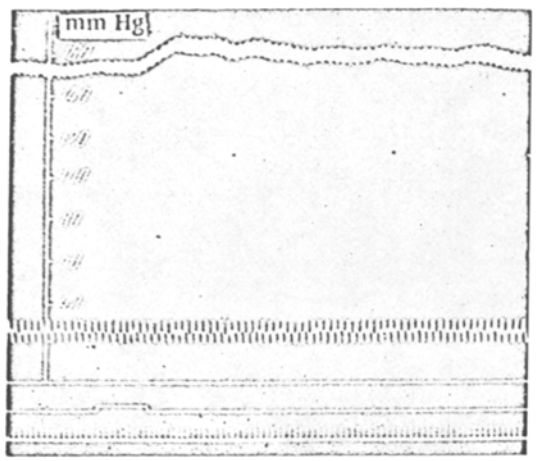

Fig. 3. Changes in blood pressure level and respiration in experiment with introduction of 20 clinical units of a chemically pure standard preparation of secretin into the vessels of a perfused area of the intestine. Records from above down: blood pressure, respiration, base line, marker denoting stimulation, time marker (1 second). Experiment No. 67, February 8, 1957.

In 1946 V. A. Alekseev [2], using the pancreatic perfusion technique, observed changed in blood pressure and respiration on introduction of secretin into the pancreatic vessels, i.e., he demonstrated the action of secretin on the receptor apparatus of the pancreas. Analogous work on the histological plane was carried out by L. V. Oleandrov [4]. The author concluded from the evidence of simultaneous staining of secretory and nervous tissue of the pancreas under the influence of intravenously administered secretin that the latter acted not only on the secretory cells of the pancreas but also on its local nervous centers. The data obtained in our experiments should be considered in the light of data reported by the above-mentioned authors. The results of the present investigation indicate that secretin, being an intestinal chemoreceptor stimulant, excites the sensory endings embedded in the walls of the small intestine at the site of its formation.

Material demonstrating the regulatory significance of these reflex influences on the functional state of the pancreas is presented in another communication.

SUMMARY

The effect of secretin on the interoceptors of the small intestine was studied in short-term experiments.

It was demonstrated that introduction of secretin into the vessels of the perfused area of intestine connected with the organism by the nerves alone caused changes in the activity of the cardiovascular and respiratory system by reflex pathways. The results of these experiments give grounds for concluding that secretin stimulates the intestinal chemoreceptors.

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