EFFECT OF SECRETIN ON BILE SECRETION UNDER CONDITIONS OF PARTIAL DENERVATION OF THE LIVER

(UDC 612.357.3-06:[612.358+612.332.84)

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 59, No. 1,
pp. 49-52, January, 1965
Original article submitted September 24, 1963

The effect of secretin and hydrochloric acid on the bile-secretory function of the liver has been demonstrated in many investigations [1, 4, 9-13], however, we do not find in the literature information on the role of the nervous system in the effect of secretin on bile secretion. Only experimental data on the value of the nervous system in accomplishing the effect of secretin and hydrochloric acid on the secretion of the pancreas are available [3, 5-8].

In the present investigation we studied the effect of secretin on bile secretion under conditions of partial denervation of the liver.

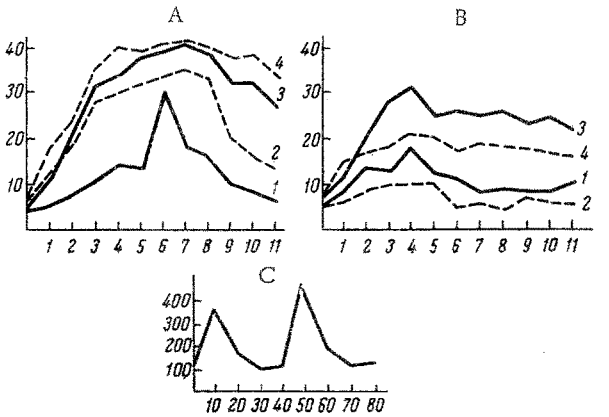

Fig. 1. Bile secretion of dogs (A) and of cats (B) with intravenous injection of secretin. The experiment on the dog was carried out on the 15th day after vagotomy with the use of 5 units of secretin (C). Time (in min) is plotted on the axis of the abscissa and the bile secretion (in drops) is plotted on the axis of the ordinate. The continuous lines indicate bile secretion of intact dogs and cats and the dashed lines indicate bile secretion of preliminarily (10 days before) vagotomized animals. A: 1 and 2) Injection of 5 units of secretin; 3 and 4) 10 units of secretin; B: 1 and 2) injection of 2 units of secretin; 3 and 4) 5 units of secretin.

EXPERIMENTAL METHOD

The investigation was carried out in acute experiments on 55 dogs and cats. Under morphine-hexobarbital sodium anesthesia for dogs and under sodium hexobarbital anesthesia for cats, a glass cannula was inserted into the common bile duct. The cystic duct was ligated. The pyloric end of the stomach was separated from the duodenum by a tight ligature. The trachea of the animal was connected with an apparatus for artificial respiration. Secretion of bile was recorded graphically by means of a recorder that we designed.

In the experiments we used crystalline secretin extracted from the mucosa of the duodenum [2].

The experiments were carried out both on animals with intact innervation of the liver and on animals on which we performed preliminary (for several days before the acute experiment) supradiaphragmatic vagotomy or splanchnicotomy, or bilateral excision of the spinal ganglia in the D_5-D_{10} segments of the spinal cord. Secretin was injected into the femoral vein in a quantity of 5-10 units in the experiments on dogs and 2-5 units in the experiments on cats. In each experiment we made not more than 3 injections of secretin and the secretion of bile was recorded not less than an hour after each injection, although the immediate effect from the injection terminated much earlier.

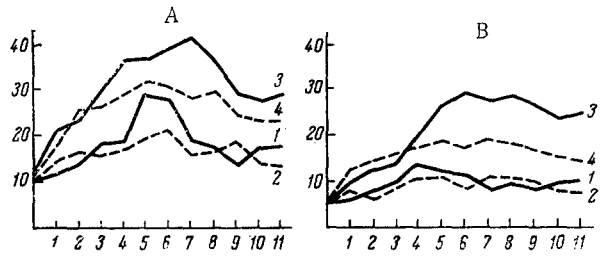

Fig. 2. Bile secretion of intact and preliminarily (15 days before) splanchnicotomized dogs (A) and cats (B). Designations are the same as in Fig. 1.

EXPERIMENTAL RESULTS

After the intravenous injection of 5-10 units of secretin into dogs with an intact innervation of the liver we noted an evident enhancement of bile secretion which usually began 2 min after injection. Bile secretion reached a maximum on the 5-6th min after injecting the secretin. Beginning with the 6th min after injection the intensity of bile secretion gradually dropped and by the 12-15th min returned to the initial level. The direct dependence of the degree of evidence of the effect on the quantity of secretin injected was established.

Then by the same method we carried out experiments on animals that had undergone surgery.

On the 10th day after bilateral supradiaphragmatic vagotomy the intravenous injection of secretin also caused an evident secretion of bile. A characteristic feature of the experiments of this series was the appearance of secondary enhancement of secretion 50-65 min after the injection of secretin. By this time the primary enhancement of secretion, which had ensued immediately after the injection of secretin, disappeared. On the 15th day after vagotomy the secondary increase in secretion in response to a single injection of secretin became more evident and frequently exceeded in magnitude the primary increase which had ensued immediately after injection of secretin (Fig. 1C).

Excision of various endocrine glands (adrenals, thyroid, pancreas) denervation of the kidneys, transection of the spinal cord under the medulla oblongata did not eliminate the secondary rises of secretion after a single injection of secretin.

The quantity of bile secreted during the 1st phase of the effect of secretin also increased. We see from Fig. 1A, in which the results of experiments on four dogs are shown, that the increase in the secretion of bile when 5 units of secretin were used was especially appreciable. A statistical analysis of the data in the investigation showed that on the 10th day after bilateral vagotomy 5 units of secretin caused bile secretion which exceeded by 44.5% that in the control experiments. Secretin in a dose of 10 units on the 10th day after vagotomy caused a 23% increase of bile secretion as compared with the control.

These facts show that transection of the vagus nerves leads to an appreciable increase in sensitivity of the secretory elements of the liver to secretin, which to a greater degree is manifested with respect to small doses of secretin. It is necessary to note that in the control experiments, just as after denervation, larger doses of secretin always causes a more appreciable secretory effect.

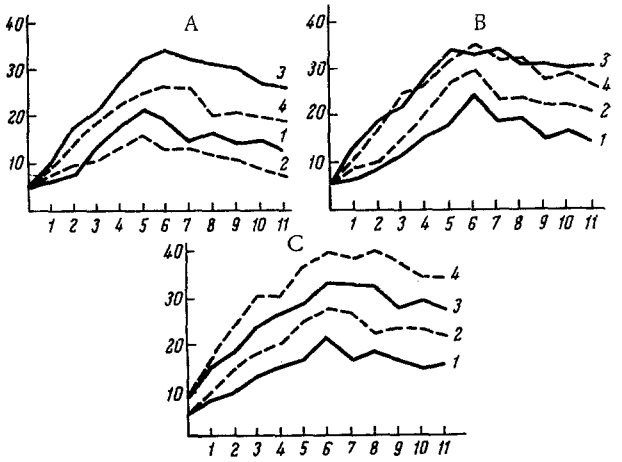

Fig. 3. Bile secretion to intravenous injections of secretin in intact dogs on the 10th (A), 50th (B), and 90th (C) days after excision of the spinal ganglia. Designations are the same as in Fig. 1.

On the 15th day after supradiaphragmatic vagotomy the secretin sensitivity of the secretory elements of the liver increased to an even greater extent.

In the experiments on cats bilateral supradiaphragmatic vagotomy also appreciably changed the reaction of the hepatic secretory elements to the injection of secretin (Fig. 1B). For cats, unlike for dogs, bilateral supradiaphragmatic vagotomy lead to an appreciable drop of bile secretion to secretin both on the 10th and on the 15th day post-operation. However, just as for the dogs, for cats there was a second phase of secretion after a single injection of secretin.

After bilateral section of the greater splanchnic nerves of dogs the secretory effect to secretin dropped considerably, (Fig. 2 A). Upon injection of 5 units of secretin after splanchnicotomy bile secretion dropped by 31.7% in comparison with the control experiments and with an

injection of 10 units, by 38.1%. In the experiments on cats bilateral splanchnicotomy also led to a decrease of bile secretion to secretin (Fig. 2 B). The reaction of the hepatic cells both of the dogs and the cats decreased especially noticeably upon injection of large doses of secretin.

In the experiments on dogs we also investigated the effect of secretin on bile secretion at various periods after spinal deafferentation of the liver (on the 10, 50, and 90th day).

On the 10th day after deafferentation we noted a proportional decrease of bile secretion upon the injection of large and small doses of secretin (Fig. 3A). On the 50th day after deafferentation in the experiments with the use of 5 units of secretin, an increase in the sensitivity of the secretory elements of the liver was elicited. Bile secretion upon injection of 5 units of secretin increased on the average by 44.3%, whereas with an injection of 10 units of secretin it, for all practical purposes, did not change (Fig. 3 B). On the 90th day after deafferentation we noted an even more intense secretion of bile with the use of both small and large doses of secretin (Fig. 3C).

On the 50th and 90th days after bilateral excision of the spinal ganglia, just as in the experiments with preliminary vagotomy, there occurred a secondary rise of secretion. However, in the experiments with deafferentation of the liver the secondary enhancement of secretion was appreciably less evident that in the experiments with vagotomy and in magnitude it never exceeded the primary increase which began immediately after injection of secretin.

It is evident from these data that the effect of secretin on bile secretion persists after all types of denervation of the liver. Disruption of the parasympathetic innervation of the liver of dogs leads, for a certain period of time after operation, to an increase of secretin sensitivity of the secretory apparatus of the liver. In cats, on the other hand, the secretin sensitivity of the liver after vagotomy dropped. The increase of secretin sensitivity of the hepatic cells of dogs also persisted for a certain time after excision of the spinal ganglia at the middle thoracic segments. We noted a phasic change of sensitivity to secretin depending on the period that had elapsed after denervation and on the quantity of secretin used.

Partial deprivation of the liver of sympathetic innervation by preliminary section of the greater splanchnic nerves of dogs and cats led to a pronounced drop of the secretin sensitivity of the hepatic secretory elements.

SUMMARY

In experiments on dogs and cats at various periods after the supradiaphragmatic vagotomy, bilateral section of the greater splanchnic nerves or excision of spinal ganglia in the D_5-D_{10} segments a study was made of bile secretion in response to the intravenous injection of purified secretin.

Disturbance of the parasympathetic innervation of the liver in dogs leads at difinite periods of time to a rise in the sensitivity of the hepatic secretory apparatus to secretin. In cats under similar conditions there is a drop of hepatic cell sensitivity to secretin. A rise of hepatic cell sensitivity to secretin was seen at definite periods after spinal deafferentation of the liver in dogs.

Partial loss of the sympathetic innervation by the liver, resulting from section of the greater splanchnic nerves, led to a marked reduction of the secretin sensitivity of hepatic secretory elements both in dogs and in cats.

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