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Liver as a Factor of Change of Gastrin Mechanisms of Regulation of Digestive Glands of the Stomach

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Abstract We studied the influence of factors affecting liver utilization of short-chain peptides as modifying mechanisms in the regulation of the digestive glands of the stomach. It was concluded that the short-chain peptide pentagastrin containing 5 amino acids is largely utilized by the liver, and the long-chain peptide gastrin-17 containing 17 amino acids is slightly utilized by the liver. Trypsin when passing through the liver reduces the utilization of pentagastrin by the liver, thereby stimulating the secretory function of the stomach. The protease inhibitor kontrakal during the passage through the liver increases the utilization ability of the liver pentagastrin, thereby reducing the secretory function of the stomach. The trypsin-inactivated pancreas and its inhibitors may be involved in the modification of the gastrin mechanisms of regulation of the digestive glands of the stomach.

Keywords Liver, Utilization, Pentagastrin, Gastrin-17, Trypsin, Contrical, Rats, Gastric secretion, Pancreatic secretion

To date, in animals and humans, most peptides are present in more than one molecular form. At the same time, at least 10 molecular forms of peptides of the gastrin (G) group were revealed, containing in their structure from 4 to 56 amino acids, the physiological role of which has been little studied [15].

The separation into short chain peptides and long chain peptides was carried out conditionally according to the results of studies where the physiological participation of the liver in increased utilization of short chain peptides containing up to 10 amino acids and low utilization of long chain peptides containing more than 10 amino acids was shown. Thus, influencing the regulation of the secretory, motor and neuromodulating functions of the digestive glands [2,10,11]. These data are consistent with the results of clinical studies, which demonstrate the presence of an excessive amount of circulating intestinal peptides that the diseased liver cannot utilize [8,13,14].

Short-chain peptides have receptors on the afferent nerve endings of peripheral neurons and on neurons of various parts of the central nervous system. In the stomach and intestines, paracrine, they interconnect endocrine cells and neurons of the submucosal nerve plexus, mesenteric and afferent neurons. Thus, short-chain peptides are of great importance in the integration of various regulatory mechanisms.

An increase in the production of short-chain peptides detected after food enters the gastrointestinal tract. In addition, short-chain peptides more efficiently stimulate the secretion of digestive glands and penetrate the blood-brain barrier. For example, due to CCK-8, a feeling of fullness is triggered, that is, a distant relationship between the cells of the digestive glands and various parts of the central nervous system is provided. This confirms the participation of short-chain peptides in the integration of peripheral and central mechanisms of regulation of the digestive glands.

The utilization capability of the liver decreases in chronic liver diseases, due to which CCK-8 increases in the peripheral blood, as a result, encephalopathy can develop [11], as well as pancreatic hypersecretory syndrome [9,12] and gastric hyposecretory syndrome [13].

In the supply of short-chain peptides to peripheral blood in the absence of physiological need, limiting mechanisms exist. So, part of short-chain peptides can be utilized in the intestine by intraorgan organ tissue and membrane proteases, and the other part in the liver, after entry through the portal system [1,10].

The described mechanisms form additional channels of peptidergic regulation of the digestive glands.

In recent years, in connection with the discovery of protease-activated receptors. It is suggested that pancreatic proteases should not be considered only from the traditional point of view as digestive enzymes, but additionally as signaling molecules that are actively involved in the spectrum of physiological and pathological conditions of both the gastrointestinal tract and other body systems. It is proposed that proteases as a whole be considered hormones, and the formation in this connection of new signaling pathways, as new regulation mechanisms in physiological

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conditions or new pathogenetic links in pathological conditions. [14].

Previously, the participation of the liver in the utilization of short-chain peptide regulators (pentagastrin, leienkephalin, and CCK-8) was shown in our laboratory, which can be considered as an additional modifying factor in the peptidergic mechanisms of regulation of the digestive glands [4]. It was also established in our laboratory that, under the influence of intravenous administration of trypsin, the enzymatic excretory activity of the gastric glands increases [5].

Objective: To study the influence of factors affecting the utilization of short-chain peptides by the liver as modifying mechanisms in the regulation of the digestive glands of the stomach.

1. Material and Methods

The studies were carried out on 98 rats in 14 series, 7 acute experiments in each series. We studied the change in gastric secretion, in 1 series (control) when 0.3 ml of physiological solution was injected into the portal vein, in 2 series (control) when 0.3 ml of physiological solution was introduced into the peripheral vein.

In the 3 series (experimental), a short-chain peptide - penta-gastrin (G-5) was injected into the portal vein at a dose of 0.1 μg / kg in 0.3 ml of physiological saline, in 4 series (experimental) - G- was introduced into the peripheral vein 5 at a dose of 0.1 μg / kg in 0.3 ml of physiological saline.

In the 5th series (experimental), a long-chain peptide gastrin-17 (G-17) was introduced into the portal vein in an equimolar dose to pentagastrin of 0.28 μg / kg in 0.3 ml of physiological saline. In the 6th series (experimental), a long-chain peptide G-17 was introduced into the peripheral vein in an equimolar dose to pentagastrin 0.28 μg / kg in 0.3 ml of physiological saline.

In the 7th of series (experimental), 0.3 ml of physiological saline was injected into the portal vein and, additionally, a contrical protease inhibitor (aprotinin) of 25,000 ATPE / kg was administered intraperitoneally.

In the 8th series (experimental), 0.3 ml of physiological saline was injected into the peripheral and, additionally, a Contrical protease inhibitor (aprotinin) of 25,000 ATPE / kg was administered intraperitoneally. In the 9th series (experimental), G-5 was injected into the portal vein at a dose of 0.1 μg / kg in 0.3 ml of physiological saline and an additional contrical protease inhibitor (aprotinin) of 25,000 ATPE / kg was additionally administered intraperitoneally.

In the 10th series (experimental), G-5 was injected into the peripheral vein at a dose of 0.1 μg / kg in 0.3 ml of physiological saline and a contrical protease inhibitor (aprotinin) of 25,000 ATPE / kg was additionally injected intraperitoneally.

In series 11 (experimental), trypsin was injected into the portal vein at a dose of 300 μg / kg in 0.3 ml of physiological saline. In the 12th series (experimental), 0.3 ml of physiological saline was injected into peripheral trypsin at a dose of 300 μg / kg.

In series 13 (experimental), G-5 was injected into the portal vein at a dose of 0.1 μg / kg, together with trypsin at a dose of 300 μg / kg in 0.3 ml of physiological saline. In series 14 (experimental), G-5 was injected into the peripheral vein at a dose of 0.1 μg / kg, together with trypsin at a dose of 300 μg / kg in 0.3 ml of physiological saline.

The study was performed under hexenal anesthesia: 0.3 ml of a 5% solution of hexenal per 100 g of body weight was intraperitoneally administered. Gastric secretion was investigated by continuous perfusion according to Ghosh and Schild [6]. Gastric perfusate was collected for 20 minutes in periods of 40 minutes (two 20-minute periods) before and 40 minutes (two 20-minute periods) after administration of 0.1 mcg / kg penta-gastrin intraportally in 0.3 ml of physiological saline.

As part of gastric perfusion solution, the following were determined: the isolation of proteases by total proteolytic activity (OPA) by spectrophotometric method [3,7], the hydrochloric acid rate by titration with NaOH perfusion solution [3,7].

2. Results and Its Discussion

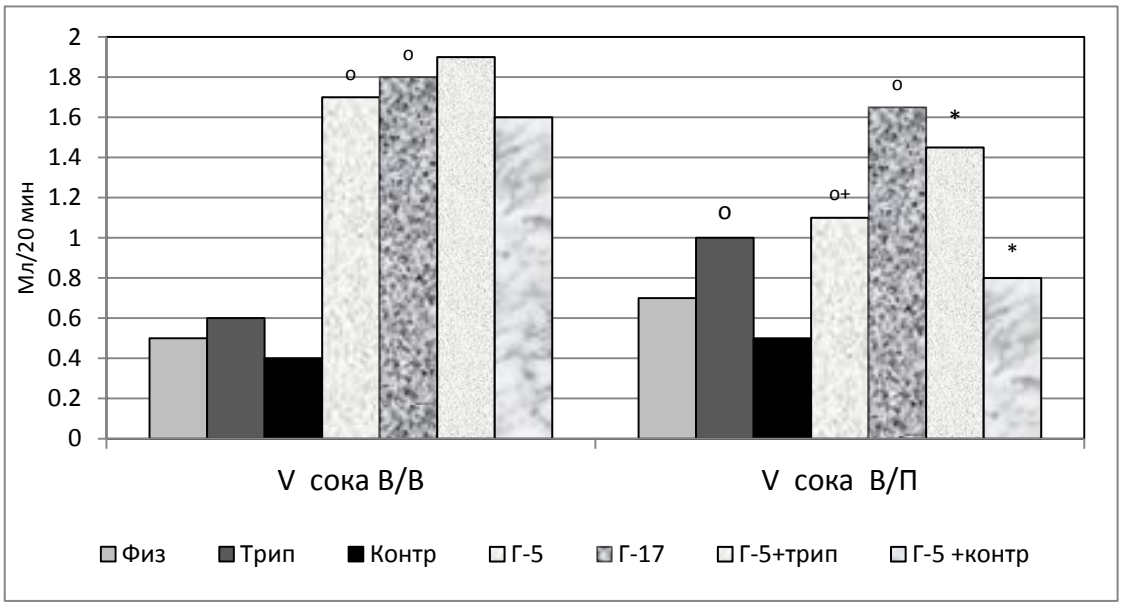
The results of experiments on rats showed that the volume of secreted gastric juice under the influence of trypsin in the peripheral vein (iv) was not significantly higher than after administration of physiological saline. And under the influence of trypsin injected into the portal vein (iv), it was significantly higher than after the introduction of physiological saline (Fig. 1).

At the same time, the volume of secreted gastric juice under the influence of contracal in the peripheral vein (iv) was not significantly lower than after the introduction of physiological saline. At the same time, under the influence of contracal introduced into the portal vein (iv), it was also not significantly lower than after the introduction of physiological saline, but this effect was more pronounced than when introduced into the peripheral vein (Fig. 1).

The volume of secreted gastric juice under the influence of G-5 injected both into the peripheral vein and the portal vein was significantly higher than those after administration of physiological saline. Moreover, the parameters under the influence of G-5 injected into the portal vein were significantly lower than the parameters introduced into the peripheral vein. At the same time, under the influence of G-17, introduced into the peripheral vein (iv), the volume of secreted gastric juice was also significantly higher than after injections of saline and slightly higher than G-5 (Fig. 1). The intra-portal administration of G-17 caused a significant increase in the volume of gastric juice, as compared with the intra-portal administration of physiological saline and an unreliable increase in comparison with G-5.

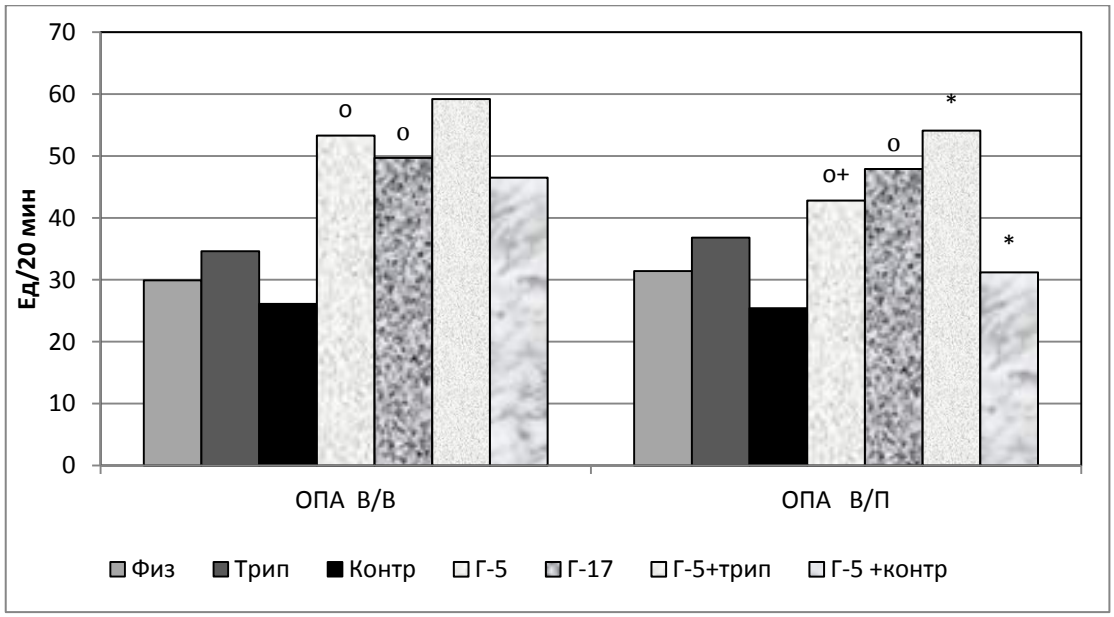
At the same time, the indices during intraportal administration of G-17 were slightly lower than when this peptide was introduced into the peripheral vein (Fig. 1).

With the combined administration of trypsin and G-5, in relation to the results of the administration of G-5 alone, there was an unreliable increase in indicators when injected into the peripheral vein and a significant increase when introduced into the portal vein. At the same time, under the influence of co-contracal and G-5, there was an unreliable decrease in indicators when injected into the peripheral vein and a significant decrease when introduced into the portal vein (Fig. 1).



about - significantly different values relative to indicators with the introduction of saline.
+ - significantly different values relative to indicators with the introduction of pentagastrin in the peripheral vein.
* - significantly different values relative to indicators with the introduction of pentagastrin into the portal vein.

Figure 1. Changes in the volume of gastric secretion in rats, when 0.3 ml of physiological saline, trypsin, kontrikal, pentagastrin G-5 (0.1 μg) is injected into the peripheral vein (B / B) and into the portal vein (B / P) / kg) and gastrin G-17 (0.28 mcg / kg), trypsin and together pentagastrin G-5, countercal and together pentagastrin G-5



about - significantly different values relative to indicators with the introduction of saline.
+ - significantly different results relative to indicators with the injection of pentagastrin in the peripheral vein.
* - significantly different results relative to indicators with the injection of pentagastrin into the portal vein.

Figure 2. Change in the OPA indices of gastric juice in rats, when 0.3 ml of physiological saline, trypsin, kontrikal, pentagastrin G-5 (0.1 μg) are injected into the peripheral vein (I / O) and into the portal vein (I / P) / kg) and. gastrin G-17 (0.28 μg / kg), trypsin and together pentagastrin G-5, contricale and together pentagastrin G-5

The gastric juice OPA after trypsin injection into both the peripheral vein and the portal vein was not significantly higher than after the administration of physiological saline, but slightly higher than when introduced into the peripheral vein. Changes in gastric juice OPA after the administration of contracal, both in the peripheral vein and in the portal vein, were unreliably lower than after the introduction of physiological saline, but more pronounced than when introduced into the peripheral vein (Fig. 2).

Under the influence of G-5, injected both in the peripheral vein and in the portal vein, the OPA indices were significantly higher than those after the administration of physiological saline. At the same time, the parameters under the influence of G-5 introduced into the portal vein were not significantly lower than the parameters introduced into the peripheral vein (Fig. 2).

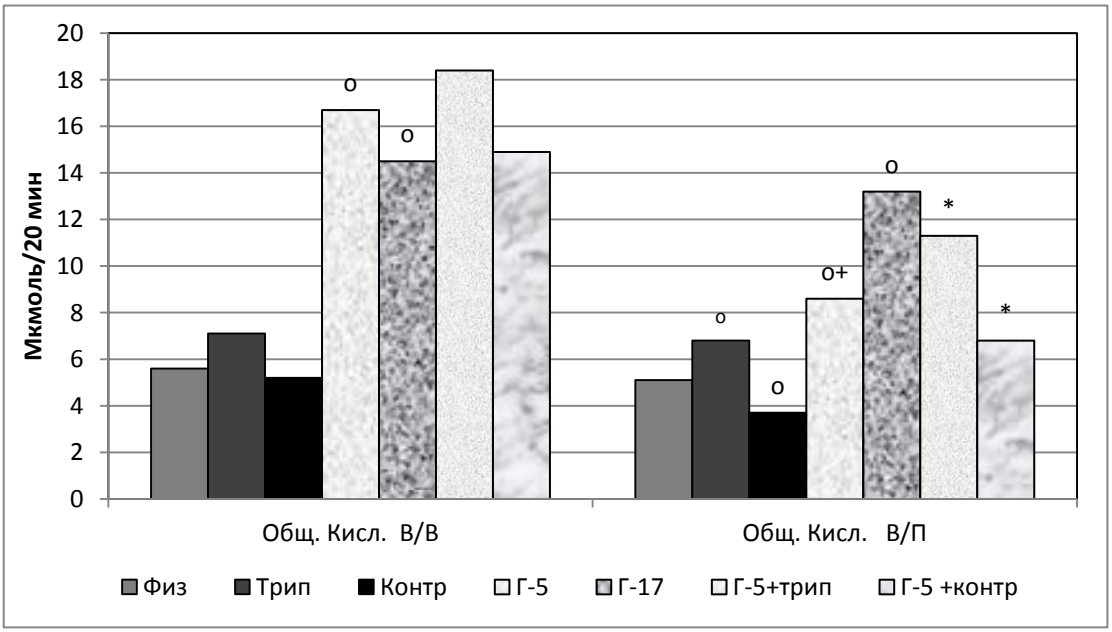
With the introduction of the G-17 peptide into the peripheral vein, the OPA results were also significantly higher in comparison with the data after the administration of physiological saline and slightly lower than after the administration of G-5. The intra-portal administration of G-17 caused a significant increase in OPA, compared with the intra-portal administration of physiological saline, and G-5. At the same time, the indices during intraportal administration of G-17 were slightly lower than when this peptide was introduced into the peripheral vein (Fig. 2).

Under the influence of the combined administration of trypsin and G-5, in relation to the results of the administration of G-5 alone, there was an unreliable increase in indicators when injected into the peripheral vein and a significant increase when introduced into the portal vein. At the same time, under the influence of co-contracal and G-5, an insignificant decrease in indicators was noted when introduced into the peripheral vein and a significant decrease when introduced into the portal vein (Fig. 2).

Indicators of total acidity of gastric juice had patterns detected in the allocation of the volume of gastric juice and OPA. After the introduction of trypsin into the peripheral vein (iv), these indicators were significantly higher than after the introduction of physiological saline. And under the influence of trypsin in the portal vein (v/p), they were significantly higher than after the introduction of physiological saline. Moreover, after the introduction of contracal into the peripheral vein (iv), these indicators were slightly lower than after the introduction of physiological saline. And under the influence of contracal in the portal vein (v/p), they were significantly lower than after the introduction of physiological saline (Fig. 3).

Under the influence of G-5 injected both into the peripheral vein and the portal vein, the indicators of total acidity of gastric juice were significantly higher than those after the introduction of physiological saline. Moreover, the parameters under the influence of G-5 injected into the portal vein were significantly lower than the parameters introduced into the peripheral vein (Fig. 3).

After introduction into the peripheral vein, the effects of G-17 were significantly higher than the effects of saline, but slightly lower than those after the introduction of G-5. At the same time, intraportal administration of G-17 caused a significant increase in the total acidity of gastric juice, compared with intraportal administration of physiological saline, as well as G-5.



about - significantly different results relative to indicators with the injection of saline.
+ - significantly different values relative to indicators with the introduction of pentagastrin in the peripheral vein.
* - significantly different values relative to indicators with the introduction of pentagastrin into the portal vein.

Figure 3. Change in the total acidity of gastric juice in rats when 0.3 ml of physiological saline, trypsin, kontrikal, pentagastrin G-5 (0.1 mcg / kg) and. gastrin G-17 (0.28 μg / kg), trypsin and together pentagastrin G-5, contricale and together pentagastrin G-5

In this case, the indices during intraportal administration of G-17 were slightly lower than when this peptide was introduced into the peripheral vein (Fig. 3).

Under the influence of trypsin and G-5 together, in comparison with the administration of G-5 alone, there was an unreliable increase in indicators when injected into the peripheral vein and a significant increase when introduced into the portal vein, as well as a significant decrease relative to those in the peripheral vein (Fig. 3).

At the same time, under the influence of co-contracal and G-5, there was an unreliable decrease in indicators when introduced into the peripheral vein and a significant decrease when introduced into the portal vein, as well as a significant decrease in relation to those in the peripheral vein (Fig. 3).

The presented data show that the introduction of trypsin into the peripheral vein caused an unreliable increase in all the considered parameters in relation to those with the introduction of physiological saline. Whereas the introduction of trypsin into the portal vein caused an unreliable increase in OPA and a significant amount of gastric juice and total acidity relative to those with the introduction of physiological saline.

At the same time, with the introduction of contracal into the peripheral vein, an insignificant decrease in all the considered indicators was noted in relation to those with the introduction of physiological saline, and its introduction into the portal vein caused an unreliable decrease in the indices of the volume of gastric juice, OPA and significant total acidity in relation to those with the introduction saline solution. This indicates a greater severity of effects with the introduction of trypsin and contracal into the portal vein.

It was found that when passing through the liver of short-chain pentagastrin, a significant decrease in secretory effects occurs, which is expressed in significantly low indices of the volume of gastric juice, OPA and general acidity. In this case, the introduction of trypsin into the peripheral vein together with pentagastrin caused an unreliable increase in all considered indicators in relation to those indicators with the introduction of only pentagastrin.

At the same time, the introduction of trypsin into the portal vein together with pentagastrin caused a more pronounced increase compared to the introduction into the peripheral vein of all the considered parameters. The introduction of contracal into the peripheral vein together with pentagastrin caused an unreliable decrease in all the considered parameters in relation to those with the introduction of only pentagastrin. And the introduction of contracal into the portal vein together with pentagastrin caused a more pronounced decrease compared to the introduction into the peripheral vein of all the considered indicators.

Thus, pancreatic hormone trypsin and its inhibitors are factors that influence the utilization of short-chain peptides by the liver, which can be involved in modifying gastrin mechanisms of regulation of the digestive glands of the stomach.

3. Conclusions

The short-chain peptide pentagastrin is largely utilized by the liver, and the long-chain peptide gastrin-17 is slightly utilized by the liver. Trypsin, when passing through the liver, reduces the ability of the liver to utilize pentagastrin, thereby stimulating the secretory function of the stomach. The protease inhibitor contrikal when passing through the liver increases the ability of the liver to utilize pentagastrin, thereby reducing the secretory function of the stomach. Pancreatic hormone trypsin and its inhibitors can be involved in the modification of gastrin mechanisms of regulation of the digestive glands of the stomach.

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