Acetylcholine and Serotonin are Neurotransmitters for the Management of Pancreatic Secretory Activity

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Abstract

The article presents data on the determination of acetylcholine and serotonin. The chemical method for the determination of acetylcholine can be applied in the determination of acetylcholine in the blood. Reliable data have been obtained that reflect the state of the parasympathetic nervous system in alcoholic chronic pancreatitis. The main stimulant of the secretion activity of the pancreas is Ash, but with the progression of the disease, the stimulation of secretion changes. It becomes autonomous, and serotonin becomes the main stimulant, damaging the excretory activity of the pancreas.

Keywords: Acetylcholine; Serotonin; Chronic Alcoholic Pancreatitis; Secretion

Introduction

Neurotransmitter (neurotransmitter - a neurotransmitter) is a signal compound released at the nerve endings, acetylcholine, adrenaline, serotonin, histaminergic and other systems and acting within the synapse, but not only [1,2].

Hormones (hormone) - a bioregulator that spreads wirelessly and has a systemic effect. And in this case, the hormones can be neurotransmitters and serotonin autacoids (tissue hormones), which are released from the cells of the APUD system [2].

All these substances are present in the digestive tract, functionally dependent on each other, enhancing or inhibiting the final result of stimulation. Neurogenic stimulation of the secretory activity of the digestive organs is carried out by the vagus nerve, or rather, its neurotransmitter, acetylcholine (Ach). Endogenous Ach is a first-order mediator; it is present in almost all body tissues, participates in the transmission of nerve impulses, and in addition it acts on the metabolic processes of the cell, being a weak mitogen. It takes part in the transmission of nervous excitement in the central nervous system, autonomic nodes, the endings of parasympathetic and motor nerves. The ends of the nerve fibers for which it serves as a mediator are called cholinergic, and the receptors that interact with it are called cholinergic receptors. Cholinergic receptors are located on the outside of the postsynaptic membrane. Endogenous Ach has a wide range of effects, mainly providing an exciting effect. Given the above, it can be assumed that the level of Ach in the blood serum will differ depending on which organ is affected. The second stimulant in the digestive tract in its importance is serotonin (5-HT). These two physiologically active agents (FAA) are in a complex relationship and interdependence. In a healthy person, the average number of EC cells per 1 mm² of the cut-off area is about 16 in the antrum, and in the stomach's body there are 10 cells that secrete and deposit serotonin. In addition,
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the release of 5-HT occurs at the nerve endings of serotonergic terminals. 5-HT is a specific gastrointestinal regulator with endocrine, paracrine and neurocrine properties, which are synthesized here in the cells of the APUD system, the diffuse neuroendocrine gland of the gastrointestinal mucosa. The most extensive part of which is the enterochromaffin-serotonin system. The 5-HT life span is short, part of serotonin is converted to melatonin in the pineal gland cells or undergoes oxidative deamination with monoamine oxidase (MAO) - the MAO pathway. MAO is localized on the inner mitochondrial membrane of cells. Serotonin is captured by cells and subjected to oxidative deamination with monoamine oxidase to form 5-hydroxyindoleacetonic acid, and partly 5-hydroxyindoleacetic acid, which is excreted in the urine, normally up to 2 - 8 mg per day.

Aim of the Study

Research studies the change in the concentration of Ac in serum and serotonin in whole blood in patients with chronic pancreatitis of alcoholic etiology in order to find out if the change in the concentration of FAA causes the formation of a local pathology [3,4].

Materials and Methods

In patients undergoing treatment at the MSC named after A.S. Loginovai in the control group in blood serum determined the concentration of acetylcholine, serotonin and the activity of cholinesterase. The obtained digital indicators were processed using statistical analysis methods. To determine acetylcholine, a chemical reaction was used based on a specific reaction for acetylcholine and a number of other substances derived from carboxylic acid. This method is based on the reaction of acetylcholine with hydroxylamine in an alkaline environment. In this case, hydroxamic acids are formed, which with ferric salts at pH = 1.2 - 1.5 give a color reaction. The method is widely used to determine acetylcholine and acetylcholine-like substances in the blood and in other biological fluids. Each time, a standard was determined in parallel with the studies. When determining cholinesterase activity, acetylcholine was used as a substrate. In the tissue, the content of serotonin was determined by extracting it into acidified butanol. In the blood, the destruction of the formed elements with perchloric acid was preliminarily carried out, followed by extraction of serotonin into the butanol fraction. Blood was taken on an empty stomach and 20 minutes after a standard breakfast. The study included 108 chronic alcohol etiology. The control group consisted of 30 volunteers regularly undergoing a dispensary preventive examination. All groups were comparable by age and gender differences.

The entire data set was subjected to a graphical test for the normality of the distribution of the obtained data on the concentration of Ach and Che, which fit into the 95% confidence interval of the distribution (confidence interval of the obtained data) (Figure 1). In the control, the concentration of Ach is shifted to the left (see box with mustache), i.e. offset to the zone of lower values.

Figure 1: Acetylcholine concentration distribution.
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As can be seen in the graph, the lower and upper values of the Ach concentration are out of the 95% confidence interval; this is possibly the result of a permissible error in the biochemical method for determining the Ach concentration.

![Figure 2: Distribution of cholinesterase activity by optical density.](image1)

As you can see on the graph, the upper values of the lower values of cholinesterase activity go out of the 95% confidence interval.

Based on these data, table 1 is compiled, where quantitative values of the content of acetylcholine (mmol/l) in the blood serum of healthy individuals are entered. Thus, acetylcholine - the average value is 1.1 ± 0.15 mmol/L, but in healthy people there may be a concentration of Ax from 0.5 to 1.5 mmol/L. According to the frequency of occurrence, the data distribution series, as already indicated, is divided into three groups: the average component is 60% of the examined, with lower values - 15% and large values - 25%.

![Figure 3: Control level of acetylcholine, frequency of distribution of quantitative values.](image2)

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Serotonin, 5-hydroxytryptamine, 5-HT - is formed by hydroxylation of the essential amino acid tryptophan through 5-hydroxytryptophan. The place of its synthesis is enterochromaffin cells (EC cells) of the digestive tract, bronchi, brain (hypothalamus). Serotonin is found in large quantities in platelets that deposit serotonin but are not able to synthesize it. In the body, 99% of tryptophan is used for the synthesis of nicotinamide and proteins, and only 1% for serotonin. 5-HT is a specific gastrointestinal regulator with endocrine, paracrine and neurocrine properties, which are synthesized here in the cells of the APUD system, the diffuse neuroendocrine gland of the gastrointestinal mucosa. The most extensive part of which is the enterochromaffin-serotonin system. The 5-HT life span is short, part of serotonin is converted to melatonin in pineal gland cells and EC cells or undergoes oxidative deamination by monoamine oxidase (MAO) - the MAO pathway. MAO is localized on the inner mitochondrial membrane of cells. Serotonin is captured by cells and subjected to oxidative deamination by monoamine oxidase to form 5-hydroxyindoleaceturonic acid, and part of 5-hydroxyindoleaceturonic acid, which is excreted in the urine, is normally up to 2 - 8 mg per day.

The secretory function of the organs of the gastroduodenal region is carried out by a complex system of interconnection and independence of all regulatory components. In a healthy person, the average number of EC cells per 1 mm² of the cut-off area is about 16 in the antrum, and in the stomach's body there are 10 cells that secrete and deposit serotonin. In addition, the release of 5-HT occurs and/or on the nerve endings of the serotonergic gastroenteric nervous system.

The study of 5-HT in healthy individuals is of interest as one of the main indicators of the violation of the complex process of regulation of the functional activity of the digestive organs, their pathogenesis and sanogenesis. The physiological role of serotonin is being studied. In the central nervous system, he is a mediator. Biosynthesis and metabolism (exchange) of serotonin and its interaction with receptors are associated with a number of psychotropic drugs (antidepressants).
The peripheral effect of serotonin is characterized by a reduction in the smooth muscles of the uterus, intestines, bronchi of the stomach and intestines. Constriction of blood vessels. Serotonin is a mediator of inflammation, with subcutaneous administration a pronounced edematous effect. Reduces bleeding time by increasing platelet count and causing spasm of arteries and arterioles. It promotes the aggregation of blood cells, especially platelets, from which serotonin is released. 5-HT is released from the cells of the APUD system of the gastrointestinal mucosa. As you know, the concept of a medical norm has significant differences related to the research method, place of residence of the subjects, genetic adaptation to external conditions. Therefore, in the laboratories in which the studies are carried out, it is necessary to have their own standards obtained during the examination of a group of practically healthy individuals. Statistical processing was applied to the total mass of data obtained. Analyzing the entire array, we arranged it in order and quantity, divided by frequency of occurrence, which made it possible to distinguish several groups according to the parameters of interest to us (Figure). Selected groups were evaluated using Student’s criterion.

An increase in the 5-HT content from $0.23 \pm 0.007$ to $0.437 \pm 0.0063 \mu g/ml \ (p < 0.05; p < 0.01)$ was revealed in the blood of patients with AP. 230 to 437 nm/ml picture based on the quantitative values of serotonin, three groups (samples) were identified in the control group. With "low", "Medium" and "high" 5-HT content. The distribution of values in groups is uniform, there are no significant differences between groups ($p > 0.05$), the values are close, they tend to average.

Thus, quantitative differences in the 5-HT content from 0.14 to 0.24 μg/ml can be distinguished, the most common value being $0.18 \pm 0.03 \mu g/ml$. In patients with chronic pancreatitis, the 5-HT value is from 0.23 to 0.39 μg/ml (Table 1).

<table>
<thead>
<tr>
<th>5-HT mcg/ml</th>
<th>Overall</th>
<th>Low</th>
<th>Average</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>31</td>
<td>11</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>m</td>
<td>$0.304 \pm 0.056$</td>
<td>$0.23 \pm 0.007$</td>
<td>$0.298 \pm 0.006$</td>
<td>$0.393 \pm 0.014$</td>
</tr>
<tr>
<td>median</td>
<td>0.3</td>
<td>0.23</td>
<td>0.3</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Table 1: Blood serotonin levels in patients with chronic pancreatitis.
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As can be seen in figure, the distribution of data by the average values of serotonin is uniform, but they are divided into three independent groups. Each group has a significant difference with the control value - $p < 0.5$; $p < 0.01$; $p < 0.001$, respectively, but they also have significant differences between themselves - $p < 0.05$. They are combined into one group - “chronic pancreatitis” but can be distinguished into independent groups. A group of asymptomatic pancreatitis was identified when there is no clarity in the analysis of instrumental and clinical data. The concentration of 5-HT tends to increase depending on the stage and duration of the disease (Table 1).

As you can see, there is no clear separation between groups in this case. In patients with chronic pancreatitis of alcoholic etiology, using standard breakfast as a secretory stimulant, changes in the level of neurotransmitters before and after standard breakfast were determined. This made it possible in patients with chronic pancreatitis to check the stability of the revealed violations.

It was found that in the control group the 5-HT level was $0.19 \pm 0.02 \mu g/ml$, Ax $0.8 \pm 0.09 \text{ mmol/ml}$ and CE activity $0.9 \pm 0.09 \text{ mmol/ml}$ 30 minutes.

In the blood serum of patients with AP, an increase in 5-HT content of $0.40 \pm 0.07 \mu g/ml$ ($p < 0.01$) and Ax $1.7 \pm 0.3 \text{ mmol/ml}$ ($p < 0.05$), a decrease in CE activity $0.15 \pm 0.01 \text{ mmol/ml}$ 30 min ($p < 0.01$). With BP - 5-HT $0.28 \pm 0.04 \mu g/ml$ ($p < 0.05$) and Ax $1.5 \pm 0.12 \text{ mmol/ml}$ ($p < 0.05$), CE activity $0.4 \text{ mmol/ml}$ 30 min ($p < 0.05$).

Using a standard breakfast as a secretory stimulant, changes in the level of neurotransmitters before and after a standard breakfast were determined. In the control group, there is a tendency to increase 5-HT from $0.19 \pm 0.02$ to $0.23 \pm 0.019 \mu g/ml$ ($p > 0.05$). The level of Ax significantly increased from $0.8 \pm 0.06$ to $1.0 \pm 0.05 \text{ mmol/L}$ ($p < 0.05$). This increase in Ax was carried out due to a decrease in CE activity from $0.9 \pm 0.1$ to $0.5 \pm 0.04 \text{ mmol/L}$ for 30 minutes ($p < 0.01$). In patients with AP, the response of biologically active substances (BAS) to a standard breakfast changed: the 5-HT concentration increased from $0.40 \pm 0.07$ to $0.55 \pm 0.05 \mu g/ml$ ($p < 0.05$) and Ax decreased from $1.7 \pm 0.3$ to $1.6 \pm 0.3 \text{ mmol/L}$ ($p > 0.05$). CE activity is low, both before and after a standard breakfast ($0.15 \pm 0.01$ and $0.2 \pm 0.01 \text{ mmol/L}$ 30 minutes respectively). The initial high level of Ah with CP does not suggest an additional increase after food stimulation. In patients with PD for a standard breakfast: the 5-HT concentration increased from $0.28 \pm 0.04$ to $0.43 \pm 0.05 \mu g/ml$ ($p < 0.05$), Ax did not change significantly - $1.5 \pm 0.12 \text{ mmol/ml}$ and $1.45 \pm 0.21 \text{ mmol/l}$ ($p > 0.05$). CE activity after a standard breakfast decreased from $0.4 \text{ mmol/ml}$ 30 minutes, $0.3 \pm 0.05 \text{ mmol/ml}$ 30 minutes (Figure 6).

![Figure 6: Level of 5-HT on an empty stomach before and after food stimulation.](image_url)
The pyloroduodenal region is the center of the system of self-regulation of the function of the digestive organs. It is provided by specific gastrointestinal regulatory peptides with endocrine, paracrine and neurocrine properties, which are synthesized here, as well as intramural plexuses that interact with the extramural autonomic nervous system. Due to the mutual duplication of their effects (stimulation, inhibition), the reliability margin of the entire gastroduodenal system of self-regulation, synchronism, consistency, integration and self-monitoring of the activity of the digestive organs included in it are achieved.

The mucous membrane of the gastroduodenal zone is an extensive information and communication system that includes all regulatory mechanisms such as the nervous, endocrine, paracrine, cellular, and blood flow regulation system. This is a huge system, which includes not only the cells of the gastrointestinal mucosa, but also includes the relationship between the brain and intestines: the brain “intestines. Carrying out both direct and feedback, in some cases it can function autonomously.

In the pyloric part of the stomach, endocrine G-cells are localized, producing the gastrointestinal hormone gastrin and enkephalins. D cells produce somatostatin, which inhibits the production of gastrin. ECL cells located in the lower third of the gastric glands, producing histamine. Histamine is a powerful stimulant of hydrochloric acid production. The release of histamine from ECL cells occurs only after binding of gastrin to receptors located on the surface of parietal cells and an increase in intracellular calcium levels.

Argentophilic cells, in which the precursor of serotonin, 5-hydroxytryptophan, are detected throughout the coolant in its deep layers. Serotonin (5-HT), which (like histamine) belongs to biogenic amines, is involved in the regulation of gastric secretion, acting as a modulator of the action of gastrin, acetylcholine and histamine.

As can be seen in figure 6, the distribution of data by the average values of serotonin is uniform, but they are divided into three independent groups. Each group has a significant difference with the control value - p < 0.5; p < 0.01; p < 0.001, respectively, but they also have significant differences between themselves - p < 0.05. They are combined into one group - “chronic pancreatitis” but can be distinguished into independent groups. A group of asymptomatic pancreatitis was identified when there is no clarity in the analysis of instrumental and clinical data. The concentration of 5-HT tends to increase depending on the stage and duration of the disease (Table 1).

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Using a standard breakfast as a secretory stimulant, changes in the level of neurotransmitters before and after a standard breakfast were determined. In the control group, there is a tendency to increase 5-HT from 0.19 ± 0.02 to 0.23 ± 0.019 μg/ml (p > 0.05). The level of Ax significantly increased from 0.8 ± 0.06 to 1.0 ± 0.05 mmol/L (p < 0.05). This increase in Ax was carried out due to a decrease in CE activity from 0.9 ± 0.1 to 0.5 ± 0.04 mmol/L for 30 min (p < 0.01). In patients with AP, the response of biologically active substances (BAS) to a standard breakfast changed: the 5-HT concentration increased from 0.40 ± 0.07 to 0.55 ± 0.05 μg/ml (p < 0.05) and Ax decreased from 1.7 ± 0.3 to 1.6 ± 0.3 mmol/L (p > 0.05). CE activity is low, both before and after a standard breakfast (0.15 ± 0.01 and 0.2 ± 0.01 mmol/L 30 minutes respectively). The initial high level of Ah with CP does not suggest an additional increase after food stimulation. In patients with PD for a standard breakfast: the 5-HT concentration increased from 0.28 ± 0.04 to 0.43 ± 0.05 μg/ml (p < 0.05), Ax did not change.
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Conclusion

Acetylcholine concentration and cholinesterase activity level can be determined by acetylcholine, a chemical reaction was used based on a specific reaction for acetylcholine and a number of other substances derived from carboxylic acid. This method is based on the reaction of acetylcholine with hydroxylamine in an alkaline environment. In this case, hydroxamic acids are formed, which with ferric salts at pH = 1.2 - 1.5 give a color reaction.

Acetylcholine and serotonin are closely related and are involved in stimulating pancreatic secretion [5-7]. The concentration of neurotransmitters changes with pancreatic disease. They are not the primary cause of the disease. the presence of a pathology that changes both the release and destruction of the FAA.

Bibliography


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