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# FUNCTIONAL STATUS OF SMALL INTESTINE AFTER APPLICATION OF GUANETIDIDE SULFATE

*G.U. Urmanova, D.A.Karshiev, Y.N.Islamov*

Tashkent pediatric medical institute

✓ ***Rezume,***

***Experiments on rats with different ages have shown that some enzymes (such as lactase amylase, saccharase, dipeptihydrolase ) precisely determine the period of adaptation to milk nutrition. Accordingly we decided to determine the type of nutrition for some enzymes. Chemical desympathetization at the early stages of postnatal ontogenesis changed the development of hydrolytic function of the small intestine.***

***Key words: guanetidine, desympathetization, CNS-central nervous system, DT- digestive tract.***

# ФУНКЦИНАЛЬНОЕ СОСТОЯНИЕ ТОНКОГО КИШЕЧНИКА ПРИ ВОЗДЕЙСТВИИ ГУАНЕТИДИНА СУЛЬФАТА

*Г.У. Урманова, Д.А.Каршиев, Й.Н. Исламов*

Ташкентский педиатрический медицинский институт

✓ ***Резюме,***

***Опыты, проведённые с крысами различных возрастных категорий, показали, что некоторые ферменты (лактаза, амилаза, сахараза, дипептигидролаза) точно определяют период адаптации к молочному питанию. Поэому мы решили определить вид питание для некоторых ферментов. На начальных этапах постнатального онтогенеза химическая десимпатизации изменяет гидролитическую функцию развитие тонкой кишки.***

***Ключевые слова: гуанетиден, десимпатизация, ЦНС-центральное нервное систем, ЖКТ-желудочное кишечное тракте.***

# ГУАНЕТИДИН СУЛЬФАТ ТАЪСИРИДА ИНГИЧКА ИЧАКНИНГ ФУНКЦИОНАЛ ҲОЛАТИ

*Г.У. Урманова, Д.А.Қаршиев, Й.Н.Исламов*

Тошкент педиатрия тиббиёт институти

✓ ***Резюме,***

***Турли ёшдаги каламушларда ўтказилган тажрибалар шуни кўрсатдики, баъзи ферментлар (лактаза, амилаза, сахараза, дипептигидролаза) сутли озуқага адаптация бўлиш даврини аниқлайди. Шунинг учун биз айрим ферментларнинг озуқа турига таъсирини аниқлашни қарор қилдик. Постнатал онтогенезнинг бошланғич босқичларида кимёвий десимпатизация, ингичка ичакнинг ривожланишида гидролитик функциясини ўзгартиради.***

***Калит сўзлар: гуанетиден, десимпатизация, МНС-марказий нерв системаси, ОИТ-ошқозон ичак тракти.***

## Relevance

With the transition from dairy nutrition to the definitive in mammals, the properties of the small intestine change, primarily the enzymatic spectrum and the distribution of enzymes in different parts of the digestive tract [1,2,5,]. The mechanisms of maturation of the functions of the digestive system are quite complex, many links of the nervous and endocrine systems are involved in them [4,7,8]. Sources indicate that, at present, the activity of the small intestine in the digestive system is not fully understood. The study of the functional state of these biological systems is of great importance.

Therefore, the study of the activity of some enzymes involved in the activity of the small intestine is of great importance.

Purpose of the research: To study the participation of sympathetic innervation in the formation of the enzymatic spectrum of the small intestine in early postnatal ontogenesis.

## Material and methods

The experiments used white laboratory rats of different ages. To obtain offspring, animals of different sexes with a body weight of 150-180 g were selected. Pregnant females were placed in individual cages. Newborns were assigned to 8 animals per lactating rat. The studies were carried out at the ages critical for the growth and development of rats: 13-24 days - the period of opening the eyes; 21-22 days - transition to definitive nutrition; 30 day emancipation from the mother, the formation of skeletal muscle tone and thermoregulation mechanisms.

For each experiment, 6 rats from at least three litters were used. In the first series of experiments, the development of the enzymatic spectrum of the small intestine in intact rats was studied. In the second, after chemical sympathization, which was carried out by the introduction of guanethidine sulfate at a dose of 20 mg / kg (daily) for 14 days. As a result of the drug administration, the number of nerve cells in the sympathetic ganglia, for example, in the upper cervical ganglion, decreases by 93-95%, and this sympathization is irreversible [2,6,12,17].

That is, this indicator decreased in the direction from the duodenum 12 in the caudal direction. On the 21st and 30th days, the gradient became more pronounced (table). distribution of amylolytic activity along the

The enzyme activity was calculated per unit weight of the raw tissue of the intestinal mucosa.

The data were statistically processed by Student and Fisher.

## Result and discussion

The activity of intestinal enzymes in intact rat pups during ontogeny undergoes significant rearrangements. So the amylase activity gradually increases from the 14th to the 21st and further up to the 30th day of life. Lactase activity gradually decreases. Sugar activity, very low on the 14th day, progressively increases until the 21st day and remains at this level on the 30th day.

During the period of pure milk feeding in the mucous membrane of the small intestine of rat pups, there is no or very low sucrase activity and a well-expressed lactase activity. By the time of the transition to definitive nutrition (21st day of life), enterocytes acquire the ability to synthesize sucrase while sharply suppressing the formation of lactase in them.

The activity of monoglyceride lipase practically does not change from the 14th to the 30th day. The activity of dipeptide hydrolase increases sharply on the 21st day and decreases by the 30th day.

Existing ideas about the functional topography of the small intestine suggest that in most cases, even complete information about the state of hydrolytic transport mechanisms in one area of the mucous membrane is insufficient for a reliable judgment about the activity of the small intestine as a whole. Changes in the activity of enteral hydrolases in different parts of the intestine during ontogenesis under the influence of various factors do not always occur in parallel.

Our studies have shown that on the 14th day of life there was a proximodistal gradient in the

**Enzyme activity in the homogenate of the mucous membrane removed along the entire rat small intestine (M ± m).**

| Enzyme | Age, days | | |
|---|---|---|---|
| | 14-th | 21-th | 30-th |
| **Amylase, mg / min • g** | 54,0±3,6<br>P<0,05 > | 120,0±0,5<br>P<0,3 | 157,0±22,4<br>P<0,05 |
| **Sucrase, µmol / min • g** | 9,4±0,4<br>P<0,05 | 20,1±1,6<br>P<0,05 | 21,0±1,5<br>P<0,001 |
| **Lactose, µmol / min • g** | 3,03±0,07<br>P<0,02 | 1,49±0,05<br>P<0,02 | 0,80±0,03<br>P<0,02 |
| **Dipeptide hydrolase, µmol / min • g** | 11,0±0,2<br>P<0,10 | 21,0±0,5<br>P<0,03 | 11,1±0,3<br>P<0,05 |
| **Monoglyceride lipase, µmol / min • g** | 4,49±0,12<br>P<0,02 | 5,59±0,18<br>P<0,10 | 5,11±0,11<br>P<0,5 |

***NOTE - The table shows the average of five experiments.***

In the homogenate of the mucous membrane, removed along the entire small intestine or separately from the duodenum and from three equal underlying areas, conventionally called proximal, medial, distal (to clarify the topography

During the period of pure milk feeding (14th day), the maximum activity of sucrase was observed mainly in the distal parts of the small intestine and moves in the oral direction during the transition to definitive nutrition.

The spatial distribution of lactase activity throughout the small intestine during the first month of life practically does not change: lactase activity is most pronounced in the proximal section, less and approximately the same in the duodenum, medial and distal segments.

During the period of milk feeding, the maximum indicator of dipeptide hydrolase was observed mainly in the distal part of the small intestine. In the duodenum and proximal part, the activity of this enzyme is minimal. By the time of the transition to definitive nutrition, there is a redistribution of activity along the small intestine. The maximum activity is found in the duodenum 12 and in the caudal region. This topography of enzyme activity remains on the 30th day.

The topography of monoglyceride lipase activity along the intestine practically does not change during ontogenesis - it is distributed relatively evenly in the three lower sections, and its maximum is noted in the duodenum.

After chemical sympathization, the body weight of experimental rat pups is less than that of intact ones (statistically significant), and is 18.6 ± 0.7 g on the 14th day and 23.8 ± 0.9 g on the 21st day 20.0 ± 0 , 7 g and 35.2 ± 1.5 g on the 30th 30.6 ± 1.8 g and 45.1 ± 1.3 g, respectively. The activity of amylase (180.0 ± 8.6 mg / min • g), sucrase (35.0 ± 2.0 μmol / min • g), dipeptide hydrolase (49.0 ± 3.3 μmol / min • g) is significantly higher , lactase (0.78 ± 0.03 μmol / min • g) is lower than in inactive individuals. Monoglyceride lipase activity in rats of both groups does not differ. After sympathization, it is 5.7 ± 0.2 μmol / min • g.

Determination of the topography of enteric hydrolases made it possible to reveal the mixing of the peak of the activity of all enzymes in the distal segment. In this regard, for almost all enzymes, a distal-proximal gradient was established, that is, a decrease in activity in the direction from the caudal to the oral parts of the small intestine.

Of enzymatic activity) sections, photoelectrocolorimetric methods were used to determine the activity of enteric enzymes: monoglyceride lipase -1-leucine dipeptide hydrolase, amylase, sucrase, lactase [2,4,17].

Such a change in the topography of enzymes after sympathization, in our opinion, is consistent with the idea that in the oral-caudal direction in the gastrointestinal tract, the regulatory role of nervous mechanisms decreases and the importance of humoral and local mechanisms increases.

The small intestine takes part in all stages of digestion, including absorption and movement of food. Here, food gruel, processed with saliva and gastric juice, is exposed to the action of intestinal juice, bile, pancreatic juice, and absorption of digestion products into the blood and lymphatic capillaries also occurs here. In the small intestine, enzymes are produced that, together with enzymes produced by the pancreas and gallbladder, help break down food into its individual components.

Then proteins are converted into amino acids, carbohydrates are broken down into simple sugars, and fats into smaller components, which contributes to the effective absorption of nutrients [5,7,15].

It is in the small intestine that most medicinal substances, poisons, toxins and xenobiotics are absorbed when administered orally. Only a few of the drugs, poisons and other xenobiotics are absorbed in the stomach. In addition to digestion, absorption and transportation of food masses, the small intestine also performs the functions of immunological protection and secretion of hormones [2,14].

In the small intestine, the gastric contents undergo deep mechanical and chemical processing. The small intestine is the main site of digestion and absorption of nutrients; cavity, parietal and intracellular digestion is carried out here [2,13].

In the small intestine, the gastric contents undergo deep mechanical and chemical processing. The small intestine is the main place for digestion and absorption of nutrients; cavity, parietal and intracellular digestion is carried out here. Intestinal digestion occurs in a neutral or weakly basic environment [4,5,6,8,10].

A special place in digestion and regulation of the functions of the digestive apparatus is occupied by the duodenum. Its contents on an empty stomach have a slightly alkaline reaction (pH 7.2-8.0). Neutralization of the acidic contents of the stomach is provided by the secretions of the pancreas, small intestine and bile, stopping the

action of gastric proteases and providing subsequent processes of cavity digestion in the small intestine [5,6,8,10,12].

The pathology of abdominal digestion may be due to insufficient intake of pancreatic juice, bile into the intestinal lumen, a violation of the formation of intestinal juice, as well as a change in the nature of nervous and humoral influences on secretory processes. A significant role in the pathology of cavity digestion is played by a change in the motor function of the intestine (increased motility or its decrease) [5,6,8,10].

In violation of membrane digestion, the main role is played by insufficient production of enzymes by enterocytes, a change in the structure of microvilli, a decrease in their number, a violation of hormonal and humoral regulation of the mitotic activity of enterocytes, as well as disorders of intestinal motility. The completeness of parietal digestion largely depends on the state of cavity digestion [5, 9, 10].

Lack of intracellular digestion is associated with primary or secondary fermentopathy, which is based on genetically determined or acquired intolerance to disaccharides or some proteins [5,6,8,10].

Guanethidine has a short-term ganglion blocking effect and some stimulating effect on β2-adrenergic receptors. Virtually no effect on the level of catecholamines in the central nervous systems of the central nervous system and the adrenal medulla. By oppressing the adrenergic innervation of the gastrointestinal tract of the gastrointestinal tract, guanethidine enhances intestinal motility [1,4].

Damage to the liver and gastrointestinal tract, tolerance, physical dependence, withdrawal syndrome, weakening of short-term memory, emotional lability, paresthesia of the extremities, Wernicke-Korsakoff syndrome, folate deficiency anemia, cardiomyopathy, arrhythmias, arterial hypertension, gynecomastia, testicular atrophy, fetal alcohol syndrome, immunodeficiency syndrome cancer, murder, suicide. Mechanism of action. They excite their own receptors in the central nervous system, coupled with the GABA receptor [2,6,17].

Guanethidine - Sympatholytic, inhibits the transmission of excitation from adrenergic neurons. Selectively accumulates in granules of sympathetic postganglionic nerve endings and displaces norepinephrine from them. Part of the released norepinephrine reaches postsynaptic α-adrenergic receptors and has a short-term pressor effect, but the main part is inactivated by MAO. As a result of depletion of norepinephrine reserves in adrenergic endings, the transmission of nerve excitation to them is weakened or stopped [1, 12,17].

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They act both at the level of peripheral organs (heart, blood vessels) and at the level of the central nervous system, which is associated with a variety of clinical and side effects of this group of drugs.

The most famous representatives are reserpine and guanethidine (octadine), used in medicine for the treatment of arterial hypertension [6, 9,17].

Sympatholytic, has a hypotensive effect. It accumulates in the granules of sympathetic nerve endings, reduces the amount of mediator entering the receptors, as a result of which the transmission of nerve excitation is weakened or stopped. Has a short-term ganglion-blocking and small beta2-adrenostimulating and local anesthetic effect. It causes a decrease in systolic and diastolic blood pressure, in terms of the strength of the hypotensive effect it is superior to reserpine, has a cardiodepressant effect, reduces myocardial contractility, conduction and heart rate (thus, a decrease in blood pressure is due to both a decrease in OPSS and IOC). At the beginning of treatment (sometimes up to several hours), a vasoconstrictor reaction may develop (massive inflow of norepinephrine into the nerve endings), which is then replaced by persistent vasodilation [3,6,11].

The sympatholytic effect of guanitedine is due to the fact that it selectively accumulates in the granules of sympathetic nerve endings and displaces the adrenergic mediator, norepinephrine, from them. Part of the released mediator reaches postsynaptic a-adrenergic receptors and has a short-term pressor effect, but the main part of the mediator is destroyed under the influence of axonal monoamine oxidase. As a result of depletion of norepinephrine reserves in adrenergic endings, the transmission of nervous excitation to them is weakened or stopped [4,6].

Violation of the transmission of nervous excitement is associated, in addition, with the fact that, accumulating in the nerve endings, octadine has a local anesthetic effect on them. Octadine affects the cardiovascular system in two phases: first, a transient pressor reaction with tachycardia and an increase in cardiac output develops, then a progressive decrease in systolic and diastolic blood

pressure occurs, the heart rate, minute volume and pulse pressure decrease, and later (after 2-3 days after oral administration) persistent hypotension occurs. The initial pressor reaction can last up to several hours. With prolonged use of the drug, the hypotensive effect may decrease due to a gradual increase in cardiac output [4,6,15].

**Conclusions**

1. Comparison of enzymatic activity of enteral hydrolases at different stages of postnatal ontogenesis suggests that lactase characterizes adaptation to milk nutrition, amylase, sucrase - to the definitive one. For monoglyceride lipase, it is not possible to establish dependence on the type of food.

2 After chemical sympathization, the body weight of rats on days 14, 21, and 30 is less than that of intact animals. The activity of most intestinal enzymes is higher, and the lactase activity is lower than in the control.

3. Chemical sympathization changes the topography of the distribution of enteric hydrolases along the small intestine due to the shift of their activity to the distal site.

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