Peculiarities of values of acethylcholine concentration and cholinesterase activity in serum of patients with alcoholic chronic pancreatitis and duodenal ulcer

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Key words: acetylcholine, cholinesterase, duodenal ulcer, alcoholic chronic pancreatitis, Kruskall-Wallis test, Nemenyi test

In the development of polytheological diseases, many equal pathological factors are intertwined. Available ideas about the mechanisms and sanogenesis digestive organs is reflected in the change of a number of hypotheses and theories, trying to give a scientific explanation of both the causes and the development of chronic relapsing diseases and on this basis to outline the ways of rational therapy [1, 2, 3]. Acute and chronic diseases of the gastroduodenal zone were considered and treated as a local pathological process. This is the result of the lack of comprehensive knowledge of biochemical, physiological, histochemical changes in regulatory activity. With the accumulation of data, it became obvious that such a representation is incorrect. The appearance of local damage is the final stage, the disturbance of the mechanisms of the regulation of physiological processes. The result is the emergence of foci of inflammation with localization in the stomach, duodenum, pancreas. Endogenous acetylcholine (AC) is a first order mediator, it is present in virtually all tissues of the body, participates in the transmission of a nerve impulse, besides it acts on the metabolic processes of the cell. Takes part in the transmission of nervous excitation in the central nervous system, vegetative nodes, endings of parasympathetic and motor nerves.

The aim of our studies was to determine the concentration of the neurotransmitter the central nervous system (or rather, the autonomic nervous system) — Arts and the level of cholinesterase (Che) activity in the serum of patients with duodenal ulcer disease (DUD) and chronic pancreatitis of alcoholic etiology (ACP), who were on treatment at the Central Scientific Research Institute of Gastroenterology and the Moscow Clinical Research Center.

Materials and methods. The study included 129 DUD, 108 ACP, the control group consisted of 30 volunteers who undergo regular check-ups. In patients and in the control group, blood was taken on an empty stomach. All groups were are comparable in terms of age and gender differences. AC and Che activity in blood serum was determined by the biochemical method of Hestrin in its own modification (2004) [2].

Statistical processing of the results obtained in control groups and patients was carried out with the help of the nonparametric analogue of the variance analysis — Kraskel-Wallistest [1] and the test of multiple pairwise comparisons of Nemenyi [5] in the software environment for statistical computations R (packages "PMCMR" and "Stats") [6, 7].

Results and discussion. Determination of the content of AC and Che activity in the blood serum in patients with DUD, pancreatitis and healthy individuals made it possible to obtain an array of data. The resulting digital data is divided into three cohorts (type) and concentration of AC Che activity: low (0,46-1,0 mmol/l) found in 6% of 0, middle (moderate) at a concentration of AC 1,02-1,5 mmol/l — in 30%, high AC level (over 1.5 mmol/l) in 10%.

To evaluate flax and visa scatter and median concentration of AC and Che in different pathologies and in control, we constructed a scatter diagram (box-plots or "boxes mustache") shown in Fig. 1 and 2.

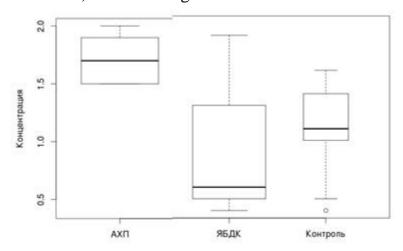


Fig. 1. Diagrams of the spread of the concentrations of AC at various pathologies and in control. Fat lines are medians, the lower and upper boundaries of the "boxes" are the first and third quartiles, respectively, the boundaries of the "whiskers" are 1, 5 interquartile ranges.

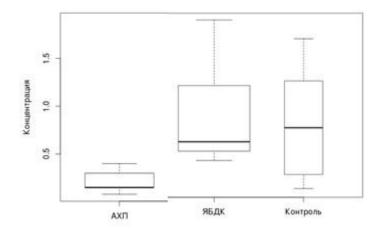


Fig. 2. Diagrams of the spread of Che activity in various pathologies in the control.

The boxplots allow us to compare the medians of the samples, and, as we see, the concentration of AC at ACP is higher than in the control group, and the activity of CE with the same pathologies is lower than in the control.

The data presented above were obtained from patients with a diagnosis, the duration of the disease is not less than 1 year.

The Kraskel-Wallis test showed the presence of statistically significant differences in the concentration of AC in the study groups; Similar results were obtained by Che activity (Table. 1).

Table 1

The results of the Kruskel-Wallis test conducted for the concentration of AC and the activity of Che

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Index	Chi-square	Degrees of	Significance level		
		freedom	(p-value)		
ОН	95.504	3	<2.2e-16		
HE	115.73	3	<2.2e-16		

For pairwise comparisons of the concentration of AC and the activity of Che between groups of pathologies and control, we used the Nemeni test, the results of which are presented in Table. 2 and 3.

The results of the Nemeni test for the concentration of AC

Table 2

The results of the Nemem test for the concentration of AC					
Groups	ACP	Control	JBDK		

Control	1.0e-05	-	-
JBDK	2.2e-15	0.76	-

Note: the significance levels of pairwise comparisons are indicated at the intersection of the corresponding rows and columns

Results of the Nemenyi test for Che activity

Table 3

Groups	ACP	Control	JBDK
Control	7.5e-06	-	-
JBDK	<2e-16	0.56	-

Note: the significance levels of pairwise comparisons are indicated at the intersection of the corresponding rows and columns

The test results show that the concentration of AC and the activity of Che statistically significantly differs between ACP and control, and ACP and DUD. Thus, the localization of the pathological process affects the concentration of AC and the activity of CE in the blood serum.

It should be taken into account that the patients had a duration of the disease for at least one year and entered the hospital for treatment, 5 to 10 days after the exacerbation. Considering this, another group of patients with JBDD was examined during the period of exacerbation and remission. It is established that during the exacerbation DUD AChlevels averaged 0.65 ± 0.1 mmol/l, Che activity — 1.1 ± 0.2 mmol/l · 30 min. AH in the period of scarring — 0.9 ± 0.1 mmol/l (in the control — 0.85 ± 0.1 mmol/l), the level of CHE decreased to 0.2 ± 0.01 mmol/l · 30 min (in control — 0.5 ± 0.09 mmol/l · 30 min).

Thus, the concentration of AC and Che activity depends not only on the location of the pathological process, but also on the stage of the disease — during inflammation (exacerbation) or scarring (remission).

At the same time, two critical areas were identified in the control group — in the zone of lower and upper values of AC concentration, which allow one to assume the possibility of developing a pathological process under the action of aggressive factors — in the duodenum with a low value of AC and pancreas at high AH values. A high serum concentration of AC in patients with HP may promote the

formation of erosions and/or ulcers in the duodenum and the release of serotonin from enterochromaffine cells (5-HT).

Conclusion:

- 1. Significant differences in the concentration of AC and Che activity between ACP and control and ACP and JBDK were established.
- 2. The concentration of AC and the activity of Che depend on the localization of the pathological process and the phase of the development of the disease.

References:

- Нарушение гуморальной регуляции внешнесекреторной функции поджелудочной железы при хроническом панкреатите / Л. В. Винокурова,
 Э. Р. Валитова, И. Е. Трубицына [и др.] // Терапевтический архив. 2007. Т. 79. № 2. С. 44–48.
- 2. Трубицына И. Е. Биологически активные вещества как факторы агрессии и защиты при язве желудка (экспериментально-клиническое исследование) : автореф. докторской диссертации / И. Е. Трубицына. М., 2004. С. 29.
- 3. Трубицына И. Е. Вариации и частота распределения количественного значения ацетилхолина и холинэстеразной активности в сыворотке крови у здоровых лиц / И. Е. Трубицына, В. Н. Дроздов, М. В. Рудь // Экспериментальная и клиническая гастроэнтерология. 2007. № 3. С. 78–81.
- 4. Kruskal W. H. Use of ranks in one-criterion variance analysis / W. H. Kruskal, W. A. Wallis // Journal of the American Statistical Association. 1952. Vol. 47, No 260. P. 583–621.
- 5. Nemenyi P. B. Distribution-free multiple comparisons: PhD thesis / P. B. Nemenyi. Princeton University, 1963.

- 6. Pohlert T. The Pairwise Multiple Comparison of Mean Ranks Package (PMCMR). R-package. 2014. Available at: http://CRAN.R-project.org/package=PMCMR
- 7. R Core Team. R: a language and environment for statistical computing / R Foundation for Statistical Computing, Vienna, Austria. 2015. Available at https://www.R-project.org/

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Introduction. There are a lot of pathogenic factors involved in development of polyetiologic diseases. Acetylcholine (AC) is known as first-order mediator as it plays an important role in development and maintenance of pathological processes. In this article we provide data on AC concentration in blood serum of patients with duodenal ulcer, alcoholic chronic pancreatitis and control group as well as activity of cholinesterase (Che).

The aim of this study was to identify a role played by AC in pathological process during a disease, which may complicate a course of the disease as a bad prognostic factor.

Results and discussion. We divided AC concentration into three types in the control group: low — 0.46-1.0 mmol/l (60% of individuals), moderate — 1.02-1.5 mmol/l (30%), and high — more than 1.5 mmol/l (10%).

Conclusion. We suppose that Che activity and AC concentration depend on localization of pathological process.