THE ROLE OF NEURON SPECIFIC ENOLASE IN HELICOBACTER PYLORI-ASSOCIATED CHRONIC GASTRODUODENITIS IN CHILDREN

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The purpose of this study was to assess the nature of changes in the level of neuron specific-enolase (NSE) in children with chronic gastroduodenitis, taking into account the severity of the disease and the presence of Helicobacter pylori (HP) infection. The study involved 73 children with chronic gastroduodenitis. Group I included children with erosive gastroduodenitis, group II – with superficial gastroduodenitis. Each of them included two subgroups: with a positive result of examination on HP-infection and with negative tests for Helicobacter pylori. In the diagnosis of the disease was used endoscopic and morphological methods; urease, microscopy, molecular biological and serological tests were carried out for the verification of HP. The results indicate a possible role of NSE in the development of severe forms of the disease in the absence of pathogenic effects of HP and do not exclude a certain link with the function of sex hormones.

Keywords: neuron specific enolase, erosive gastroduodenitis, surface gastroduodenitis, Helicobacter pylori, children

Among children's digestive system diseases the leading place is taken by chronic upper parts inflammatory diseases of digestive tract, in particular chronic gastroduodenit (CGD) [1]. A special role in chronic gastroduodenit development is played by Helicobacter pylori (HP-infection) [2, 3]. Up to 75 % of CGD is associated with the HP-infection [4].

At the same time, there is a number of endogenous etiological factors influencing the stomach mucous membrane (MM) state and duodenum through neuro-reflex and endocrine-humoral effects [5, 6].

Recently, some attention has been paid to the biochemical indicators study to clarify the formation and development mechanisms of chronic gastroduodenitis. In particular, to the study of the neuron-specific enolase (NSE) role in these processes [7, 8]. In fundamental studies was noted that NSE is found in all human tissues and organs, including the gastrointestinal tract tissues. The significant enzyme activity is determined in the blood serum [9].

Therefore, in the study of the NSE level changes (children with CGD), depending on the HP infection, the MM gastric inflammatory changes severity and duodenal, we taking into account the gender factor as it has a certain relevance.

Research objective: to estimate the nature of the NSE level changes (children suffering from CGD) depending on disease severity and existence of the HP-infection.

Materials and methods of research

In the research group there are 73 children at the age of 8 – 15 with CGD, 34 (46,6 %) girls and 39 (53,4 %) boys were observed.

The I-st group 32 (43,8 %) included children with an erosive gastroduodenit (EGD), 20 (62,5 %) boys and 12 (37,5 %) girls.

The II-nd group 41 (56,2 %) included children with a superficial gastroduodenit (SGD), 19 (46,3 %) boys and 22 (53,7 %) girls.

The I-st group included 16 (50 %) children with an erosive gastroduodenit (EGD) associated with the HP-infection (EGD HP (+) – the 1-st subgroup) and 16 (50 %) – with negative results of HP (EGD HP (-) – the 2-nd subgroup). In the 1-st subgroup of the I-st group 12 (75 %) boys and 4 girls (25 %) were observed; in the 2nd subgroup of the I-st group – 8 (50 %) boys and 8 (50 %) girls.

The II-nd group included 14 (34,1 %) children with the superficial gastroduodenit associated with HP (SGD HP (+) – the1-st subgroup) and 27 (65,9 %) children with SGD with negative Helicobacter pylori tests (SGD HP (-) – the 2nd subgroup). The 1-st subgroup of the II-nd group included 8 (57,1 %) boys and 6 (42,9 %) girls; The 2nd subgroup of the II-nd group included 13 (48,1 %) boys and 14 (51,9 %) girls.

28 children (I-II health group) at the age of 8-15, entered the control group (CG). 17 (60,7 %) boys and 11 (39,3 %) girls.

To include in the study, we obtained the parents consent and they were fully informed about the research progress.

The chronic inflammatory pathology of the upper digestive tract (UDT) diagnosis was established on the complaints basis, data of anamnesis, general clinical and instrumental examination results. All children underwent endoscopic examination, including NBI-technology, histological examination.

The blood serum NSE research was determined by an enzyme immunoassay sets method of Can Ag Diagnostics (Sweden) in the standardized conditions (in the morning; empty stomach). The results were recorded and estimated by means of a SUNRISE photometer produced by TECAN (Austria).

To diagnosis the HP infection all the patients underwent three methods. Bacterioscopic method we used biopsy medicines in MM antralny stomach department; polymerase chain reaction for detection of Helicobacter pylori DNA in the MM antralny stomach department biopsy (test systems "Liteks" Russia) urease method – determination of urease activity in the MM stomach biopsy placing it in a liquid medium containing standard RU-Test Helicobacter pylori (Russia); enzyme immunoassay of blood serum on existence of immunoglobulins of A class and total immunoglobulins to Helicobacter pylori the "DRG" test systems (Germany).

Statistical processing of the research results was carried out by means of the Statistica for Windows program packages (version 6.1) by nonparametric statistics methods (Mann-Whitney's criterion), taking into account that distribution of NSE number didn't correspond to the normal distribution law. Data are presented in the form of a median (Me) and also the 25 and 75 quartile [25%-75%]. Reliable considered significance value of $p \leq 0,05$.

Results of research and their discussion

The analysis of the research results of the NSE level (boys with an erosive gastroduodenit (the I group)) showed the comparable indicator values which don't have statistically significant differences both in 1, and in 2 subgroups: 12,04 (10,78-13,34) μg/li and 10,7 (10,61-12,26) μg/li respectively, $p \geq 0,05$. At the same time the NSE level in blood serum (boys with EGD HP (+)) significantly exceeded control values: 12,04 (10,78-13,34) μg/li and 9,65 (8,96-11,2) μg/li respectively, $p \leq 0,05$. As for indicator values (patients with EGD HP (-)), they didn't differ from CG ($p \geq 0,05$) (Table. 1). The obtained data, apparently, don't exclude probability of formation of interrelation of the NSE level changes in blood serum (boys suffering from EGD with the HP-infection).

A similar situation of NSE level changes was found in group II with SGD, in particular: the NSE values in subgroup 1 (SGD HP +) did not differ significantly from the 2 subgroup (SGD HP-): 11,18 (9,98-11, 54) μg/li and 12,37 (10,87-13,02) μg/li, respectively, $p \geq 0,05$ (Table 1).

However, the NSE content in patients' blood (boys with SGD HP (-) significantly exceeded the control values: 12,37 (10,87-13,02) μg/li and 9,65 (8,96-11,2) μg/li, respectively ($p \leq 0,01$). Boys of subgroup 1 (SGD HP +), there was only a certain tendency to increase the indicator level relatively to the control group ($p \geq 0,05$), which probably calls into question the existence of the interrelation between the NSE dynamics and the development of HP-associated SGD in this patients category (Table.1).

It was also found that boys with SGD HP (-), the NSE values exceeded the level in the blood of EGD HP (-) patients: 12,37 (10,87-13,02) μg/li and 10,7 (10,61-12,26) μg/li, respectively ($p \leq 0,05$), which may indicate the probability of a NSE marker effect in the development of a different disease severity regardless of HP infection in this children category.

Table 1

Neuron-specific enolase indicators in blood serum (boys with chronic gastroduodenitis)

Groups	Boys, n = 39				
Indicators	CG n = 17	1 subgroup Group I EGD HP (+) n = 12	2 subgroup Group I EGD HP (-) n = 8	1subgroup Group II SGD HP (+) n = 6	2subgroup Group II SGD HP (-) n = 13
NSE μg/li Me Quartos [25-75]	9,65 [8,96-11,2]	12,04** [10,78-13,34]	10,7* [10,61-12,26]	11,18 [9,98-11,54]	12,37*** [10,87-13,02]

Note: * – the differences are statistically significant when comparing boys of subgroup 2-nd and groups I and II ($p \leq 0,05$); ** – the differences are statistically significant when comparing the boys of the CG and the boys of group I of the 1-st subgroup ($p \leq 0,01$); *** – the differences are statistically significant when comparing the boys of the CG and the boys of group II of the 2-nd subgroup ($p \leq 0,01$).

Boys with EGD HP (+), only a certain tendency was found to increase the NSE level in comparison with children diagnosed with SGD HP (+): 12,04 (10,78-13,34) μg/li, and 11,18 (9,98-11,54) μg/li, respectively ($p \geq 0,05$), which also does not exclude the above assumption (Table 1).

The study of the NSE dynamics in the girls' blood established that the index values (patients with EGD HP (+)) significantly exceeded its level in the blood, determined at EGD HP (-) and in CG: 10,62 (10,24-10,89) μg/li; 9,48 (8,74-10,08) μg/li, and 9,0 (7,8-10,0) μg/li, respectively ($p \leq 0,05$; $p \leq 0,01$). The girls suffering from EGD not associated with HP infection, the NSE level corresponded to the indicator values in the CG, with only a tendency to increase ($p \geq 0,05$) (Table 2). This circumstance makes it possible to assume a certain interaction existence of the HP-infection factor and the NSE dynamics in the formation of erosive lesion of MM of UDT (girls).

Besides, the revealed statistically significant NSE differences ($p \leq 0,01$) in the blood of girls with SGD HP (-) in comparison with patients with EGD HP (-), indicate the possible role of NSE in morphological changes aggravation in MM of UDT, not associated with participation of HP-infection (Table 2).

The study also found that the boys with EGD HP (+) and EGD HP (-), the NSE level was significantly higher than the enzyme serum levels in girls' blood in similar subgroups: 12,04 (10,78-13,34) μg/li and 10,7 (10,61-12,26) μg/li, respectively, for boys and girls of subgroup 1, $p \leq 0,05$; 10,7 (10,61-12,26) μg/li and 9,48 (8,74-10,08) μg/li, respectively, for boys and girls of the 2nd subgroup, $p \leq 0,01$. The same statistically significant trend was observed in the NSE level changes in the corresponding subgroups of boys and girls with SGD (Table 1, Table 2).

The unidirectionality of changes in the studied indicator (patients with both SGD and EGD), regardless of the HP infection presence, associated with the gender factor, can probably be explained by a certain continuum existence of action of NSE and sex hormones in the CGD pathogenetic model.

Conclusions

1. The study results showed the probability of association changes in NSE serum level with Helicobacter pylori effects in the development of erosive gastroduodenitis both boys and girls.

2. It has been proved that severe (erosive) forms of CGD associated with Helicobacter pylori infection are more often detected in boys (62,5% and 66,7%, respectively), which indicates gender differences during the disease course.

Table 2

Indicators of neuron-specific enolase in serum in girls with chronic gastroduodenitis

Groups / Indicators	girls, n = 34				
	CG n = 11	1 subgroup Group I EGD HP (+) n = 4	2 subgroup Group I EGD HP (-) n = 8	1subgroup Group II SGD HP (+) n = 8	2subgroup Group II SGD HP (-) n = 14
NSE (μg/li) Me Quartos [25-75]	9,0 [7,8-10,0]	10,62*, **** [10,24-10,89]	9,48*** [8,74-10,08]	10,07**,***** [9,91-10,12]	10,56****** [10,15-11,18]

Note: * – the differences are statistically significant when comparing girls of subgroup 1-st and 2-nd groups I ($p \leq 0,05$); ** – the differences are statistically significant when comparing girls 1-st and 2-nd of subgroup II of the group ($p \leq 0,01$); *** – the differences are statistically significant when comparing girls of 2-nd subgroups of I and II group ($p \leq 0,01$); **** – the differences are statistically significant when comparing girls of the CG and girls of the I group of the 1-st subgroup ($p \leq 0,05$); ***** – the differences are statistically significant when comparing GC girls and girls of the II group of the 2-nd subgroups ($p \leq 0,05$); ****** – the differences are statistically significant when comparing girls of the CG and girls of the II group of the 2-nd subgroups ($p \leq 0,01$);

Girls of group II. The NSE values for SGD HP (-) in comparison with patients with SGD HP (+) and CG were dominated: 10,56 (10,15-11,18) μg/li; 10,07 (9,91-10,12) μg/li and 9,0 (7,8-10,0) μg/li, respectively ($p \leq 0,01$; $p \leq 0,01$) (Table 2). These results may indicate the possible studied enzyme involvement in a pathogenetic mechanisms complex for the formation of catarrhal MM of UDT inflammation associated with HP-infection. The NSE level (girls with SGD HP (+)) also exceeded the values in the CG: 10,07 (9,91-10,12) μg/li and 9,0 (7,8-10,0) μg/li, respectively $p \leq 0,05$), which does not contradict the previously stated assumption.

3. The study revealed a NSE serum increase (boys with superficial gastroduodenitis without association with Helicobacter pylori, which casts doubt on the enzyme involvement in the genesis of catarrhal gastroduodenal mucosa inflammation. Also, an increase in the NSE level relative to the control values found in girls with SDG HP (+) may indicate the existence of a specific interaction of the Helicobacter pylori pathological effects and the specific dynamics of NSE during the superficial gastroduodenitis formation in this category of patients.

4. Higher NSE levels in the blood were detected in both boys and girls with SGD HP (-) compared with the value of this parameter of patients with EGD HP (-), which allows us to consider the possibility of using NSE as an auxiliary noninvasive marker of gravity morphological damage of the mucosa of the gastroduodenal zone in the absence of pathogenic effects of Helicobacter pylori.

5. Unidirectional changes in boys' NSE serum compared with girls, regardless of the disease severity and the of Helicobacter pylori infection involvement, indicate a certain association of effects of NSE with the functional sex hormones characteristics in the CGD pathogenesis.

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