State of connective tissue biopolymers in digestive tract diseases

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Abstract. The study presents the results of qualitative and quantitative content of connective tissue biopolymers in children suffering from the chronic gastritis. The main group consists of 56 children with confirmed diagnosis of chronic gastritis enrolled in the study using the principle of randominization and inclusion criteria. There was a considerable decrease in the content of glycosaminoglycans in the examined children, considerable morphological changes to the mucosa in the form of inflammation, atrophy, erosions, lymphoid and plasmacytic infiltration, severe to moderate contamination by Helicobacter pylory, intestinal metaplasia. There was a considerable proportion of children with endoscopic signs of parasitosis. Changing in the state of the mucosa, composition of the mucosal mucus as connective tissue derivatives is one of additional mechanisms of chronic gastritis. Connective tissue failure in the form of modified composition of mucus as well as epithelial cells failure in pediatric patients are the main reason of facilitation of Helicobacter pylory penetration through these barriers. These factors also cause the formation of pathological process in children and determine its clinical manifestations. The successful treatment of this disease also depends on these factors.
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Introduction

Despite important advances in the study of etiology and pathogenesis, we can see a great prevalence and significant trend towards further increase in the incidence of chronic gastritis in children. This causes the necessity for the further study of pathogenetic mechanisms of formation and development of pathogenetic kinds of treatment of this disease in childhood1, 2, 3, 4, 5

According to some researchers, the prevalence of digestive diseases increased from 58.8% in 3-6 years old children to 97.4% in 12-14 years old children 6, 7, 8. This leads to the fact that more than half of all adults suffer from chronic diseases of the digestive tract 9, 10.

Analyzing the main lines of pathogenesis of chronic gastritis, it should be noted about the importance of various mechanisms, including the impact of Helicobacter pylory produced by various enzymes, inflammatory mediators, cytotoxins; immune reactions; functional disorders of acid and pepsin production; morphofunctional immaturity of the nervous system; residual-organic background of the CNS damage, morphological changes. The proper organization and functioning of structural elements of the "first and second lines of defense" are of particular importance. It is well known that Helicobacter pylory penetrates into the mucosal mucus covering mucosa, destroying its mucopolysaccharides and glycoprotein complexes. Therefore H. pylori colonize the apical part of the epithelial cells, disrupting its integrity following by subsequent penetrating directly into the cells of the mucous membrane, causing its destruction and replacement of more primitive mucus-producing cells.

Obviously, connective tissue failure in the form of altered composition of mucus and epithelial cells failure facilitates penetration of Helicobacter and causes the formation of pathological process.

Consequently, the condition of connective tissue biopolymers apparently can be considered as criterion of evaluating the pathological process in chronic gastritis.

Study of gastrointestinal diseases with regard to changes of the connective tissue on the basis of the study of its biopolymers allows for new insights into formation of chronic diseases of the stomach taking into account phenotypic signs of connective tissue dysplasia.

Hence, we have set out an aim to examine the state of the connective tissue biopolymers, namely glycosaminoglycans in children with chronic gastritis.

In order to avoid systematic errors the enrollment of patients was performed in compliance with the principle of randomization.

Criteria for inclusion in the experiment were the following: patients with verified diagnosis - chronic gastritis, patient's consent, an absence of contraindications and the absence of other urological subcompensated states.

Principle of randomization means selection of patients using randomization technique (every even sick child).

Exclusion criteria were the following: adverse side effects, no effect within 14 days of treatment, patient's refusal. Statistical analysis of the study data was performed using the software package Microsoft Excel-2003.

Scheme and dates of examination:

Medical examination was conducted during the treatment: objective assessment of physical status, EGD with biopsy followed by histological and biochemical studies of the samples, biochemical blood analysis with the determination of activity of connective tissue biopolymers (glycosaminoglycans). The level of hexuronic acid and hexosamines was determined by the carbazole method of Dische (1947) modified by Bitten and Muir (1965), Merkur'eva R.V. and Altynbekova B.E. (1982).

Results and Discussion

Examination of children with chronic gastritis was carried out on the basis of Gastroenterological Department in the Regional Children's Clinical Hospital, Karaganda.

The main group consists of 56 sick children with confirmed diagnosis of chronic gastritis. Verification of the diagnosis in sick children was conducted on the basis of clinical, laboratory and instrumental standardized survey methods.

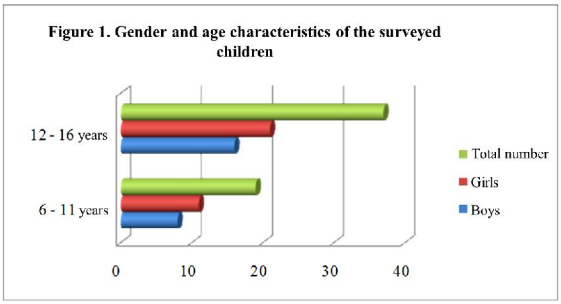
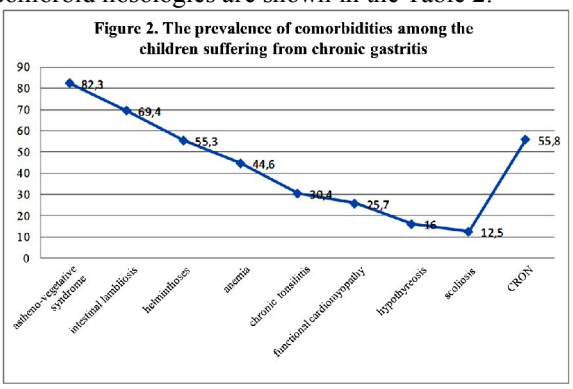


Figure 1. Gender and age characteristics of the surveyed children

Of the total number of the surveyed children there were 25 boys (44.6%) and 31 (55.4%) girls. The age stratification of the surveyed children was carried out in accordance with conventional periodization of childhood. Analysis of the age structure revealed that 19 children belonged to the category "primary school age" (6 to 11 years) and the proportion of such children was equal to 33.9%. At the same time the age category "senior school age" (12 to 16 years) included 37 surveyed children (56%).

The duration of the disease in 15% of children was less than 3 years, in 30% it varied in the range from 3 to 5 years. In 55% of the surveyed children the duration of the disease didn't exceed 5 years.

It is important to note that comorbid diseases were considerably more common among the surveyed children suffering from the chronic gastritis. Main comorbid nosologies are shown in the Table 2.



The control group consisted of 35 children suffering from the chronic gastritis. Children matched by sex and age.

Evaluation of morphological changes of gastric mucosa was carried out in accordance with the International Sydney Classification (1990). There were 5 parameters that were taken into consideration - atrophy, inflammation, activity, intestinal metaplasia, and the presence of *Helicobacter pylori*. These parameters were evaluated using a 4-point scale: absence of parameter, light, moderate and severe degree of the parameter.

The clinical picture of chronic gastritis in the examined children was manifested by pain, dyspeptic and astheno-vegetative syndrome. In our study we established the frequency of these syndromes among the surveyed children. In 82.6% pain syndrome was typical for the epigastric region, and in 61.7% it was combined with soreness in the right and left upper quadrant. Dyspeptic disorders were revealed in 76% of cases. Various manifestations of astheno-vegetative syndrome were typical for two thirds of the surveyed children.

In 65.6% of the surveyed children there were signs of polyhypovitaminosis and micronutrient deficiencies in the form of dry skin and desquamation, tarnishing and increased fragility of hair, changes to the nail plates (striations, fragility, etc.).

The study found that the average level of physical development was considerably low and below the average according to centile table more likely (86.7%, $p < 0.05$) among the studied patients suffering from the chronic gastritis. Along with this, the revealed types of physical development were characterized by disharmony (20%, $p < 0.05$) and severe disharmony (66.7%, $p < 0.05$). The mean level combined with harmony of physical development of

the surveyed children was established in 13.3% (p <0.05) of cases.

We have found that children suffering from the chronic gastritis were considerably more likely (p <0.05) to have minor anomalies of the oral cavity (69.1%) compared to healthy children, i.e. gothic palate, striated tongue, teeth dysplasia, trema, diastema. Minor anomalies of dermatological nature were revealed in 56.7%: they included depigmentation, hyperpigmentation, transverse fold on the abdomen. Also such typical signs as «sandal gap» (53.5%) and joint hypermobility (43.2%) were recorded considerably often. Minor anomalies were more prevalent among boys than girls. We should assume that considerable prevalence of minor developmental anomalies of connective tissue of the surveyed children was related to the exposure to pathological effects of different strength on the connective tissue in the prenatal period.

An objective medical examination of the oral cavity revealed that majority of children had white coating of tongue, its dryness, smoothness of papillae, predominant mucosa of crimson hue. Palpation of the digestive tract organs revealed tenderness in the epigastric region in 82.6% of which 61.7% was determined in the right upper quadrant and 22.7% in the left one. Patients with hypoacidic gastritis (11.7%) revealed tenderness in the projection of intestine.

It should be emphasized that clinical signs of chronic gastritis in children were polymorphic, often atypical, especially in young children and depended on the morphological status of fundus and antrum mucosa, microcirculatory disorders in the mucosal stroma, proteolytic activity of gastric contents, comorbidity.

In the surveyed children we found the following endoscopic types of gastritis: superficial (42.2%), erosive (31.8%), atrophic (18.8%), hyperplastic (3.2%) and autoimmune (3.8%). Inflammatory changes in the stomach combined with motor-evacuation disorders in the form of duodenal reflux in 22% of cases. In 26.6% of the surveyed children we have recorded endoscopic signs of parasitosis. Moreover, we were unable to determine the dependence of the endoscopic picture of parasitosis (in the absence of clinical symptoms) on morphological forms of chronic gastritis.

Superficial helicobacter-associated active gastritis was found on endoscopic examination in 42.2% (p <0.05) of the surveyed children. The gastric mucosa was pale pink, edematous, dull, hyperemic with pronounced infiltration of lymphocytes, plasmocytes, neutrophils. Besides diffuse mucosal changes were revealed in both antrum and pylorus in 51.2% (p <0.05) of cases, and in 48.8% (p <0.05) of cases in antrum only.

Considerably higher prevalence of erosive gastritis in the surveyed children (31.8%, p <0.05) is a matter of particular attention. It's more frequent in patients of the older school age. These are acute erosions that were prevalent on endoscopic picture of these patients. On endoscopic examination these erosions were presented as flat superficial defects of mucosa covered by fibrin and hydrochloridic hematin (hemorrhagic). Multiple erosions were more prevalent (63.2%, p <0.05) compared to the single ones (36.8%, p <0.05) among the examined children. At the same time hemorrhage in the mucosa was considerably more common (55%) among sick children, especially the older ones. A typical feature of hemorrhages in the mucosa in 24.4% of the children was its considerable area (islands). While in other cases (55.5%) dot petechiae were recorded. Histological characteristics of acute erosions were represented by superficial desquamation of epithelium. In 42.9% of cases it affected large areas and in 57.2% of cases it affected the restricted areas of the gastric mucosa.

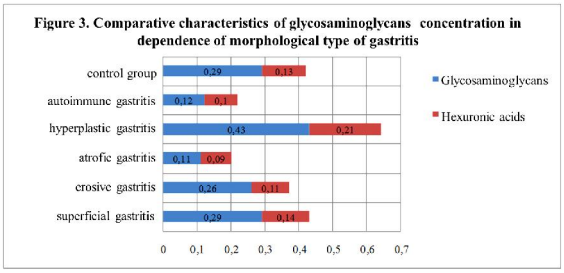
Atrophic form was diagnosed in 18.8% (p <0.05) of cases among children suffering from the chronic gastritis. On endoscopic examination this morphological form of gastritis was characterized by pasty, friable, easy vulnerable, motley (foci of bright red and pink color on the background of pale coloring) mucosa. At the same time in children with atrophic gastritis we revealed smoothness relief and thinning of the mucosa. In 37.9% of cases it combined with shortening of fundic glands, focal hemorrhages, severe lymphoplasmacytic infiltration.

Hyperplastic gastritis was revealed in 3.2% (p <0.05) of the surveyed children of the school age with long duration of the disease. Endoscopic picture of hyperplastic gastritis is characterized by thickening of the gastric mucosa with many grains of different sizes on its surface, resulting in cobblestone appearance of the mucosa. Along with this, there was proliferation of gentle connective tissue between glands.

While assessing the presence of Helicobacter pylori we revealed their presence in 94.8% (p <0.05) of cases. On staining the tissue sections with methylene blue Helicobacter pylori were rod-shaped and were identified in the mucus covering the mucosa. However, Helicobacter pyloric contamination was considerably more common at the surface and erosive forms of chronic gastritis. At the same time a high degree of Helicobacter pylori contamination was established in 17.4% (p <0.05) of cases, medium degree was established in 43.5% (p <0.05) of cases, and low degree of H. pylori contamination was established in 39.1% (p <0.05) of cases. In the literature there are evidences that the degree of Helicobacter pylori contamination decreases along

with the development of atrophic changes. In our study we have obtained the similar results.

The examination of the status of connective tissue biopolymers in the mucus and mucosa showed changes in their quantity. Comparative analysis of quantitative assay of hexuronic acid and hexosamine in the mucus revealed the dependence of connective tissue biopolymers on the morphological forms of chronic gastritis of the surveyed children. The data obtained are shown in Table 3.



Based on the data presented in the table, we can say that the content of both hexosamine and hexuronic acid changes in various morphological types of chronic gastritis, being the causative factor affecting dystrophic, atrophic, and dysregenerative processes. Moreover, the greatest reduction of connective tissue biopolymers occurred in patients suffering from autoimmune atrophic and erosive gastritis. A trend towards reduction in the quantity of investigated connective tissue biopolymers was revealed in superficial gastritis. However, in comparison with the above noted forms of gastritis the revealed changes were less pronounced.

Hyperplastic gastritis was characterized by an increased content of hexosamine and hexuronic acid compared with the control group. Probably it can be explained as a compensatory response of the connective tissue in the form of regenerating of undifferentiated epithelium with the loss of its ability to differentiate into mature cell forms.

Thus, the quantitative and qualitative composition of connective tissue biopolymers has its own characteristics in different types of chronic gastritis in children. Presumably, characteristics of pathogenetic and clinical manifestations in children with chronic gastritis are mediated by the above-noted qualitative and quantitative changes in the content of connective tissue biopolymers.

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