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# Interconnection between aggression and protection factors of gastric juice and oral liquid of the patients with precancerous changes of gastric mucosa

**A. I. Rudenko[1], L. M. Mosiychuck[1], O. M. Khomenko[2], O. P. Petishko[1]**

**[1]SI "Institute of Gastroenterology of NAMS of Ukraine", Dnipro, Ukraine**
**[2]Oles Honchar Dnipro National University, Dnipro, Ukraine**

## Absract

This article is about learning of the aggression factors and the gastric juice and oral liquid protection of the patients with precancerous changes in the mucous gastric membrane of stomach.

32 middle-aged people were researched, who were at the inpatient treatment at the SI "Institute of Gastroenterology of NAMS of Ukraine": 6 of them were with the atrophic changes of mucous membrane of stomach with different rate of severity (the I group), 12 people were with the intestinal metaplasia in the antrum (the II group), 14 patients were with intestinal metaplasia in the body and in the antrum of mucous membrane of stomach (the III group). The diagnosis was established after meticulous endoscopic and histological researches of biopsy

material of mucous membrane of stomach. During the esophagogastroscopic research the gastric juice was being collected. It was determined its pH, pepsin, glycoprotein, sialic acids, fucose and hexosamines concentration. Also there were conducted the investigations of oral liquid, where the content of glycoprotein, sialic acid, fucose and hexosamines was determined.

In the gastric juice of patients of the II and III groups, the content of sialic acids was increased, in the III – the acid secretion increased the hexosamines, with anacid – of fucose and it was decreased the amount of pepsin. In the oral liquid, the content of sialic acids in all researching groups was increased, fucose - only in the I group, hexosamines and glycoproteins - only in the III group.

The further complex study of functional-morphological changes of gastric secretion and salivary glands activity will allow to assess the condition of reserve capabilities of the protection factors of the mucous membrane of the stomach and to determine the risk groups of patients with the precancerous condition.

**Keywords: intestinal metaplasia, gastric juice, oral liquid.**

## Introduction

In spite of some success in solving cancer problems and particularly stomach cancer in learning of influence of etiological factors and pathogenetic mechanisms of this disease, nowadays there aren't any reliable diagnostic tests of timely development of this pathology. Untimely diagnostic of stomach cancer, certainly, influences adversely on efficiency of committing the therapy and it's very dangerous of serious complications like: anemia, stenosis of cardiac or pyloric stomach section, bleeding, metastatic formations and etc. [2, 4, 10, 12, 14, 19]. Thus, the early detection of stomach mucous membrane and making relevant therapeutic- wellness methods will cause the development of gastro carcinogenesis complication.

A lot of scientists think, the main pathogenetic factors of development the pathological process in mucous gastroduodenal section are, first of all, chronic, atrophic gastritis, (especially during achlorhydria), smoking, alcoholism, stomach and duodenum ulcer, insufficient supply into the organism of biologically important nutrients, that carries out a coenzyme function, taking products of nutrition and water that contain chemical compounds with carcinogenic and mutagenic activity, hereditary predisposition, unsatisfied condition of manufacturing surroundings and environment, chronical inflammatory diseases of internal organs and tissues, operations with organs of abdominal cavity and etc. [2, 6, 15, 21]. There are some violations of signaling, integration and regulatory cellular systems that provide the

adequacy of plastic, energetic, proliferative processes, as well as the process of differentiation, which change can lead to malignant cell transformation [16, 20, 21]. We need to note that in most cases the development of adenocarcinoma of the stomach intestinal type is the culmination of the so-called sequence Correa cascade: "inflammation - metaplasia - dysplasia - cancer" [1].

Oxidative stress and free radicals play an important role in the formation of malignant cell transformation that can lead to chemical modifications of DNA structure, interacting with oncogenes and genes - suppressors of tumor growth. Anti-radical and anti-peroxide cell's protection depends on the condition of enzymes superoxide dismutase catalase activity, glutathione peroxidase, ceruloplasmin, content of alpha tocopherol, vitamins C, A, hapthoglobin, selenium in the organism and, in particular, the renewed glutathione and glutathione-dependent enzymes [1, 10, 11, 13, 14, 15, 16]. Renewed glutathione, except for providing antioxidant protection, detoxification of electrophilic xenobiotics, is known for its involvement in modulation of redox-regulated signal transmission, cellular regulation proliferation, apoptosis and cell differentiation. This tripeptide provides accumulation and cysteine transport, participates in deoxyribonucleotides synthesis, regulation of the immune response, leukotrienes and prostaglandins metabolism, folding and protein synthesis, modulates the cellular response to redox changes that are associated with the presence of active forms of oxygen.

Nowadays, researchers pay great attention to the role of protective structures of the gastric mucosa (GM). Transmembrane glycoproteins (TP) or, as they are otherwise called, gel forming mucins (MUC2, MUC5AC, MUC5B, MUC6) are intensively being studied with using the immunohistochemical method, the method of hybridization 'in situ' and Western blotting method. If normally, the GM is expressed by mucin: MUC1, MUC5AC and MUC6, then during the development of the pathological condition the mucinous compound changes. Thus, it has been found that MUC13 expression is the characteristic for the intestinal type of cancer and GM-fragments with intestinal metaplasia (IM), which is not detected on intact GM [4, 8, 10, 19].

It's known that today is the fact that the presence of GM and IM atrophy are associated with a high risk of stomach cancer as they make up a background where dysplasia and adenocarcinoma of intestinal stomach is developing [1, 6, 14, 15]. The detection and observation of patients with such pre-existing conditions may lead to early diagnosis of stomach cancer.

Analyzing the literature data, it should be noted that the search for the newest approaches for the identification of groups of risk for the development of stomach cancer is continuing. So, the interest of scientists to study the compound of the mouth liquid has increased for the diagnosis of diseases of the digestive system, as one of alternatives to blood analysis [3, 5]. The study of this biological liquid is non-invasive method that can be used many times and almost unlimited in terms of collecting the material [5].

The mouth liquid contains in its compound an epidermal growth factor, which stimulates the proliferation of epithelial tongue cells, esophagus, stomach and intestines, and inhibits the stomach hydrochloric acid secretion, and it almost does not influence on the pepsin release and the concentration of gastrin in blood. Also, the epidermal growth factor causes trophic action on organs of digestion; it is connected with its cytoprotective effect on the mucous membrane stomach interconnection. So, intragastric injection of saliva with high content of the epidermal growth factor reliably reduces ulceration in rats with removed submandibular glands [3].

The purpose of the research: is studying the aggression and protection factors of gastric juice and oral liquid of the patients with precancerous changes of gastric mucosa.

**Materials and methods**

The research was done with 32 people in the age between 40 to 55 years old with precancerous changes in the mucous membrane of the stomach, who were in stationary treatment at the Gastroenterology Institute NAMS of Ukraine “. The object of the research was the compound of gastric juice and patients ‘mouth liquid.

All patients after a thorough endoscopic and histological examination of GM biopsy were divided into three groups. In group I there were 6 patients with atrophic changes of GM of different degrees of severity, in group II - 12 people with IM in the antral department of the stomach, in group III – 14 patients with IM in the body and anterol department of GM. People from the 1st and 2nd groups had acidic condition of gastric secretion. Patients of the III group depending on the acidity of gastric juice were divided into subgroups: IIIa subgroup included 8 patients with acid secretion, IIIb subgroup - 6 patients with anatase. The control group consisted of 16 practically healthy people.

During the esophagogastroscopic examination gastric juice was collected by a suction method in a graduated tube. The pH gastric juice, pepsin concentration [17], TP [18], sialic acid (SA) were determined - by the method I. Warren, fucose - for L. Dische, hexosamines - forreaction with acetylacetone in an alkaline medium using R. Palmer's method [9].

They also conducted a study of the mouth liquid collected in the morning, on an empty stomach, after rinsing your mouth with warm boiled water using the splicing method for 10 minutes. In the mouth liquid it was determined the content of TP, SA, fucose, hexoamines too using the previous techniques.

All output data to optimize mathematical processing was input into the Microsoft Excel database. It was used descriptive statistics for statistical analysis of data comparison of average values; variables were carried out using parametric methods (t-criterion Student) for the normal distribution of evidence. Ratio of the distribution types of the signs of the law of normal distribution was checked by using Shapito-Whisk's method. In other cases it was used non-parametric method (U-criterion Mana-Whitney). For comparison the particle dividing of two or more variables, it was used the $\chi^2$ - test. The difference was considered reliable if the level of significance reached (p) was lower than 0,05 [7].

**Results and discussion**

In the result of the conducted studies in the control group, I, II and IIIa groups it was shown the acid state of the gastric secretion (2,51±0,35, 2,50±0,30, 2,83±0,63, 2,50±0,35 respectively), whereas in the IIIb group, the pH value was equal to 7,40±0,21.

As for the number of pepsin (Fig. 1), the individuals of group I the average indicator was 0,35±0,22 mg/ml, the second – 0,44±0,008 mg/ml and IIIa group - 0,53±0,007 mg/ml, that was not almost different from the control (0,62±0,004 mg/ml). Probable changes the quantity of pepsin compared to the control group was acquired only in the IIIb group, decreasing by 15,5 times. Analyzing personal data, it should be noted that in 75,0% of the examined people of I group, 54,5 - II and 66,7% - III group, there was a decrease of pepsin concentration, more changes (pepsin content was lower than 0,1 mg/ml) were observed in 65,0% of patients with atrophic changes, 16,7% - II group and 70,0% - patients with total IM. As to the quantitative composition of the protective factor of glycoprotein gel, the level of TP was: in the I group - 0,11±0,01 mg/ml, in II - 0,14±0,03 mg/ml, in IIIa - 0,14±0,01 mg/ml, in IIIb - 0,15±0,03 mg/ml in comparison with 0,1±0,01 mg/ml in control group. Thus, in spite of the changes of GM and its localization, the TP amount in the studied patients almost was not different.

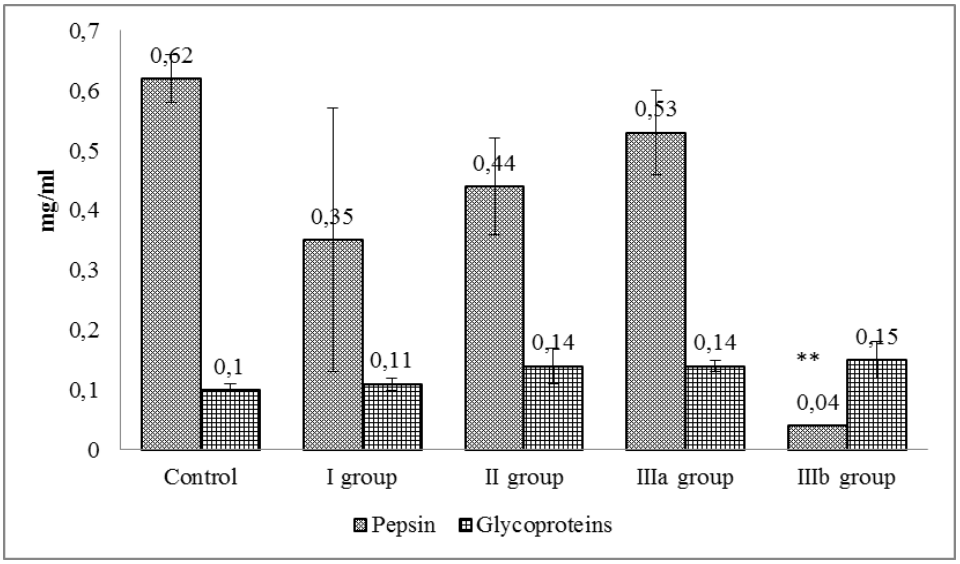


Figure 1. Pepsin and glycoproteins amount in gastric juice of researched people.

Note: ** - p<0,001.

In the study of the SA level, which is a marker of the altemative processes in GM, the results were following (look at Fig. 2): in group I this indicator slightly has changed from 0,086±0,01 mmol/l to 0,22±0,12 mmol/l, in the 2nd group it has increased by 2,5 times (to 1,21±0,05 mmol/l, p<0,10), in the III group - 3 times up to (0,26±0,04 mmol/l, p<0.01), in IIIb group – 3,25 times up to (0,28±0,01 mmol/l p<0,001).

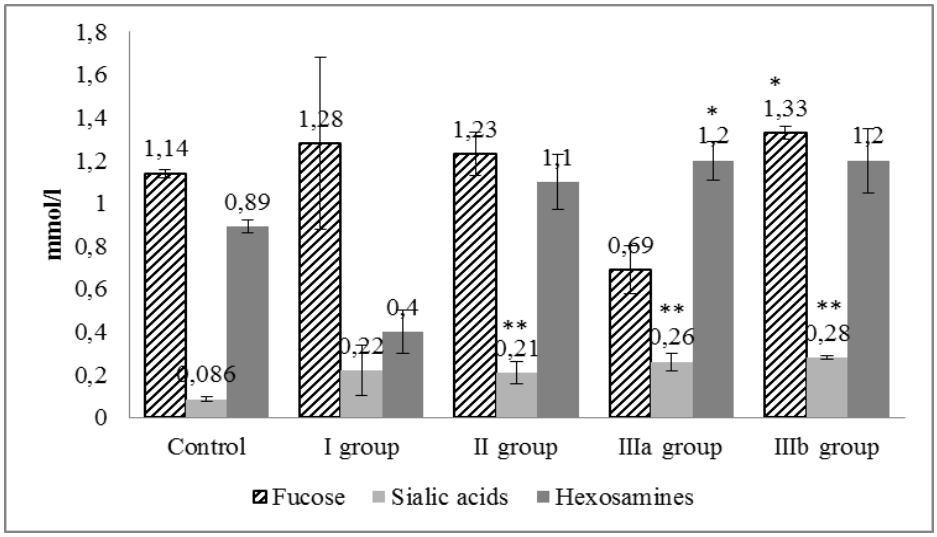


Figure 2. Fucose, sialic acids and hexosamines amount in the gastric juice of investigated people.

Notes: * - p<0,05; ** - p<0,001.

As for the protective component structures of the mucous gel - fucose and hexosamines, its content was different. Thus, in group I, the level of fucose in gastric juice has slightly changed - from 1,14±0,02 mmol/l to 1,28±0,4 mmol/l, in the second group - up to 1,23±0,1 mmol/l, in IIIa group - up to 0,69±0,11 mmol/l, and in IIIb group it has increased to 1,33±0,03 mmol/l (16%, $p<0,05$). The level of hexosamines in group I had the tendency to decrease and was 0,4±0,1 mmol l in comparison with 0,89±0,03 mmol/l in the control group, in the II and IIIb groups there was a tendency to increase (1,1±0,13 mmol/l and 1,2±0,15 mmol/l, respectively), increasing by 35% (up to 1,2±0,09 mmol/l, $p<0,05$) in the III group of the subjects.

Analyzing the ratio of aggression and protection factors of the SJ were the following adaptive-compensatory variants selected into: 1 (hyperreactive) - simultaneous increase in both the factors of aggression and protection; 2 (compensatory) - with an increase in the level of aggressive factors the concentration of protective was within the norm; 3 (decompensating) – with an increase in the content of aggressive factors of the gastric juice was a decrease in it compensatory indicators.

The distribution in groups according to definite variants has showen that in all patients with atrophic changes in GM in 100,0% of cases a hyperreactive variant was established (Fig. 3).

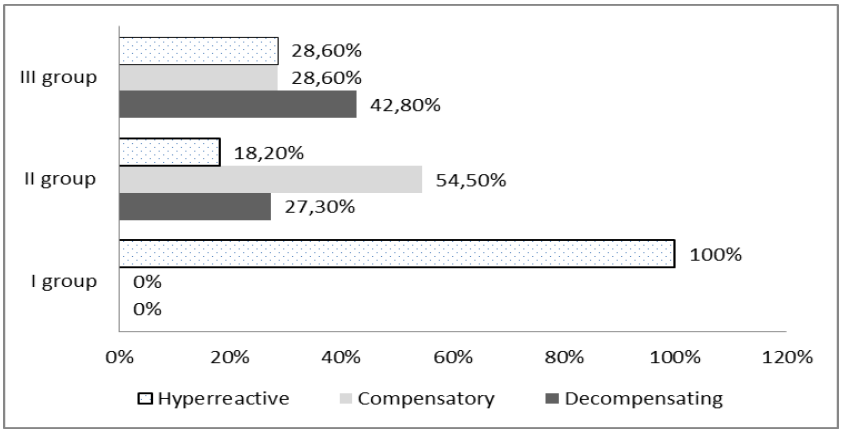


Figure 3. Aggressive and protective factors distribution in groups for variants of correlations.

In the II group, there is a compensatory version of the ratio (54,5%). In patients with total IM with an increase in the content of aggressive factors shock reduction of its compensatory indicators was noted at 42,8% of cases that is 1,6 times the frequency of observations of this option in the second group.

As a result of the mouth liquid study, there is a decrease of its pH (<7) in 25% of the studied group II and 50% of the patients of the IIIrd. Number of TPs in the investigated subjects (Fig. 4) was: in the I group - 0,12±0,006 mg/ml, in the II – 0,12±0,002 mg/ml, in IIIa and IIIb groups it was significantly increased - up to 0,24±0,005 mg/ml and 0,21±0,04 mg/ml versus 0,1±0,01 mg/ml in the control group (p<0,001).

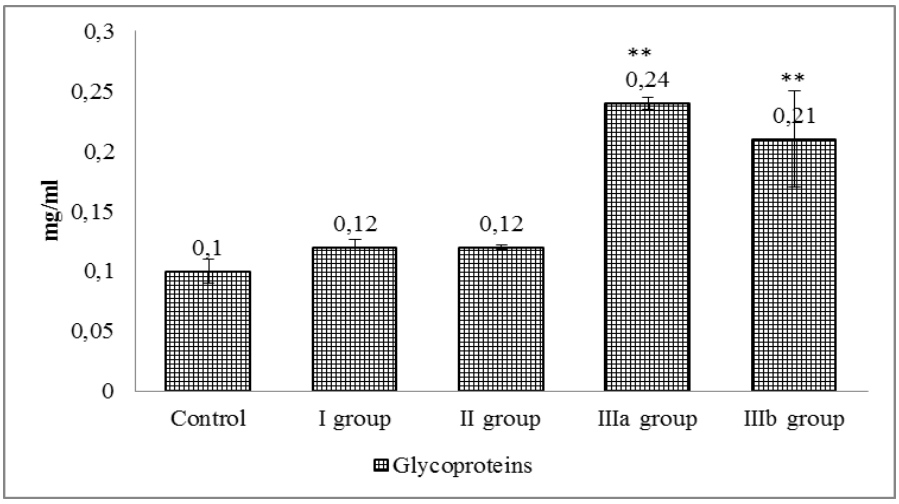


Figure 4. Glycoproteins amount in the mouth liquid of the patients.

Note: ** - p<0,001.

Regarding the level of SA (Fig. 5), it has risen in the mouth liquid of all people of the examined groups: 64% in the I (from 0,14±0,01 mmol/l to 0,23±0,004 mmol/l, p<0,001), by 42% - in II (up to 0,2±0,003 mmol/l, p<0,05), on 85% - in the III group (up to 0,26±0,004 mmol/l, p<0,001), and, mostly, by 92%, in IIIb group (up to 0,27±0,03 mmol/l, p<0,001).

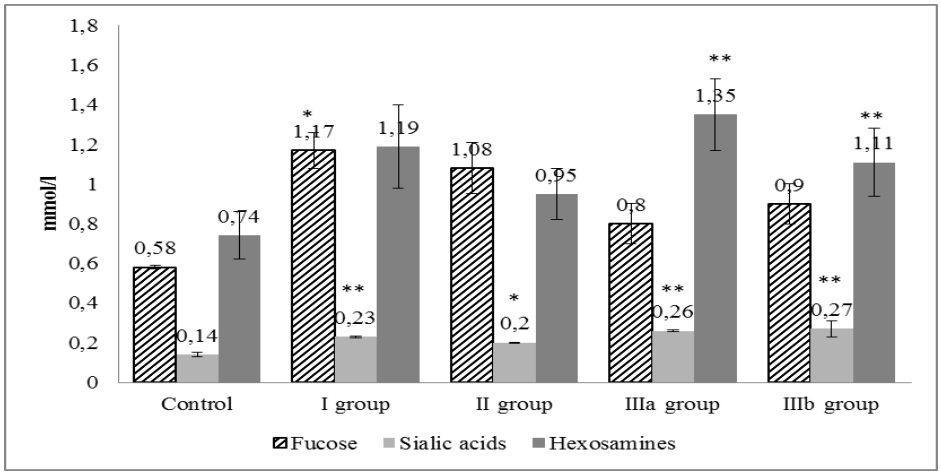


Figure 5. Fucose, sialic acids and hexosamines amount in the mouth liquid of investigated people.

Notes: * - p<0,05, ** - p<0,001.

The content of fucose in the mouth liquid of patients in the control group was 0,58±0,001 mmol/l. Its increasing, in 2 times, occurred only at the examined group I (up to 1,17±0,09 mmol/l, p<0,05). In the II, IIIa and IIIb groups this figure was 1,08±0,13 mmol/l, 0,8±0,1 mmol/l and 0,9±0,1 mmol/l, respectively.

Similar changes were in the mouth liquid and the amount of hexosamines. In the I group, this indicator has changed from 0,74±0,12 mmol/l to 2,29±0,21 mmol/l, in IInd - up to 0,95±0,13 mmol/l, gaining a probable increase in IIIa group up to 1,35±0,18 mmol/l (82%, p<0,001), and in the IIIb group - up to 1,11±0,17 mmol/l (50%, p<0,001).

Thus, the disproportion of polymer components of the mucous gel structures is detected, indicating a violation of the TP biosynthesis and may be due to the secretion of the "immature" TP. The last ones do not provide adequate level of physical and chemical characteristics of the gel that covers the lumen surface of GM, which influence on its aggressive damage factors.

**Conclusions**

Estimating the correlation between aggression and protection factors of gastric juice were selected adaptive-compensatory variants, the distribution of which ones in groups has shown that patients with only atrophic changes in GM in 100% of cases is set simultaneous increase as the aggression and protection factors. In the II group it was (54,5%) compensatory variant (with an increase of the level of aggressive factors the concentration of protective was within the norm). In patients with total IM in 42,8% of cases with an increase of the content of aggressive gastric factors juice was diagnosed with a decrease of its compensatory indicators, which is 1,6 times exceeds the frequency of observations of this option in the second group. IM is accompanied by increasing the amount of glycoproteins and hexosamines in oral liquids of patients, while sialic acids in this biological liquid is increased in all studied groups.

Comprehensive study functional-morphological changes of gastric secretion and activity salivary glands make it possible to assess the condition of reserve factors of factors protect the gastric mucosa and determine the risk groups of patients with precancerous state.

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