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# Activity dynamics of liver secretory enzymes in the blood serum of the patients with generalized periodontitis on a background of hepatobiliary system chronic pathology under the influence of combined treatment

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**Abstract**
The article presents data of the completed prospective clinical, controlled, parallel, longitudinal, public research of 126 patients (age of 22-44): 23 with the healthy periodontal without somatic diseases (control group) and 103 patients with chronic generalized periodontitis of the I degree (32 – without pathology of internal organs, 49 – with concomitant cryptogenic hepatitis and 22 – with concomitant sub compensated liver cirrhosis). We studied the secretory liver enzymes activity (cholinesterase and ceruloplasmin) in the blood serum and there changes under the influence of the combined treatment, conducted for 17 patients with generalized periodontitis without concomitant pathology and 29 patients with generalized periodontitis with concomitant cryptogenic hepatitis. An amino acid with antioxidant and hepatotropic action and mineral-vitamin complex were prescribed endogenously. An initial periodontal therapy, antiseptic medication and extemporaneous mixture of the same amino acid and enterosorbent were prescribed topically. During the data processing using package "Statistika 6,0" Microsoft Excel 2010 the parametric methods of descriptive statistics were used. In patients with generalized periodontitis without concomitant pathology the cholinesterase activity was unchanged in comparison with indicators of healthy people and in the case of comparison with cryptogenic hepatitis and sub compensated liver cirrhosis - significantly reduced ($p_1$<0,001). The difference in data in patients with generalized periodontitis without and with concomitant diseases was authentic ($p_2$<0,001). In combination of generalized periodontitis with sub compensated liver cirrhosis decrease in cholinesterase activity was the highest and other than indicators of generalized periodontitis and cryptogenic hepatitis ($p_3$<0,001). The ceruloplasmin activity increased especially during concomitant liver disease ($p_1$<0,005; $p_1$<0,001). The difference in ceruloplasmin activity in combination with generalized periodontitis with liver pathology and data of patients without concomitant pathology was authentic ($p_2$<0,001), as of the indicators in the case of generalized periodontitis on the background of sub compensated liver cirrhosis and generalized periodontitis in combination with cryptogenic hepatitis ($p_3$<0,05). After the treatment the cholinesterase activity increased achieving the rate of healthy in patients with generalized periodontitis without concomitant pathology. The cholinesterase activity was well regulated during simultaneous generalized periodontitis and cryptogenic hepatitis, the difference in data before the treatment was authentic ($p_1$<0,01), and the difference of healthy people indicators –insignificant ($p_2$>0,05). The regulation of ceruloplasmin activity in patients with generalized periodontitis without somatic diseases was achieved by the treatment ($p_2$>0,05). It also significantly reduced ($p_1$<0,05) during generalized periodontitis on the background of cryptogenic hepatitis, however the difference of healthy people indicators was significant ($p_2$<0,005).

**Keywords:** generalized periodontitis, cholinesterase, ceruloplasmin, combined treatment, amino acid.

## 1. Introduction
Periodontics occupies one of the leading places among the topical problems of modern dentistry. This causes an increased interest of scientists to the study of reasons of their origin and connection of periodontal disease with other dental and somatic illnesses [1]. Numerous studies have confirmed that the development and course of periodontal diseases is pathogenetically closely associated with systemic disorders of the body, and inflammatory and dystrophic-inflammatory lesions of periodontium are mostly secondary concerning system processes in the body which are the basis of a number of internal organs diseases [2].
During many diseases the destruction of cells occurs and its content, including enzymes, goes out into the blood stream. Diseases of such kind are chronic generalized periodontitis (GP) and chronic liver disease. Reasons that cause the release of intracellular contents into blood stream are violations of the permeability of cell membranes (inflammatory processes) or violation of

the integrity of the cells (necrosis). Determination of hepatic enzymes activity in blood is used to diagnose various diseases because their plasma level correlates with the degree of cell damage [3]. Considering these facts the study of activity of secretory liver enzymes in the case of GP, combined with chronic liver pathology and its changes under the influence of treatment is topical.

The purpose of our study was to establish activity changes of secretory liver enzymes cholinesterase (CE) and ceruloplasmin (CP) in the serum of patients with GP on a background of chronic diseases of the hepatobiliary system and the possibility of its drug correction.

## 2. Materials and Methods

Research was conducted at the University Hospital Dental Center of Ivano-Frankivsk National Medical University and gastroenterological department of Municipal Clinical Hospital №1 (Ivano-Frankivsk city). The study involved 126 patients - 23 persons with clinically healthy periodontal without somatic diseases (control group) and 103 patients with GP of I degree chronic course, including: 32 – without pathology of internal organs, 49 - with concomitant cryptogenic hepatitis and 22 - with concomitant subcompensated liver cirrhosis. The distribution to the groups was conducted by the method of stratified randomization (by diagnosis and age). The development degree and progression of GP was determined according to the classification of M.F. Danilevskiy (1994), which is recommended as a working one in educational and health care institutions of Ukraine [4]. The specified clinical classification was agreed upon with international statistical classification of diseases of 10th revision (MKX-10) – code MKX-10 K 05.31. The work was executed in accordance with ethical guidelines of carrying out biomedical investigations involving human that have been adopted by Helsinki Declaration (1964).

The criteria for inclusion were: age of 22-44 years, GP patients of I degree of development without concomitant somatic pathology; GP patients of I degree of development with concomitant cryptogenic hepatitis and subcompensated hepatic cirrhosis; absence of contraindications to treatment with investigational means and pharmacological medications; sanitated carious teeth, signing of informed consent for participation in research.

Exclusion criteria were: patients with viral hepatitis B and C and decompensated hepatic cirrhosis with a high degree of activity; patients who: have a contraindication to treatment with investigational techniques and pharmacological medications; did not appear for the next examination or breached the rules of controlled research.

Research design: prospective, clinical, controlled, parallel, longitudinal, open. The research was conducted without the involvement of pharmaceutical companies and applied medical products are registered in Ukraine in the established order.

In all examined persons was determined CE activity in blood serum using standard biotests kits of "Filisit-Diagnostika" company (Ukraine), CP - by using the method of G.O. Babenko [5].

For complex treatment and re-examination were selected 17 GP patients without concomitant pathology and 29 patients with GP combined with CH. We prescribed amino acid with antioxidant and hepatotrophic effect endogenously - GLUTARGIN: in the absence of concomitant pathology - 2 pills (0.25) 2 times per day for 15-20 days, in the presence of concomitant CH - 2 pills (0.75) 2 times per day for 15-20 days, and mineral-vitamin complex - Calcemin (1 pill 2 times per day for 15 days). We applied initial periodontal therapy locally (removal of soft and hard dental deposits, detoxification and roots polishing, closed curettage), an antiseptic drug of natural origin - Stomatofit (mouthwash) and extemporaneous mixture of 4.5 ml of 4% solution of GLUTARGIN and 2 g of enterosorbent Atoxil (for applications and instillations). We used parametric methods of descriptive statistics when processing the received data via package "Statistica 6,0" Microsoft Excel 2010.

## 3. Results and Discussion

While analyzing the received data, we defined that in patients with chronic generalized periodontitis of I degree the indicators of liver secretory enzymes activity underwent certain changes (see. Table 1).

**Table 1:** Liver secretory enzymes activity in the blood serum of the patients with chronic generalized periodontitis of I degree with concomitant cryptogenic hepatitis and sub compensated liver cirrhosis (M±m)

| Indicators | Researched groups | | | |
|---|---|---|---|---|
| | Healthy people | Patients with GP | Patients with GP and CH | Patients with GP and SLC |
| CE, mmol /s·l | n=23 | n=32 | n=40 | n=22 |
| | 77,28±2,46 | 74,15±1,89<br>$p_1$>0,05 | 64,25±1,39<br>$p_1$<0,001<br>$p_2$<0,001 | 51,84±1,12<br>$p_1$<0,001<br>$p_2$<0,001<br>$p_3$<0,001 |
| CP, u.o | n=22 | n=31 | n=49 | n=22 |
| | 21,89±1,42 | 27,59±0,91<br>$p_1$<0,005 | 33,62±1,24<br>$p_1$<0,001<br>$p_2$<0,001 | 39,99±2,59<br>$p_1$<0,001<br>$p_2$<0,001<br>$p_3$<0,05 |

**Notes:** GP − generalized periodontitis; CH – cryptogenic hepatitis; SLC – sub compensated liver cirrhosis; CE – cholinesterase; CP – ceruloplasmin. The probability of indicators difference is denoted: $p_1$ – healthy people indicators quantity; $p_2$ – patients with GP indicators quantity; $p_3$ − patients with GP and CH indicators quantity.

So, the level of CE activity in the blood serum of patients with GP without concomitant pathology slightly decreased - at 4.22% ($p_1$>0,05), slightly differed from the indicator of healthy people (77,28±2,46 mmol /s·l). In the case of combined GP and CH the CE activity decreased by 20.28% ($p_1$<0,001) in comparison with the data of control group and by 15,41% ($p_2$<0,005) relatively to indicators of patients with GP without internal organs destruction. In patients with GP on the background of SLC the CE activity indicator reduced even more – by 49,07%; $p_1$<0,001 (to 51,84±1,12 mmol /s·l) in comparison with the data of healthy people, and as to the indicators of patients with GP without concomitant pathology– by 43,04% ($p_2$<0,001). Analyzing the state of CE activity during both concomitant liver diseases we defined that in patients with GP on the background of SLC in comparison with received data in the case of GP this indicator significantly decreased and the difference was 23,94% ($p_3$<0,001). In all examined patients CE activity in the blood serum did not extend beyond the accepted norm (45-95 mmol /s·l), however in the case of GP with concomitant SLC this indicator approached norm lower limit. The study of CP activity level allowed to define that in patients with chronic GP of I degree this indicator was 27,59±0,91 u.o and higher than in healthy people by 26.04% ($p_1$<0,005). It was detected much growth of CP activity in patients with GP on the background of CH (to

33,62±1,24 u.o.) in comparison with healthy people and patients with GP without concomitant pathology, and the difference was 53,59% ($p_1$<0,001) and 21,86% ($p_2$<0,001) accordingly. The CP activity significantly increased in the case of GP and concomitant SLC – to 39,99±2,59 u.o. If relatively to the data of control group this difference was 82,69%($p_1$<0,001), then concerning indicators of somatically healthy people with periodontal disease it reached 44,94% ($p_2$<0,001). Comparing CP activity in the blood serum in the case of GP and it combination with liver cirrhosis with the data of GP on the background of CH the highest CP activity was detected in the case of GP and SLC – by 18,95% ($p_3$<0,05).

Under the influence of combined treatment of patients with GP the changes in activity of both studied by us liver secretory enzymes were detected (see. Table 2). So, CE activity, that before the treatment was 74,12±2,68 mmol /s·l, after the conducted therapy increased - at 4,38% ($p_1$>0,05; $p_2$>0,05). In the case of GP combined with CH CE activity before the treatment was 64,31±1,90 mmol /s·l and after it increased at 12,74% ($p_1$<0,01), approaching the data of healthy people ($p_2$>0,05).

**Table 2:** Activity dynamics of liver secretory enzymes in the blood serum of the patients with chronic generalized periodontitis of I degree with concomitant cryptogenic hepatitis under the influence of the treatment (M±m)

| Indicators | Healthy people | Researched groups | | | |
|---|---|---|---|---|---|
| | | Patients with GP | | Patients with GP + CH | |
| | | before the treatment | immediately after the treatment | before the treatment | immediately after the treatment |
| CE, mmol /s·l | n=23<br>77,28±2,46 | n=17<br>74,12±2,68 | n=17<br>77,37±2,37<br>$p_1$>0,05<br>$p_2$>0,05 | n=22<br>64,31±1,90 | n=21<br>72,50±2,17<br>$p_1$<0,01<br>$p_2$>0,05 |
| CP, u.o | n=22<br>21,89±1,42 | n=17<br>27,58±1,36 | n=17<br>22,74±1,51<br>$p_1$<0,05<br>$p_2$>0,05 | n=29<br>33,60±1,73 | n=25<br>27,90±1,23<br>$p_1$<0,05<br>$p_2$<0,005 |

**Notes:** GP − generalized periodontitis; CH – cryptogenic hepatitis; CE – cholinesterase; CP – ceruloplasmin. The probability of indicators difference is denoted: $p_1$ – to indicators quantity before treatment; $p_2$ – to indicators quantity of healthy people.

Complex therapeutic measures helped to reduce CP activity in patients with GP to 22,74±1,51 c.u., that is to 21,28% ($p_1$<0,05) and reached the indicator practically healthy persons ($p_2$>0,05). CP activity also decreased to 27, 90 ± 1,23 c.u. as a result of similar treatment of patients with concomitant CH, and the difference from the original data was 20.43% ($p_1$<0,05). However, the resulting figure was close to that in patients with GP without concomitant liver pathology, and the difference from data of healthy persons remained significant (27,46%; $p_2$<0,005).

In summary, it should be mentioned that some decrease of the CE activity in blood serum of GP patients points to a slight irregularities in their protein-synthetic liver function. Similar data were received also by other scientists [6]. Decrease in activity of this early marker of protein-synthetic liver function in patients with GP combined with chronic liver pathology indicates its considerable violation [7], especially in case of simultaneous lesions with GP and SLC. Severe decrease of the CE activity in blood serum of these patients indicates a deep trophic disruption in organism due to increase of hepatodepressive syndrome [8].

An increase of CP activity as a secretory liver enzyme and antioxidant in blood serum of patients with GP is an evidence of antioxidant system tension [9]. The increase of CP activity in the case of GP and concomitant chronic liver pathology (CH and especially SLC) also points to a simultaneous intensification of inflammation in periodontal and liver tissues, since it is a marker of acute phase of inflammation [7].

Our received data testified that breach of secretory activity of liver enzymes in blood serum promotes development and deepening of the pathological process in periodontal tissues requiring the prescription of medication that would have a combined effect on these organs, including medications Glutargin and Calcemin.

Activity regulation of secretory liver enzymes under the influence of complex GP treatment was provided primarily by antioxidant and hepatoprotective effect of the drug Glutargin [10, 11], which allows widely recommend it not only to patients with liver disease, but also with the presence of GP burdened with somatic pathology and without it.

## 4. Conclusions

1. In patients with GP without concomitant somatic pathology CE activity in the blood serum practically unchanged in comparison with healthy people indicators, and in the case of GP on the background of CH and SLC - significantly reduced ($p_1$<0,001). The difference of data of patients with GP with and without concomitant liver diseases was authentic ($p_2$<0,001). In combination of GP and SLC CE activity was the most and reliably different from the indicators of patients with GP on the background of CH ($p_3$<0,001).
2. CP activity indicators in the blood serum of all examined patients with GP significantly increased, especially with concomitant liver disease ($p_1$<0,005; $p_1$<0,001). The difference of CP activity indicators in combination of GP with CH and GP with SLC was authentic ($p_2$<0,001) in comparison with the data of patients with GP without concomitant liver pathology, and as between the indicators in the case of GP on the background of SLC and GP in combination with CH ($p_3$<0,05).
3. Under the influence of the combined treatment the CE activity increased in patients with GP without concomitant liver pathology reaching the indicator of healthy people. In the case of simultaneous GP and CH HE activity is well regulated, the difference of data before the treatment was authentic ($p_1$<0,01), and of healthy people indicators - not significant ($p_2$>0,05).
4. The regulation of CP activity in the blood serum of the patients with GP without somatic diseases was reached by the combined treatment ($p_2$>0,05). In patients with GP on the background of CH CP activity also significantly

reduced ($p_1$<0,05), however the difference form the similar indicator of healthy people was significant ($p_2$<0,005).

The perspective for further research is to study the activity of other liver enzymes during the diseases of periodontal tissues on the background of concomitant chronic liver pathology and there indicators in the blood serum and the possibility of there correction.

**Conflict of Interest Statement**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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