ASPECTS OF HEPATIC FUNCTION AT PERSONS WITH CHRONIC INTOXICATION WITH ALCOHOL

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Summary

The recognition of alcoholic hepatic injury is difficult because of both long clinical-biological latency of hepatopathy and the fact that alcohol consumption is recognized in less than half of cases. Performed researches proved the value and utility of complex of tests for detecting of persons with alcoholic intoxication. The evaluation of clinical syndromes at patients with alcoholic disease of liver revealed the presence more frequently of hepatomegaly, icteric syndrome and portal hypertension, unlike to the patients with chronic viral hepatitis, at whom manifestations of neuro-asthenic syndrome prevailed. Clinical perturbations are more severe in chronic mixed hepatitis (viral and alcoholic) versus alcoholic and viral hepatitis taken apart. The essential immunological modifications are characterized by rise of IgA at patients with alcoholic intoxication and chronic hepatitis and alcoholic liver cirrhosis and by rise of IgG at patients with chronic viral hepatitis. In chronic hepatitis and liver cirrhosis by alcoholic/viral etiology in association with chronic alcoholic intoxication, significant rise of γ-GT, carbohydrate-deficient transferrin (CDT), alcohol dehydrogenase (ADH) and glutamate dehydrogenase (GDH) were discovered, versus liver pathology by viral etiology without alcoholic intoxication.

Key words: alcoholic hepatitis, alcohol, carbohydrate deficient transferrin.

Introduction

Among the somatic diseases, induced by the chronic alcoholic intoxication, those digestive ones are the first and foremost, mainly hepatopathy and alcoholic pancreatitis (Nelson et al., 2008). In the context of hepatic diseases, alcoholic hepatic disease, according to its spreading and its social importance, holds the second place after the viral affections. The report of World Health Organization presents the list of the first 10 causes of death in the world depending on seriousness and the consumption of alcohol holds the 5th place (WHO, 2007).

Epidemiological studies proved the existence of a positive corelation between the consumption of alcohol allocated on each inhabitant and the mortality by liver cirrhosis (Maher, 1999; Nalpas, 2003). In Europe, the alcohol is considered to be the most frequent cause of liver cirrhosis (50-70%) (Nelson et al., 2008), and the american statistics shows that near 96% of alcoholics die by somatic complications.

The difficulty of the problem consist on the late diagnosis of somatic consequences as part of chronic alcoholic intoxication (Radu et al., 2011). Also, the complexity of the problem resides in the fact that the patients with alcoholic liver disease presents various clinic aspects, as a measure of its morphologic variability, influenced by the presence of accoholic abuse (Haber, et al., 2003), genetic susceptibility (Wong et al. 2000; Lesch et al., 2011), immune agression (Yin, et al., 2001; Neuman 2002), infection with hepatic viruses B and C (Zoulim et al., 2003; Grigorescu et al., 2003), as well as by the fact that the alcohol consumption is denied in more than 50% of cases (Trifan et al, 2004), and the serologic markers of hepatic injury due to alcohol are imperfects.
with still argued utility (Nanji, 2001 et al., Chiapelli et al. 2005).

The purpose of our study was the analysis of clinical-paraclinical particularities of the hepatic function at patients with chronic alcoholic intoxication in association with chronic hepatitis and liver cirrhosis (alcoholic, viral).

Material and methods
The clinical material was selected in „Sf. Apostol Andrei” Clinical Emergency County Hospital Galati. The study group was made of 117 patients with chronic liver pathology.

Depending on sex and age, the patients were divided in the following way:
• 49,1% (74) women and
• 50,9% (78) men; among who 24,6% (22) were below 40 years age, and 75,4% (95) – over 40 years age,
• the average age was 47,6 ± 1,4 years.

The duration of hepatic patology was less than 5 years at 53,2% (91) patients.

All the persons included in the study group were questioned using the complex of tests for estimation of chronic alcoholic intoxication. Thus, at 64,9% (97) of patients chronic alcoholic intoxication was identified.

When asked, only 44,1% (49) of patients sincerely admit the chronic consumption of alcohol, and more than half of them - 55,9% (62)- denies the alcohol abuse.

Depending on the presence or absence of chronic alcoholic intoxication and on the nosological form of liver pathology, the patients were distributed into the following groups:
• 19,8% (23) patients at who diagnosis of chronic alcoholic hepatitis (CAH) was established;
• 17,5% (19)- chronic viral hepatitis (CVH);
• 18,2% (21)- chronic hepatitis by mixed etiology (viral and alcoholic) (CVAH);
• 26,9% (26)- alcoholic liver cirrhosis (ALC);
• 17,5% (19)- viral liver cirrhosis (VLC).

The groups of patients were about similar by social standing, age, sex, body weight.

In the study were not included patients with obesity of II and III degree, diabetes mellitus, selfimmune diseases, primary and secondary biliary cirrhosis, pulmonary and renal patology.

As a witness group 20 persons that were clinically healthy were used: 55% (11) men and 45% (9) women, without alcohol consumption, without aggravating hereditary anamnesis, in the absence of hepatic and gastrointestinal patology.

For the appreciation of chronic alcoholic intoxication, a complex of tests was used: the CAGE; AUDIT questionnaire; the inquiry for the estimation of the intensity of alcoholic postintoxication syndrome; the modified „Le Go” map, which consists in detecting the objective signs of chronic alcoholic intoxication.

For the evaluation of the degree of hepatic alteration, a complex of tests was made, what reflects: the cytolytic syndrome (ALT, AST), the colestatic syndrome (total bilirubin and conjugated bilirubin, alkaline phosphatase, total cholesterol, HDL and LDL, β-lipoproteins, triglycerides), hepatocarential (proteins, albumins, transferrin, prothrombin time), the immuno-inflammatory syndrome (the level of IgA, IgM, IgG, circulating immune complexes, total T-lymphocytes and their subgroups: T-act, T-tfs and T-tfr by theophylline method).

The characteristic of this study aimed the determination of specific markers which indicate the chronic consumption of alcohol: gamma-glutamyl transpeptidase (G-GT), glutamate dehydrogenase (GDH), alcohol dehydrogenase (ADH), the level of alcohol into the serum and a new marker-carbohydrate-deficient transferrin (CDT).

For the purpose of detection of the etiology of viral hepatitides, markers of viral hepatitides B, C and D were determined. The research of the liver status were completed by the efectuation of
abdominal ecography.

The obtained results were evaluated by statistical analysis method, by using arithmetic mean and its error; the t-Student criterion and the “r” correlation coefficient.

**Results and discussions**

The clinical features of patients with alcoholic, viral and mixed (alcoholic and viral) hepatopathy were established, pointing out the syndromes that were present the most frequently (Table I). By studying the quantity and the duration of alcohol consumption at the patients included in the study, we found the longest duration (18.76±2.4 years) and the biggest quantity of pure alcohol used by day (54.6±2.6 g) at the patients with alcoholic cirrhosis. In all the groups it was established that the duration of alcohol consumption were more prolonged and the quantity of alcohol were bigger in men versus women.

**Table I** The most frequent encountered syndroms by clinical examination of patients from the groups of chronic alcoholic hepatitis (CAH), chronic viral hepatitis (CVH), chronic hepatitis by mixed etiology (viral and alcoholic) (CVAH), alcoholic liver cirrhosis (ALC), viral liver cirrhosis (VLC).

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>CAH group</th>
<th>CVH group</th>
<th>CVAH group</th>
<th>ALC group</th>
<th>VLC group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatomegaly</td>
<td>94.1% (32)</td>
<td>73.3% (22)</td>
<td>100% (31)</td>
<td>89.1% (41)</td>
<td>76.6% (23)</td>
</tr>
<tr>
<td>Neuro-astenic syndrome</td>
<td>70.5% (24)</td>
<td>83.3% (25)</td>
<td>83.8% (26)</td>
<td>76.1% (35)</td>
<td>86.6% (26)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>67.6% (21)</td>
<td>63.3% (19)</td>
<td>70.9% (22)</td>
<td>78.2% (36)</td>
<td>53.3% (16)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>58.8% (20)</td>
<td>63.3% (19)</td>
<td>67.7% (21)</td>
<td>58.7% (27)</td>
<td></td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>14.7% (5)</td>
<td>6.7% (2)</td>
<td>32.3% (10)</td>
<td>36.9% (17)</td>
<td>66.6% (20)</td>
</tr>
<tr>
<td>Edema</td>
<td>29.4% (10)</td>
<td>-</td>
<td>16.1% (5)</td>
<td>47.8% (22)</td>
<td>43.3% (13)</td>
</tr>
<tr>
<td>Ascites</td>
<td>11.7% (4)</td>
<td>-</td>
<td>12.9% (4)</td>
<td>71.7% (33)</td>
<td>50% (15)</td>
</tr>
<tr>
<td>Jaundice</td>
<td>29.4% (10)</td>
<td>-</td>
<td>25.8% (8)</td>
<td>80.43% (37)</td>
<td>46.6% (14)</td>
</tr>
</tbody>
</table>

**Fig.1** Clinical examination of patients with chronic alcoholic hepatitis (CAH) showed the presence more frequently of the following syndroms

Patients with CAH at clinical examination presented prevalent hepatomegaly (Fig.1, Table 1), a special attention was accorded to characteristic objective signs of chronic alcoholic intoxication: facial telangiectasis 91.2% (31), conjunctival hyperemia - 55.8% (19), tremor of extremities - 61.7% (21), peripheric neuropathy - 52.9% (18), muscular atrophy - 44.4% (15), Dupuytren’s contracture - 32.3% (11), mark of trauma - 17.6% (6), palmar erythema 50% (17), vascular stars 23.5% (8), gynecomastia 38.2% (13) (Fig. 2).
It was significant that at patients with CVH, unlike those with CAH (at whom the most frequent sign is hepatomegaly), predominant were: neuro-astenic syndrome - 83.3% (25), followed by hepatomegaly - 73.3% (22), nausea and pain syndrome finded at 63.3% (19) patients (Fig. 3, Table I). Splenomegaly was finded at only 6.7% (2) cases. At these patients were’n find jaundice, ascites, edema, signs of gonadic deficiency- signs that are present at patients with CAH and CVAH.

At patients with CVAH, clinical manifestations were more marked by comparison with CAH and CVH. The hepatomegaly was present at all patients-100% (31). The neuro-astenic syndrome was present in - 83.8% (26) cases, the pain syndrome - 67.7% (21), the nausea and vomiting syndrome -70.9% (22), splenomegaly 32.3% (10), jaundice 25.8% (8), edema 16.1% (5), ascites 12.9% (4) (Fig. 4, Table I).

At patients with CAH and CVAH, in clinical features hepatomegaly prevailed, unlike CVH at whom the neuro-astenic syndrome were finded more frequently. In CAH and CVAH were finded signs of portal hypertension and hypogonadism, signs that weren’t finded in CVH. It was concluded that the clinical manifestations were more severe in CVAH than in CAH and CVH.

Clinical examination at patients with CAH revealed more frequently the following clinical syndroms: hepatomegaly present at 89.1% (41) patients, jaundice - 80.43% (37), nausea and vomiting -78.2% (36), neuro-astenic syndrome - 76.1% (35), ascites - 71.7% (33), edema - 47.8% (22), pain at 58.7% (27) patients, splenomegaly was finded in 36.9% (17) cases. At 45.6% (21) patients, fever was finded. Skin-mucous syndrome was finded, consisting of: spider angiomas - 56.5% (26), palmar erythema -91.3% (42), gynecomastia - 50% (23), bruises - 17.4% (8) and epistaxis - 45.7% (21). Coagulation anomalies were noticed, as well as the objective signs suggestive for alcoholic etiology of hepatopathy (Fig.5).
In viral liver cirrhosis (VLC): neuroasthenic syndrome was found at 86.6% (26) patients; hepatomegaly - 76.6% (23); nausea, vomiting and pain at 53.3% (16) patients. It was noticed that splenomegaly - 66.6% (20) - was found more frequently, and jaundice 46.6% (14) less frequently, by comparison with ALC. As well, signs of portal hypertension were finded: ascites 50% (15), edema 43.3% (13) and collateral circulation 26.6% (8). Signs of gonadic deficiency were more reduced than in alcoholic cirrhosis (Fig. 6).

At patients with ALC were finded hepatomegaly, nausea and vomiting and jaundice by comparison with VLC at which neuroasthenic syndrome and splenomegaly were finded more frequently.

The recognition of alcoholic liver injury is difficult due to the latency of clinical-biological hepatopathy, and to the fact that the alcohol consumption is admit in less than half of cases. Research that were made proved the value and utility of group of tests for detecting the persons with alcohol intoxication. The evaluation of clinical syndroms at patients with alcoholic liver disease showed the presence more
frequently of hepatomegaly, jaundice syndrome and portal hypertension.

According to literature, hepatomegaly is the most constant and often the only sign, that is found in chronic alcoholic hepatitis and it is due both to fat accumulation and protein, aminoacid, water accumulation into the hepatocytes (Neuman, 2001, Neuman, et al., 2002). The presence of portal hypertension in CAH and CVAH is due to the compression of the sinusoids and hepatic veins by lipid deposits and perivenular sclerosis (colagenesation of the 3rd zone) (Navder, et al., 2002, Lesch et al. 2011].

Regarding of the laboratory markers for the hepatopathy syndroms at the patients with chronic hepatic patology due to alcohol, viruses and mixed (alcoholic and viral), we obtained the following results:

The cytolytic syndrome

At patients with CAH, the activity of ALT (67,7±8,8 U/l) was find to be significant elevated comparing to witness group (p<0,001), but veridical reduced as compared to patients with CVH (111,7±13,6 U/l) (p<0,01) and CVAH (119,7±14,5 U/l) (p<0,01). The level of AST (61,36±10,4 U/l) in CAH, in the same way, was higher comparing to witness group (p<0,001). Veridic differencies between AST levels at patients with CAH and those with CVH (76,65±7,9 U/l) and CVAH (78,5±10,1 U/l) weren’t noticed.

The proportion AST/ALT in CAH were 0,94±0,07, beeing elevated as compared to CVH (0,71±0,05) (p<0,01).

In ALC the level of ALT (91,2±7,4 U/l) was higher than at witness group (p<0,001), but there wasn’t differenced versus VLC (83,18±9,15 U/l). The activity of AST (64,65±6,1 U/l) in ALC exceeded by 3.3 times the level in witness group (p<0,001), and it was higher than in VLC (46,19±6,7 U/l) (p<0,05), too. De Rittis’s coefficient was 0,79±0,08, higher than in VLC (0,55±0,04) (p<0,01).

The comparative analysis of aminotransferases showed higher levels of ALT (TGP) in CVH (p<0,01) and CVAH (p<0,001) by comparison with CAH. The level of AST (TGO) was higher in ALC versus VLC (p<0,05).

The cholestatic syndrome

The level of total bilirubin and direct bilirubin were finded higher at all groups of patients with chronic hepatitides by comparison with the witness group, the highest values of total bilirubin (28,12±2,68 mmol/l) and direct bilirubin (7,24±1,37 mmol/l) were finded in CVAH, the total bilirubin being significantly higher versus CVH (20,41±2,5 mmol/l) (p<0,05). At CAH, total bilirubin (27,19±2,9 mmol/l, p<0,001) and the conjugated fraction (7,36±1,29 mmol/l, p<0,001) were higer versus those at witness group.

The levels of alkaline phosphatase in CAH (263,9±18,72 U/l, p<0,001) and CVAH (271,09±23,74 U/l, p<0,001) were higher than in witness group. As well, in CVAH, it was higher than at patients with CVH (263,9±18,7 U/l) (p<0,05).

The analysis of lipids showed high triglycerides (2,38±0,21 mmol/l) at patients with CAH by comparison with healthy subjects (p<0,001) and with CVH patients (1,20±0,07 mmol/l) (p<0,001). The levels of β-lipoproteins (65,2±3,44 IU/l) (p<0,001) and HDL (2,06±0,17 mmol/l) (p<0,001) in CAH were significantly rised by comparison with healthy persons. As well, significant statistical differences to patients with CVH were finded, at the last ones levels of β-lipoproteins being lower (43,22±3,0 IU/l) (p<0,001) and HDL too (0,93±0,13 mmol/l) (p<0,001). A similary tendency was recorded at CVAH, too: triglycerides (2,29±0,26 mmol/l) (p<0,001), β-lipoproteins (60,38±4,17 IU/l) (p<0,001) and HDL (1,94±0,2 mmol/l) (p<0,001) in CVAH were higer by comparison with witness group and CVH. The modifications of the cholestatic syndrome proved to be more marked at the group of patients with CAH and CVAH, by comparison to CVH, manifesting by rising of total bilirubin and conjugated fraction, alkaline phosphatase, triglycerides, HDL and β-lipoproteins.
The research of the lipids emphasized the rise of triglycerides (2.12±0.21 mmol/l) by comparison to witness group (p<0.05) and VLC (1.13±0.13 mmol/l) (p<0.05). Total cholesterol raised (5.27±0.23 mmol/l, p<0.01), LDL, too (3.1±0.21 mmol/l, p<0.05) at patients with ALC by comparison to healthy persons. The level of cholesterol was higher than in VLC, too (4.07±0.32 mmol/l) (p<0.01).

**The hepato-deficiency syndrome**

It was showed the reduction of total proteins at patients with CAH (72.57±1.32 g/l, p<0.01) and CVAH (72.59±0.97 g/l, p<0.01) versus CVH (78.56±1.6 g/l). A similar tendency was noticed at seric albumins, too, in CAH (38.13±1.41 g/l, p<0.001) and CVAH (37.64±1.25 g/l, p<0.001) they were lower than in VCH (44.97±1.40 g/l).

It was noticed the reduction of total transferrin, too, at patients with CAH (2.24±0.09 g/l, p<0.001) and CVAH (2.37±0.09 g/l, p<0.001) as compared to CVH (3.02±0.14 g/l).

By researching the hepato-deficiency syndrome at patients with ALC, it was noticed the significant lowering of total proteins (68.87±0.96 g/l, p<0.001), albumins (33.38±0.89 g/l, p<0.001) and transferrin (1.98±0.04 g/l; p<0.001) as compared to respective levels at healthy persons. There weren’t determined statistical differencies between the above parameters and the similar levels of patients with VLC, the parameters being lowered in both cases.

The prothrombin time (65.22±1.87%) in ALC was lower, both versus the witness group (p<0.001), and the VLC (74.37±1.62%) (p<0.001).

**The immuno-inflammatory syndrome**

The most relevant, by meaning of detecting the perturbation of immune response at patients with CAH, were: IgA (4.67±0.27 g/l) (p<0.001), IgM (2.02±0.14 g/l) (p<0.001), IgG (17.54±0.69 g/l) (p<0.001), their levels were significantly raised compared to witness group. A special remark is given to IgA, it’s level rised 1.9 times above the healthy individuals, and it was significantly raised compared to CVH (p<0.01).

The evaluation of cellular immunity demonstrated a decreasing of T lymphocytes =0.77±0.07x10/l (49.33±1.56%) (p<0.05) and raising Th=0.63±0.06x10/l (42.67±2.6%) compared to similar parameters in witness group.

At patients with CVH we noticed: rise of IgM (1.92±0.11 g/l) (p<0.001) and IgG (28.71±10.26 g/l) (p<0.001) versus witness group. At patients of this group was noticed the highest level of IgG compared to CAH (p<0.01) and CVAH (p<0.01).

The study of cellular immunity revealed the rise of lymphocytes Th=0.72±0.07x10/l (41.33±3.04%) compared to witness group (p<0.01).

**The evaluation of the markers of chronic consumption of alcohol**

The study of markers that indicates the chronic impregnation with alcohol (table I) revealed:

- At the patients with CAH, G-GT was significantly raised (153.4±18.2 U/l) compared to witness group (p<0.001), exceeding these values by 4.8 times, at the same time this marker was proved to be statistic significant raised compared to patients with CVH (68.9±6.44 U/l) (p<0.001).
- In CAH, GDH (14.46±1.35 U/l) exceeded its value at healthy people by 3 times and
- ADH level (10.95±0.79 IU/l) was 5 times rised versus witness group (p<0.001). There were noticed statistic significant differences with these values at patients with CVH (p<0.001).

- A distinct significance had the research of carbohydrate-deficient transferrin (CDT), that revealed essential raised values at patients with CAH (11.07±0.42%) compared to the healthy subjects (p<0.001) and the patients with CVH (5.17±0.20 %) (p<0.001), at who this marker was normal
- The CDT/transferrin ratio
(5.31±0.35) was significant raised in this group, too, versus healthy subjects (p<0.001) and patients with CVH (1.80±0.10) (p<0.001).

- The level of alcohol into the blood was 0.014±0.002 g/l, that was no different to witness group and patients with CVH.

At patients with CVAH, as the same, there were founded significant raised levels of:

G-GT (177.43±25.43 U/l) (p<0.001), GDH (15.63±1.42 U/l) (p<0.001) and ADH (9.82±1.13 IU/l) (p<0.001) compared to these markers at healthy subjects and patients with CVH (p<0.001) (Table II).

The level of CDT (10.84±0.49%), was raised comparing to the witness group (p<0.001) and CVH (p<0.001).

### Table II Markers of chronic excessive consumption of alcohol at patients with CAH, CVH and CVAH

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Witness group – I (n=20)</th>
<th>CAH – II (n=34)</th>
<th>CVH – III (n=30)</th>
<th>CVAH – IV (n=31)</th>
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</thead>
<tbody>
<tr>
<td>G-GT (U/l)</td>
<td>29.16±2.45</td>
<td>153.4±18.1***</td>
<td>68.9±6.44**</td>
<td>177.4±25.4***</td>
</tr>
<tr>
<td>GDH (U/l)</td>
<td>3.86±0.18</td>
<td>10.5±1.35***</td>
<td>4.9±0.41</td>
<td>11.6±1.42***</td>
</tr>
<tr>
<td>ADH (IU/l)</td>
<td>1.92±0.11</td>
<td>8.9±0.79***</td>
<td>2.36±0.36</td>
<td>9.82±1.13***</td>
</tr>
<tr>
<td>CDT (%)</td>
<td>4.7±0.41</td>
<td>11.07±0.42***</td>
<td>5.17±0.20</td>
<td>10.8±0.49***</td>
</tr>
<tr>
<td>CDT/transferin</td>
<td>1.56±0.20</td>
<td>5.31±0.35***</td>
<td>1.8±0.10</td>
<td>4.78±0.39***</td>
</tr>
<tr>
<td>Unconjugated bilirubin (mcmol/l)</td>
<td>10.44±1.10</td>
<td>19.51±1.89*</td>
<td>14.33±2.17</td>
<td>20.8±2.83**</td>
</tr>
<tr>
<td>Blood alcohol</td>
<td>0.01±0.002</td>
<td>0.014±0.002</td>
<td>0.009±0.001</td>
<td>0.015±0.002</td>
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</table>

Note: *p<0.05; **p<0.01; ***p<0.001 – difference between the study groups and the witness group

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Witness group – I (n=20)</th>
<th>ALC – V (n=46)</th>
<th>VLC – VI (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G-GT (U/l)</td>
<td>29.16±2.45</td>
<td>269.4±35.7***##</td>
<td>72.6±9.5**</td>
</tr>
<tr>
<td>GDH (U/l)</td>
<td>3.86±0.18</td>
<td>17.4±1.07***#</td>
<td>9.91±1.21***</td>
</tr>
<tr>
<td>ADH (IU/l)</td>
<td>1.92±0.11</td>
<td>8.04±0.97***##</td>
<td>2.56±0.41</td>
</tr>
<tr>
<td>CDT (%)</td>
<td>4.7±0.41</td>
<td>12.5±0.37***#</td>
<td>5.35±0.68</td>
</tr>
<tr>
<td>CDT/transferin</td>
<td>1.56±0.20</td>
<td>6.6±0.35***##</td>
<td>2.9±0.26</td>
</tr>
<tr>
<td>Unconjugated bilirubin (mcmol/l)</td>
<td>10.44±1.10</td>
<td>52.6±6.7***</td>
<td>61.3±4.2**</td>
</tr>
<tr>
<td>Blood alcohol concentration (g/l)</td>
<td>0.01±0.002</td>
<td>0.23±0.001## #</td>
<td>0.01±0.002</td>
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</tbody>
</table>

Note: *p<0.05; **p<0.01; ***p<0.001 – the difference between the study groups and the witness group

Analising biochemistry tests that shows excessive consumption of alcohol at patients with ALC (Table III), we obtained: the most rised levels of G-GT (269.38±35.7 U/l), that exceeds by 6 times the values obtained in the group of healthy subjects (p<0.001). The level of G-GT was significantly rised compared to the similar marker of patients with VLC (72.65±9.55 U/l) (p<0.001) and those with chronic viral hepatitis (p<0.001), CAH (p<0.01) and CVAH (p<0.05). The concentration of GDH (17.38±1.07 U/l), that was 4 times higher than at the witness group, was proved to be significant rised both versus healthy persons (p<0.001), and compared to patients with VLC (9.91±1.21 U/l) (p<0.001), at who this marker was rised, too, but not significantly.

### Table III The specific markers of chronic excessive consumption of alcohol at patients with ALC and VLC

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Witness group – I (n=20)</th>
<th>ALC – V (n=46)</th>
<th>VLC – VI (n=30)</th>
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<td>GDH (U/l)</td>
<td>3.86±0.18</td>
<td>17.4±1.07***##</td>
<td>9.91±1.21***</td>
</tr>
<tr>
<td>ADH (IU/l)</td>
<td>1.92±0.11</td>
<td>8.04±0.97***##</td>
<td>2.56±0.41</td>
</tr>
<tr>
<td>CDT (%)</td>
<td>4.7±0.41</td>
<td>12.5±0.37***##</td>
<td>5.35±0.68</td>
</tr>
<tr>
<td>CDT/transferin</td>
<td>1.56±0.20</td>
<td>6.6±0.35***##</td>
<td>2.9±0.26</td>
</tr>
<tr>
<td>Unconjugated bilirubin (mcmol/l)</td>
<td>10.44±1.10</td>
<td>52.6±6.7***</td>
<td>61.3±4.2**</td>
</tr>
<tr>
<td>Blood alcohol concentration (g/l)</td>
<td>0.01±0.002</td>
<td>0.23±0.001##</td>
<td>0.01±0.002</td>
</tr>
</tbody>
</table>

Note: *p<0.05; **p<0.01; ***p<0.001 – the difference between the study groups and the witness group

# # # p<0.001 – the difference between ALC and VLC
There were found significantly statistic differences of ADH level (8,04±0,97 IU/l) at patients with ALC compared to the witness group (p<0,001) and to the patients with VLC (2,56±0,41 IU/l) (p<0,001). CDT (12,54±0,37 %) and CDT/transferrin ration (6,6±0,35) were proved to be significantly rised versus these parameters of the witness group (p<0,001) and of the patients with VLC (p<0,001). At the patients with ALC it was found a significantly rised level of blood alcohol concentration (0,23±0,01 g/l) both compared to the healthy persons (p<0,001) and VLC (p<0,001), and compared to the persons with chronic hepatitides by any etiology (p<0,001), at these patients finding a normal level of blood alcohol concentration.

The evaluation of results of the imagistic examination

At the patients with CAH and CVAH there were finded: rised and uniform ecogenericity of the hepatic parenchyma; at 41,2% (14) cases signs of hepatic steatosis were finded in CAH and in 38,7% (12) cases- in CVAH. The dimensions of the liver were finded rised in CAH (right lobe 16,39±0,33 cm, p<0,01; left 8,87±0,26 cm, p<0,01) and CVAH (the right lobe 15,1±0,3 cm, p<0,01; left 8,5±0,27 cm, p<0,01) compared to the respective parameters at patients with CVH (right lobe 13,4±0,64 cm, left 7,0±0,36 cm).

The endoscopy showed the presence of incipient esophageal varices at 11,8% (4) patients and in only 1 case (2,94%)- varices of II-nd degree, in contrast to CVH at which there were not detected varices of esophagal veins.

At the patients with ALC there have been finded: non-homogeneous image of the liver parenchyma, with an alternance of ecogenic zones and ecodense zones. There have been detected signs of steatosis at 21,7% (10) patients. The dimensions of the liver- the right lobe (16,39±0,33 cm) and the left one (8,9±0,26 cm)- were proved to be obviously rised compared to patients with VLC- respectively 14,4± 0,4 cm (p<0,01) and 8,0± 0,3 cm (p<0,05). The longitudinal dimension of the spleen (14,3±0,49 cm) were significantly reduced comparing to the similar values of the patients with VLC (15,8±0,6 cm) (p<0,05). The endoscopy confirmed the presence of advanced signs of portal hypertension and of significants altertations of the liver both in the alcoholic cirrhosis and in the viral one.

A special attention was accorded to the modification of the biochemistry parameters of hepatic syndroms, that could facilitate both recognition of alcoholic hepatopathy and the evaluation of the degree of hepatic lezions induced by the alcohol.

According to the previously presented results, there are known the important modifications of the parameters that caracterizes the cytolytic syndrome, cholestatic syndrome and the hepatodeficiency syndrome at the patients with CAH. There are numerous literature data (Burns et al., 2001, Neuman, et al., 2002, Lesch et al. 2011) that shows hyperlipidemia that is present in the alcoholic hepatopathy.

The study that was presented evidentiated the rise of HDL, triglycerides and β-lipoproteins at the patients with CAH and CVAH compared to CVH, so that these values can be used as suplimentar criteria for diagnosis of alcoholic hepatopathy.

The modifications of the humoural immunity at the patients are in conformity with the opinions found in the literature (Tilg, et al., 2000) where rise of IgA into the serum is remarqued at 60-70% of persons with prolonged alcoholic impregnation at toxic levels.

The evaluation of the values of abusive alcohol consumption at the studied patients revealed important modifications that should contribute at the diagnostication of alcoholic liver patology. The level of G-GT was obviously rised at the patients with CAH. According to the bibliographic sources (Maher 1999; Nalpas, 2003; Nelson et al., 2008), the rised values of G-GT represents the most frequent biochimic anomaly founded at the alcoholics.

Our study estimated the importance of the determination of CDT at the patients
with alcoholic liver. Into the groups with alcoholic liver patology, the level of CDT was significantly raised compared to the levels at the patients with viral patology without alcoholic intoxication.

By difference of G-GT, which raised non-significantly both at the patients with viral liver patology, the level of carbohydrate-deficient transferrin both at the patients with CVH and those with VLC did not essentially variate from the value finded at healthy subjects. Literature sources (Chen et al., 2003, Lesch, et al. 2011, Nelson et al., 2008) consider CDT as the one of the most specific markers of alcohol consumption. The rise of the CDT, as well as the rise of disialic- and asialic transferrine permit the identification of chronic consumers of alcohol. These are specific markers of the alcoholic impregnation, much more efficient than GGT and transaminases, low specificity tests. The daily average consumption of 50-80 g of alcohol for 2 weeks modifies the level of transfferin isomorofes. The technique permits the separation depending of pH of the 5 isomorofes of the transferrin by the mean of the different degree of transferrin sialisation: asialo- di-, tri-, tetra- and penta-transferrin.

In the present day, there continues the studies for finding a combination of tests that should increase de confidence in the diagnosis. Chen et al. (2003) proved that for men the association of CDT and G-GT assures the highest degree of confidence for the detection of daily consumption of 60 g alcohol and over.

In contrast with G-GT and CDT, which can reflect only the presence of alcohol consumption, GDH reflect the depth of hepatocyte cytolysis in hepatic patology (Chen et al., 2003, Lesch et al. 2011, Nelson et al., 2008). But GDH can be increased at the patients with active cirrhosis by other etiology, including viral one, being a sign of unfavourable prognostication.

The data referring to the activity of ADH in the alcoholic hepatopathy are contradictory. We recorded the rise of the level of ADH in all groups of patients with liver patology and CAH. A recent study accomplished by Nanji et al. (2001) demonstrated the importance of raised seric ADH as an indicator of alcoholic hepatic malfunction, but didn’t confirmed its signification as a marker of alcoholic dependency.

**Conclusions**

1. In the clinical manifestations of the patients with chronic alcoholic intoxication and with chronic hepatitis and alcoholic liver cirrhosis predominates hepatomegaly, jaundice and portal hypertension versus the patients with chronic viral hepatitis, at who prevails the manifestation of neuro-astenic syndrome. The clinical perturbations are more severe in mixed chronic hepatitis (viral and alcoholic) versus alcoholic hepatites and separately the viral one.

At the patients with ALC randomly were assessed hepatomegaly, dispeptic manifestations and jaundice, by comparison with VLC at what more frequently were determined neuro-astenic syndrome and splenomegaly.

2. At the patients with chronic alcoholic intoxication associated with chronic hepatitis and alcoholic liver cirrhosis it was finded more pronounced the cholestasis and the hepato-deficiency syndrome compared to the chronic viral hepatitis, at which the cytolysis syndrome were finded more pronounced.

3. The essential immune modifications are the increase of IgA at the patients with alcoholic intoxication and chronic hepatitis and alcoholic liver cirrhosis and the increase of IgG at the patients with chronic viral hepatitis.

4. At chronic hepatitis and liver cirrhosis by alcoholic/viral associated with alcohol etiology, significant increases of gamma-glutamyl transpeptidase, carbohydrate-deficient transferrin, alcohol dehydrogenase and glutamate dehydrogenase were determined, versus hepatic patology by viral etiology without alcoholic intoxication.

5. For the detection of chronic alcoholic intoxication it is necessary to use the complex of tests CAGE, the inquiry for detection of
the alcoholic postintoxication syndrome, the map of the signs of the chronic alcoholic intoxication „Le Go”.

6. For the argumentation of alcoholic etiology

References


