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ABSTRACT

FEATURES OF CHANGES IN INTEGRATIVE INDICATORS OF ENDOGENOUS INTOXICATION, REACTIVITY, INFLAMMATION ACTIVITY IN PATIENTS WITH CHRONIC VIRAL HEPATITIS AND CHRONIC RENAL FAILURE

The aim: to study the peculiarities of changes in integrative indicators of endogenous intoxication, reactivity and activity of inflammation in patients with chronic viral hepatitis B and C, and with chronic renal failure undergoing hemodialysis.

Materials and methods. 19 patients with chronic viral hepatitis B (HBV) and chronic viral hepatitis C (HCV) with chronic renal failure and patients with chronic kidney disease (KD) were examined. Comparison group included 40 healthy blood donors. Epidemiological, clinical and laboratory examination was performed. Indicators of endogenous intoxication, nonspecific reactivity and inflammatory activity were calculated and analyzed using statistical criteria (M ± m, Student's test and Mann–Whitney test).

Results: an increase in the integrative indicators of endogenous intoxication in patients with the combined pathology of chronic KD and chronic viral hepatitis (VH) is a consequence of the activation of tissue disintegration, cytolysis of hepatocytes and a significant impairment of liver function. A change in the indices of non-specific inflammation indicate expressed activity of the inflammatory process and immunological disorder of reactivity. These changes also suggest decompensated endotoxicosis, as a possible consequence of a chronic infectious process and decompensated endogenous intoxication.

Indicators of leukocyte intoxication index (LII), leukocyte shift index (ISL), hematological intoxication index (HII), intoxication index severity (IIS), immunoreactivity index (IR), neutrophil-monocyte ratio (NMR) are increased in all patients with chronic KD, which may be related to the actual cause of development –

glomerulonephritis, chronic pyelonephritis, concomitant pathology. More pronounced deviations were found in men of both groups than in women, which may be related to greater adherence to diet, water load between hemodialysis procedures in the latter.

Conclusions. Patients receiving invasive manipulations, including hemodialysis, belong to the risk group and are more susceptible, taking into account immunodeficiency, to infection with hepatitis viruses than the general population. CVH is one of the most common types of lesions in them. The obtained changes, namely, a more pronounced increase in the integrative indicators of endogenous intoxication, in patients with the combined pathology of CKD and CVH indicate the activation of the processes of tissue decay, cytolysis of hepatocytes and significant liver function impairment. At the same time, a change in indices of non-specific inflammation indicates a pronounced activity of the inflammatory process and an immunological disorder of reactivity. A clear systemic reaction to inflammatory processes in the body of patients is determined, the probable development of decompensated endogenous intoxication, which is possible consequence of a chronic infectious process. A simultaneous increase in ISL and a decrease in ILG was established, which is associated with the development of endogenous intoxication and a violation of immunological reactivity due to autointoxication of the body. A decrease in Ilymph indicates an active adaptive reaction of white blood cells and a cell-type immunodeficiency, in particular, a decrease in non-specific anti-infective protection. Indicators of LII, ISL, HII, IIS, IR, NMR are increased in all patients with CKD, which may be related to the actual cause of development – glomerulonephritis, chronic pyelonephritis, etc. The difference of integrative indicators between men and women was established, more pronounced deviations from normal were found in men of both groups than in women, which may be associated with greater adherence to diet, water load between hemodialysis procedures in the latter.

Key words: chronic viral hepatitis B and C, coinfection, hemodialysis, chronic renal failure, health, intoxication, reactivity, inflammation.

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ОСОБЛИВОСТІ ЗМІН ІНТЕГРАТИВНИХ ПОКАЗНИКІВ ЕНДОГЕННОЇ ІНТОКСИКАЦІЇ, РЕАКТИВНОСТІ, АКТИВНОСТІ ЗАПАЛЕННЯ У ПАЦІЄНТІВ З ХРОНІЧНИМ ВІРУСНИМ ГЕПАТИТОМ ТА ХРОНІЧНОЮ НИРКОВОЮ НЕДОСТАТНІСТЮ

Мета: вивчити особливості змін інтегративних показників ендогенної інтоксикації, реактивності, активності запалення у пацієнтів з хронічними вірусними гепатитами В і С, і хронічною нирковою недостатністю, що знаходяться на гемодіалізі.

Матеріали і методи: обстежено 19 осіб (з хронічним вірусним гепатитом В (ХВГ), хронічним вірусним гепатитом С

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та з хронічною нирковою недостатністю (ХНН), пацієнти з хронічною хворобою нирок). Групу порівняння склали 40 здорових донорів крові. Зібрано епідеміологічні, клінічні та лабораторні дані (загальний та біохімічний аналізи крові). Показники ендогенної інтоксикації, неспецифічної реактивності та активності запалення були розраховані та проаналізовані за допомогою статистичних критеріїв (M ± m, критерій Стьюдента і критерій Манна– Уїтні).

Результати: збільшення інтегративних показників ендогенної інтоксикації, у пацієнтів з поєднаною патологією ХНН та ХВГ є наслідком активації процесів розпаду тканин, цитолізу гепатоцитів та значного порушення функції печінки. Встановлені зміни індексів неспецифічного запалення вказують на виражену активність запального процесу та імунологічне порушення реактивності, а також на декомпенсований ендотоксикоз, як можливий наслідок хронічного інфекційного процесу та виразну ендогенну інтоксикацію.

Показники ЛІІ, ІЗЛК, ГПІ, ПІ, ІІР, ІСНМ підвищені в усіх пацієнтів з ХНН, що може бути пов’язано з власне причиною розвитку – гломерулонефритом, хронічним пієлонефритом, супутньою патологією. Більш виражені відхилення від нормальних були виявлені у чоловіків обох груп, ніж у жінок, що може бути пов’язане з більшою прихильністю до дієти, водного навантаження між процедурами ГД в останніх.

Висновки. Пацієнти, що отримують інвазивні маніпуляції, у тому числі гемодіаліз, відносяться до групи ризику і більш сприйнятливі, враховуючи імунодефіцит, до інфікування вірусами гепатитів, ніж загальна популяція. ХВГ є одними із найпоширеніших типів уражень у них. Отримані зміни, а саме виразніше збільшення інтегративних показників ендогенної інтоксикації, у пацієнтів з поєднаною патологією ХНН та ХВГ свідчить про активацію процесів розпаду тканин, цитолізу гепатоцитів та значне порушення функції печінки. Разом з тим, зміна індексів неспецифічного запалення вказує на виражену активність запального процесу та імунологічне порушення реактивності. Визначається чітка системна реакція на запальні процеси в організмі хворих, вірогідний розвиток декомпенсованої ендогенної інтоксикації. Вказані зміни свідчать про декомпенсований ендотоксикоз, як можливий наслідок хронічного інфекційного процесу. Встановлене одночасне підвищення ІЗЛК та зниження ІЛГ, що пов'язано з розвитком ендогенної інтоксикації та порушенням імунологічної реактивності внаслідок автоінтоксикації організму. Зниження Ілімф вказує на активну адаптивну реакцію білої крові та імунодефіцит клітинного типу, зокрема на зниження неспецифічного протиінфекційного захисту. Показники ЛІІ, ІЗЛК, ГПІ, ПІ, ІІР, ІСНМ підвищені в усіх пацієнтів з ХНН, що може бути пов’язане з власне причиною розвитку ниркової недостатності – гломерулонефритом, хронічним пієлонефритом тощо. Встановлена різниця інтегративних показників між чоловічою та жіночою статтю, більш виразні відхилення від нормальних були виявлені у

чоловіків обох груп, ніж у жінок, що може бути пов'язане з більшою прихильністю до дієти, водного навантаження між процедурами гемодіалізу в останніх.

Ключові слова: хронічні вірусні гепатити В і С, коінфекція, гемодіаліз, хронічна ниркова недостатність, здоров'я, інтоксикація, реактивність, запалення.

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INTRODUCTION / ВСТУП

Almost 4 million people in the world require renal replacement therapy (RRT), and hemodialysis (HD) remains the most common form, accounting for about 69% of all RRT and 89% of all dialysis [1]. According to the Institute of Nephrology of the Medical Academy of Ukraine, there are 57 hemodialysis centers in Ukraine, where about 3.5 thousand patients undergo extracorporeal detoxification [2]. Treatment technology and availability have improved significantly in recent decades, but access, cost, and treatment outcomes vary widely around the world, and overall, rates of impaired quality of life, morbidity, and mortality are high, representing a major public health problem [1] The interpretation of laboratory parameters of patients with HD is extremely important for the analysis and improvement of the quality of treatment, but the issue of significant heterogeneity in monitoring and reporting of these results in different centers becomes relevant.

The risk of infection with hepatitis B, C and D viruses (HBV, HCV and HDV) is quite high during the HD procedure [3]. Patients and employees of hemodialysis departments are at risk of HBV, HCV, HDV infection. According to the DOPPS (Dialysis Outcomes and Practice Patterns Study), the incidence of hepatitis C virus (HCV) among 76,689 patients was 7.5% (5.9% in North America, 6.7% in Europe, and 12.4% in Japan) . The prevalence of hepatitis B (HBV) among patients treated for HD in the same study in North America, Europe and Asia was 3.3% (ranging from 0% in the UK to 6.6% in Italy) [4].

HCV infection remains the most common cause of liver damage in patients with chronic kidney disease (CKD). In patients with HD more than 12 months, this indicator is higher than in patients with shorter (up to 12 months) periods of replacement therapy [5].

Some patients have serological signs of simultaneous infection with several hepatotropic viruses (HBV, HCV), which can complicate the clinical course of the disease.

The problem of combined pathology, chronic viral hepatitis (CVH) and chronic renal failure in Ukraine, despite its importance and significant economic losses, remains unstudied. Absence of a common accounting base for HBV, HCV, HDV infection of medical staff of medical institutions. The influence of HD on the course of combined pathology (CVH and CKD) has not been studied.

MATERIALS AND METHODS

19 patients aged (59.0 ± 2.92) years old were examined (examinations were carried out during 2019–2022, at least once a month, a total of 327 examinations were carried out) with CKD stage 5, who underwent HD in one of the centers of nephrology and hemodialysis with the experience of performing the procedure from one to 20 years (10.58 ± 4.8). The patients were divided into two groups: the first – patients with CVH (9 people; CVH B – 3, CVH C – 5, CVH B+C – 1); the second group included 10 patients with CKD without CVH. The average age of the examinees in the first group was (61.8 ± 4.06) years, in the second – (57.0 ± 3.57) years ($p < 0.05$, Mann–Whitney test). Regarding the distribution by gender, in the first group, men make up 90% (average age (60.7 ± 4.24) years), women 10% (age – 69.0 years) ($p > 0.05$). In the second group, the ratio is 1:1 (average age of women (61.0 ± 2.53) years, men (52.6 ± 6.13) years) ($p > 0.05$).

It was performed: collecting of epidemiological, clinical and anamnestic data, clinical and laboratory studies. The observation was carried out during 2019–2022. The obtained data are entered into the tables of the Microsoft Office Excel package with the creation of a database. The calculation of integrative indicators of: endogenous intoxication (leukocyte intoxication index (LII), , hematological intoxication index (HII), index of intoxication severity (IIS) leukocyte shift index (ISL), neutrophils reactive response (NRR)); non-specific

reactivity (immunoreactivity index (IR), neutrophil-monocyte ratio (NMR), lymphocyte-monocyte ratio index (LMR), lymphocyte index (I_{lymph}), eosinophil-lymphocyte ratio index (ELR), allergy index (IA); indices inflammation activity (Krebs index (KI), lymphocyte-granulocyte index (ILG), index of leukocyte and ESR ratio (ILESR) [6, 7].

Indicators were compared with data obtained from healthy individuals. This group consisted of 40 clinically and anamnestically healthy blood donors from the Sumy Regional Center of the Blood and Transfusion Service, aged (37.95 ± 1.72). The group had equally 20 men and women

All data were recorded in the electronic system. The results of clinical observation and conducted research were processed with the help of Microsoft Office Excel 2010 software. We used parametric methods in patient groups, since the obtained data correspond to a normal distribution – the Student's t-test was used to analyze quantitative data, the Mann–Whitney test was used for age calculations. For the calculation, we used the application created by us for the Android platform – Android Studio. This program is free and is licensed under Apache 2.0. Android Studio is based on IntelliJ IDEA Community Edition supported by JetBrains [8].

RESULTS

Medical records of 19 patients of the first and second groups were calculated, analysed and compared integrative indicators of endogenous intoxication, indices of non-specific reactivity, indices of inflammatory activity between groups, compared to the norm and depending on sex.

In patients from the first group, an increase in the indices of endogenous intoxication was found relative to the norm: LII – by 1.9 times; HII – by 2.5; IIS– by 9.1; ISL, NRR – by 1.8 times ($p < 0.05$–0.001) (Table 1). Which may be related with stimulation of the cytokine response to the virus, liver dysfunction and intoxication by decay products.

In patients from the second group, an increase was found: LII – by 1.5 times; HII – by 1.9; IIS – by 5.6; ISL – by 1.7; NRR by 1.6 times relative to the normal values, which can be associated with a multifactorial clinical and laboratory syndrome caused by an inflammatory response due to residual uremic syndrome and/or concomitant diseases (MIA syndrome) ($p < 0.05$–0.001) [2].

If we compare the indicators of endogenous intoxication between the examined first and second groups, they are higher in the first group (LII – by 1.2 times; HII – by 1.3; IIS – by 1.6;) (Table 1), which confirms the influence of aggravating infectious pathology, impaired liver function and pronounced cytolytic syndrome. This is also confirmed by the data presented in Table 2, so in patients of the first group, the AlAT indicator is higher by 1.3 times; AsAT – by 1.5 times compared to the second group ($p < 0.05$–0.001).

In male patients from the first group, a significant increase in the indices of endogenous intoxication was found – LII (by 2.0 times), HII (by 3.1), IIS (by 9.4), ISL (in 1.7), NRR (in 1.8) compared to normal indicators. Regarding the indicators of men in the second group, we also observed an increase in these parameters relative to the norm (LII – by 1.6 times; HII – by 1.9; IIS – by 5.7; ISL – by 1.9; NRR – by 1.5 times; ($p < 0.05$–0.001). When comparing the indicators endogenous intoxication between the men of the first and second groups, it was found that the men of the first group have higher indicators: LII – by 1.2, HII, IIS – by 1.6 times ($p < 0.05$–0.001).

Integrative indicators of endogenous intoxication are increase at female patients of the first group (LII – by 1.5 times; HII, ISL – by 2.0; IIS – by 7.6; NRR – by 1.8), and indicators of LII , HII, IIS were lower (by 1.3, 1.5, and 1.2 times, respectively), compared to the indicators of the male patients in the same group, and the indicator of ISL was slightly higher (by 1.1 times) ($p < 0.05$–0.001), which is associated with less decompensated intoxication in women.

If we analyze the indicators of women of the first group compared to the indicators of all patients in the corresponding group, the level of LII and HII is lower in the female population – by 1.2 times. During the examination female patients of the second group, these indicators were also increased compared to the group of healthy persons: LII – by 1.4 times; HII – by 1.7; IIS – by 5.5; ISL and NRR – by 1.7 times ($p < 0.05$–0.001), which is probably related to the pronounced MIA syndrome. If we compare the indicators of female patients with CKD and men in this group, a higher level of intoxication indicators was found in men (LII, HII, ISL by 1.1 times.

However, if we compare the groups of women with CVH and concomitant renal failure with patients without CVH, then the indexes of endogenous intoxication are greater in the first group, namely HII and ISL – by 1.1 times, IIS – by 1.4, which indicates the aggravating effect of the infectious load associated with viral hepatitis (Table 1).

Table 1 – Integrative indicators of intoxication, reactivity, inflammation in patients who were on hemodialysis

Indicator	Norma, healthy individuals, n=40	Patients, n, number of studies					
		Group 1 (CVH + CKD, n=9)			Group 2 (CKD, n=10)		
		All	Man 158 studies	Women 38 studies	All	Man 70 studies	Women 61 studies
Index of endogenous intoxication							
LII	0,70 ± 0,07	1,35 ± 0,12 a	1,40 ± 0,14 a	1,09 ± 0,06 a, b, c	1,11 ± 0,07 a, e	1,16 ± 0,01 a, d	1,04 ± 0,08 a, c
HII	0,64 ± 0.06	1,62 ± 0,13 a	2,01 ± 0,15 a	1,29 ± 0,08 a, b, c	1,20 ± 0,08 a, e	1,24 ± 0,13 a, d	1,15 ± 0,10 a, c, d
IIS	0,16 ± 0,02	1,47 ± 0,11 a	1,51 ± 0,12 a	1,22 ± 0,14 a, c	0,89 ± 0,08 a, e	0,91 ± 0,13 a, d	0,88 ± 0,08 a, d
ISL	1,62 ± 0,10	2,92 ± 0,08 a	2,89 ± 0,10 a	3,22 ± 0,16 a, c	2,92 ± 0,11 a	3,04 ± 0,17 a	2,78 ± 0,15 a, c, d
NRR	12,75 ± 1,82	23,17 ± 1,60 a	23,06 ± 1,74 a	23,76 ± 2,11 a	21,38 ± 1,56 a, e	19,30 ± 2,40 a	22,20 ± 2,02 a
Index of non-specific reactivity							
IR	4,65 ± 0,36	22,54 ± 0,8 a	23,75 ± 0,82 a	15,78 ± 1,20 a, b, c	19,39 ± 1,01 a, e	20,55 ± 1,10 a, d	14,46 ± 1,27 a, b, c
NMR	8,88 ± 0,91	50,85 ± 1,78 a	59,46 ± 1,84 a, b,	42,35 ± 2,12 a, b, c	30,12 ± 1,94 a, e	39,13 ± 2,48 a, b, d	21,14 ± 1,37 a, b, c, d
LMR	4,77 ± 0,45	20,76 ± 0,77 a	21,91 ± 0,79 a	14,38 ± 1,15 a, b, c	19,18 ± 0,93 a	21,21 ± 1,29 a	18,22 ± 1,25 a, c, d
I_{lymph}	0,59 ± 0,04	0,38 ± 0,01 a	0,39 ± 0,01 a	0,33 ± 0,01 a, b, c	0,34 ± 0,01 a	0,39 ± 0,02 a	0,30 ± 0,02 a, c
ELR	0,08 ± 0,009	0,09 ± 0,01 a	0,08 ± 0,01 a	0,11 ± 0,01 a, c	0,09 ± 0,01 a	0,05 ± 0,01 a, b, d	0,08 ± 0,01 a, c, d
IA	1,05 ± 0,07	0,80 ± 0,02 a	0,81 ± 0,02 a	0,77 ± 0,02 a	0,88 ± 0,03 a, e	0,90 ± 0,05 a, d	0,86 ± 0,04 a, d
Indices of inflammatory activity							
KI	2,02 ± 0,94	3,04 ± 0,10 a	2,95 ± 0,10 a	3,5 ± 0,15 a, b, c, d	3,05 ± 0,13 a	3,19 ± 0,19 a	2,8 ± 0,23 a, c, d
ILG	4,85 ± 0,29	3,57 ± 0,10 a	3,66 ± 0,11 a	3,08 ± 0,20 a, b, c	3,74 ± 0,13 a	3,64 ± 0,19 a	2,85 ± 0,16 a, b, c
ILESR	1,33 ± 0,20	0,41 ± 0,01 a	0,42 ± 0,01 a	0,37 ± 0,01 a, b, c	0,31 ± 0,01 a, e	0,31 ± 0,01 a, d	0,31 ± 0,02 a, d

Notes. A significant difference in indicators compared to the following: a – healthy people (norm); b – all in the relevant group, c – men in the relevant group; d – of the same sex in another group, e – all of the first group; p < 0.05–0.001, Student's t-test was used

During analyzing the indices of non-specific reactivity (Table 1), we found that in the patients of the first group, IR was 4.8 times higher than the indicators of healthy individuals, NMR – by 5.7, LMR – by 4.3 times($p < 0.05–0.001$). The Ilymph indicator is reduced compared to the healthy group, which indicates an active adaptive reaction of white blood and an immunodeficiency stage of the cell type, in particular, a decrease in non-specific anti-infective protection due to intoxication [11]. ELR is within normal limits, and IA is reduced by 1.3 times ($p < 0.05–0.001$). In the patients of the CKD group, an increase in IR indicators by 3.4 times, NMR – by 4.8, and LMR – by 3.0 was found ($p < 0.05–0.001$), which indicates a violation of immunoreactivity, mainly associated with an increase in relative the number of neutrophils and a decrease in the relative number of lymphocytes. The greater the shift of the

leukocyte blood formula to the left, the greater the ISL [12]. Indicators Ilymph decreased – by 1.7 times, IA – by 1.2 ($p < 0.05–0.001$), and ELR within normal limits. In male patients with CKD + CVH, an increase in IR was found 5.1 times higher than the indicators in healthy individuals, and by 6.6 times higher in NMR; LMR – in 4.6 ($p < 0.05–0.001$). ELR – the indicator was within the normal range.We were found by 1.5 times decrease in Ilymph, and by 1.3 times decrease in IA ($p < 0.05–0.001$). As for the indicators of men in the CKD group, there is an increase in IR, NMR, LMR – by 4.4 times compared to the norm; on the contrary, Ilymph, ELR, and IA decreased by 1.5, 1.6, and 1.2 times ($p < 0.05–0.001$).

Table 2 – Biochemical indicators in patients undergoing hemodialysis

Indicator	Group 1 (CVH + CKD, n=9) 235 studies	Group 2 (CKD n=10) 202 studies
Bilirubin, μmol/l General indirect	 8,16 ± 0,54 4,64 ± 0,41	 6,2 ± 0,19 *a* 4,2 ± 0,41 *a*
AlAT, Units/l	22,56 ± 0,93	17,2 ± 0,71 *a*
AsAT, Units/l	25,68 ± 1,30	16,7 ± 0,79 *a*

Note: a – a significant difference in indicators compared to the first group; p < 0.05–0.001, Student's t-test was used

After comparing the indicators in men with concomitant CVH and all patients, it was established that NMR higher in men by 1.2 times, which may indicate greater immunoreactivity in the male population. If we compare patients – men from the first and second groups, then in the first group the IR is greater than in the second – by 1.2 times, NMR – by 1.5, ELR – by 1.6 ($p < 0.05–0.001$), which is associated with a greater immunological load in patients with CVH than in patients with CKD. However, there was a tendency to increase IA in the second group (by 1.1 times). When comparing the indices of inflammatory activity of men with CKD with the results of all patients in the corresponding group, the index of NMR, similar to the results of group 1, was increased by 1.3 times, and ELR in the population of all – by 1.8 ($p < 0.05–0.001$) (Table 1).

The women of the first group had an increase in IR index by 3.4, NMR – by 5.2, LMR – by 3 times, ELR – by 1.3 was found compared to normal parameters. On the contrary, Ilymph and IA indicators were reduced – by 1.5 times and by 1.4, respectively ($p < 0.05–0.001$). In women of the second group, indicators – IR, NMR, LMR are 3.1, 2.4, 3.8 times higher than the norm, respectively. ELR – relative to the norm. And Ilymph and IA decreased – by 2 times and 1.2 ($p < 0.05–0.001$) (Table 1). Comparing the changes in indices of non-specific reactivity in women of the first group with the indicators of all in this group, this indices are lower, namely: IR, LMR – by 1.4 times, NMR and Ilymph – by 1.2 ($p < 0.05–0.001$). When the indicators of the women of the second group were identically compared with the indicators of all patients from this group, similar changes were established: a decrease in IR – by 1.3 times, NMR – by 1.4 ($p < 0.05–0.001$).

If we compare male and female indices of non-specific reactivity of the first group, then: IR, LMR is higher in men – by 1.5 times, NMR – by 1.4, Ilymph – by 1.2 ($p < 0.05–0.001$). When comparing the indicators of the females from group HVH+ CKD and CKD, the index of NLR is by 2 times higher in women of the first group, and LMR in the second group is 1.3 times higher ($p < 0.05–0.001$). When comparing men and women in the group of CKD without hepatitis, all indicators are higher in men, namely IR – by 1.4 times, NMR – by 1.8, LMR – by 1.2, Ilymph – by 1.3 times ($p < 0.05–0.001$) (Table 1).

The indices of inflammatory activity, KI in patients of the first group is 1.5 times higher than normal, ILG and ILESR are lower – by 1.3 and 3.2 times, respectively. The same changes were observed in the patients of the second group: KI increased by 1.5 times; ILG and ILESR decreased by 1.3 and 4.3 times, respectively, which may indicate a decrease in the activity of a nonspecific cellular immune link in a pronounced inflammatory process [12]. If we compare the ILESR indicator in the first and second groups, then in the second group it is reduced more ($p < 0.05–0.001$). In men, patients of the CKD + CVH group, KI is 1.4 times higher than normal, in the comparison group (the second) it is

also increased by 1.5 times. ILG in men of the first and second groups decreased by 1.3 times. ILESR is also reduced, compared to healthy individuals – in the first group by 3.2 times, in the second – by 4.2 times. As for women with CKD + CVH, KI was increased 1.7 times from the normal value. This indicator was increased in women in comparison: with all, with men in this group, as well as with women in the group without accompanying CVH – by 1.2 times.

In the first group, in women, the ILG indicator is reduced – 1.6 times from normal indicators, also compared to the group of all and to men of this group (by 1.2) ($p < 0.05–0.001$). Taking into account the ILESR indicator, a decrease was found in women of the first group – by 3.6 times the norm and by 1.1 compared to men and all in the same group ($p < 0.05–0.001$).

As for women in the second group, the KI is by 1.4 times higher than normal, which indicates increased inflammatory activity. This indicator is lower compared to men and women in the first group by 1.2 ($p < 0.05–0.001$). ILG decreased relative to the norm – by 1.7 times ($p < 0.05–0.001$). Also, this indicator is lower, if we compare the group of all and men in the corresponding group – by 1.3 times. All of this helps to diagnose and confirm the severity of intoxication [12].

During the study, a decrease in the ILESR index was found in the group of women – by 4.3 times ($p < 0.05–0.001$). The index value can be a sign of a decrease in the activity of the non-specific cellular immune link in the presence of a pronounced inflammatory process [12]. However, this indicator was lower than in the group of women with concomitant viral pathology – by 1.2 times ($p < 0.05–0.001$) (Table 1).

CONCLUSIONS / ВИСНОВКИ

1. Patients receiving invasive manipulations, including hemodialysis, belong to the risk group and are more susceptible, taking into account immunodeficiency, to infection with hepatitis viruses than the general population. CVH is one of the most common types of lesions in them.

2. The obtained changes, namely, a more pronounced increase in the integrative indicators of endogenous intoxication, in patients with the combined pathology of CKD and CVH indicate the activation of the processes of tissue decay, cytolysis of hepatocytes and significant liver function impairment. At the same time, a change in indices of non-specific inflammation indicates a pronounced activity of the inflammatory process and an immunological disorder of reactivity. A clear systemic reaction to inflammatory processes in the body of patients is determined, the probable development of decompensated endogenous intoxication, which is possible consequence of a chronic infectious process.

A simultaneous increase in ISL and a decrease in ILG was established, which is associated with the development of endogenous intoxication and a violation of immunological reactivity due to autointoxication of the body.

A decrease in Ilymph indicates an active adaptive reaction of white blood cells and a cell-type

At the terminal stage of chronic renal failure, the humoral and cellular links of immunity are disrupted up to the general suppression of the specific immune response. Uremic toxins that permanently exceed normal values have a significant impact on metabolic processes, as well as the presence of MIA syndrome, which is caused by an inflammatory response due to residual uremic syndrome and/or concomitant diseases (diabetes mellitus, complications of chronic renal failure, such as hydrothorax, ascites),which led to changes reflected in changes in integrative indicators of endogenous intoxication, non-specific reactivity and inflammatory activity, which did not correspond to the norm, but were lower than in patients with concomitant viral hepatitis.

Violation of infection control is the main factor responsible for outbreaks of viral hepatitis B and C in centers [9]. Therefore, regular screening for infection with hepatitis viruses and compliance with infection control rules are key to preventing these infections. This should include: vaccination of the vulnerable contingent, patients on HD at the terminal stage of CKD are recommended to use double doses of the vaccine according to the modified method – 0–1–2–6 months, and if there are indication – booster immunization after 12 months; admission of employees to work only after a full course of vaccination against CVH B; checking post-vaccination immunity by monitoring antibodies; at least annual screening for markers of viral hepatitis of patients and medical staff with rapid tests followed by an algorithm, monitoring of functional indicators of the liver; compliance with the rules and the action of the medical staff in accordance with the order in matters of disinfection, pre-sterilization treatment, sterilization, disposal of waste of various categories.

immunodeficiency, in particular, a decrease in non-specific anti-infective protection.

3. Indicators of LII, ISL, HII, IIS, IR, NMR are increased in all patients with CKD, which may be related to the actual cause of development – glomerulonephritis, chronic pyelonephritis, etc.

4. The difference of integrative indicators between men and women was established, more pronounced deviations from normal were found in men of both groups than in women, which may be associated with greater adherence to diet, water load between hemodialysis procedures in the latter.

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

The issue of incidence structure of virus hepatitis among medical workers and among patients of the HD departments remains relevant and unstudied as well as determination of routine indicators of the effectiveness of treatment procedures in patients with CKD and development of effective measures to reducing the possibility of nosocomial infection.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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1. A significant contribution to the design or construction of the manuscript; acquisition, analysis, or interpretation of data for the manuscript;
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