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FEATURES OF LIVER DAMAGE ACCORDING TO ULTRASOUND ELASTOMETRY IN PATIENTS WITH CHRONIC VIRAL HEPATITIS C AMONG THE POPULATION OF VARIOUS REGIONS OF AZERBAIJAN (ACCORDING TO THE RESULTS OF THE APPEAL)

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The purpose of the study was to establish the frequency of registration of various degrees of liver tissue damage in chronic viral hepatitis C infection.

Materials and methods. People who applied to the Medical Center "Medikus clinic" were studied. 1611 people were examined, including 830 males and 771 females. The proportion of people with viral hepatitis C was 972 people, of whom there were 432 men and 540 women. Among the surveyed such age groups were identified: 1st – 18–29 years, 2nd – 30–39, 3rd – 40–49, 4th – 50–59 and 5th – 60 years and older. In order to verify the presence of viral hepatitis C, specific laboratory methods and their evaluation criteria were used, and it was HCV [ifa]. The studies were carried out on the Beckman Coulter Access 2 device according to the ELISA methodology. For hepatitis C virus, the analytical sensitivity was 15/m IU/ml. Polymerase chain reaction was used to confirm the presence of viral hepatitis C in the examined patient. The study was carried out on the device "Rotor Gene Q" (Germany). Elastometry was performed on a 2D-Supersonic Aixplorer SWE (France). The examination of patients was carried out according to the Cut-offs scale, and liver fibrosis was determined by the METAVIR scale. Ultrasound elastometry of the liver made it possible to assess the degree of fibrosis of hepatic tissue in patients with chronic viral hepatitis C, which is important in predicting complications of the disease and their consequences.

Results and discussion. In males in all age groups, relatively high indicators characterizing the stiffness of liver tissue were recorded, without significant dynamics (1st – 8.2 ± 1.2 kPa; 2nd – 9.5 ± 0.8 kPa; 3rd – 11.4 ± 0.8 kPa; 4th – 11.8 ± 1.0 kPa; 5th – 11.0 ± ± 1.1 kPa, p>0.05). Almost all of them corresponded to the compensated stage of liver cirrhosis. Among females in the presence of viral hepatitis C, the indicator characterizing the degree of liver tissue fibrosis showed a statistically significant increase from the minimum value in the 1st age group to the maximum in the 5th (1st – 5.9 ± 0.5 kPa; 2nd – 7.6 ± 0 kPa; 3rd – 8.2 ± 0.7 kPa; 4th – 10.9 ± 0.8 kPa; 5th – 12.9 ± ± 0.9 kPa, p<0.001) and everywhere it was higher than the standard indicator (5.0 kPa).

Conclusion. It is quite obvious that the presence of viral hepatitis C is characterized by a pronounced progressive development of fibrous tissue. The peculiarity lies in the fact that this trend is observed in men starting from 40, and in women from 50 years. In all age groups, it was higher in males. Basically, fibrosis progressed after 50 years. The male sex and age of patients had a significant influence on the development of fibrous tissue in the liver. The highest values of the studied indicator were observed in the regions of the Republic of Azerbaijan. The increase in the degree of liver tissue damage after 50 years is probably due to the development of the atherosclerotic process and the presence of comorbid diseases.

Keywords: chronic viral hepatitis C, liver elastometry, fibrosis.

Introduction. In recent decades, the chronic form of viral hepatitis C (HCV) has attracted a lot of attention. The reason for this is the growing frequency of registration of its transformation into non-alcoholic fatty liver disease (NAFLD), liver cirrhosis (LC), hepatocellular carcinoma (HCC). These pathological conditions significantly reduce the quality of life of patients, increase the rates of disability and mortality [1, 2]. Patients with HCV have a number of metabolic disorders due to its extrahepatic effects caused by the formation of insulin resistance and further metabolic syndrome [3], which is the basis for cardiovascular pathology, lipid and carbohydrate metabolism disorders, which in themselves pose a danger to the patient's life. Therefore, timely detection of fibrous changes in the liver is of priority importance. The degree of fibrosis determines the prognosis of the disease [4, 5, 6].

Previously, in people with chronic liver diseases, a biopsy was used to verify the lesion of its tissue. However, the method had a number of significant drawbacks: the impossibility of dynamic control of the fibrosis process, coverage of a wider lesion area, high cost and invasiveness of the technique with the risk of potentially life-threatening complications. Taking into account the above, a number of non-invasive methods for assessing fibrosis have been developed – ultrasound elastometry based on measuring the stiffness of liver tissue. This method measures the velocity of

a low-frequency elastic transverse wave propagating through the liver. The stiffer the fabric, the higher the velocity of propagation of the transverse wave. The result is recorded in the kPa. The advantages of ultrasonic elastometry are a short procedure time (less than 5 minutes), and immediate results. The test can be performed at the patient's bedside, as well as on an outpatient basis and repeatedly [7, 8, 9, 10].

The main importance is given to the timely detection of changes that can subsequently lead to the development of life-threatening complications of the patient. Based on the above, we have set the following goal for the first time in the region.

The purpose of the study was to establish the frequency of registration of various degrees of liver tissue damage in chronic HCV infection.

Materials and methods. The object of the study was the population of various regions of Azerbaijan, including Baku, Sumgait and certain districts, who applied to the "Medikal Clinic". 1611 people were examined, including 830 males and 771 females. The proportion of people with HCV was 972 people, of whom there were 432 men and 540 women. Among the surveyed such age groups were identified: 1st – 18–29 years, 2nd – 30–39, 3rd – 40–49, 4th – 50–59 and 5th – 60 years and older. In order to verify the presence of HCV, specific laboratory methods and their evaluation criteria were used, and it was HCV [ifa]. The studies were carried out on the Beckman Coulter Access 2 device according to the ELISA methodology. For hepatitis C virus, the analytical sensitivity was 15/m IU/ml. PCR was used to confirm the presence of HCV in the examined patient. The study was carried out on the device "Rotor Gene Q" (Germany).

Elastometry was performed on a 2D-Supersonic Aixplorer SWE (France). The examination of patients was carried out according to the Cut-offs scale, and liver fibrosis was determined by the METAVIR scale. According to this scale, the stages of fibrosis are estimated from F0 to F4, where F0 is the absence of cirrhosis, F1 is mild fibrosis, F2 is moderate fibrosis, F3 is severe fibrosis, F4 is cirrhosis. According to available data, the sensitivity of this method is more than 80%, and the specificity is more than 90%. In order to verify structural fibrotic changes in the liver, ultrasound elastographic examination was performed in all persons with HCV. The liver stiffness index at the stage of F4≥30 kPa indicates compensated, and F4≥40 kPa indicates decompensated cirrhosis of the liver.

The study was carried out in compliance with the basic provisions of the "Rules of ethical principles of scientific medical research with human participation", approved by the Declaration of Helsinki (1964-2013), ICH GCP (1996), EEC Directive No. 609 (dated 24.11.1986). All the participants were informed about the goals, organization, methods of examination and signed an informed consent to participate in the completely anonymous study.

Statistical processing of the obtained data was carried out using the analytical program Microsoft Excel 2010 using the following techniques: for quantitative indicators with the correct distribution of averages, statistical evaluation of significant differences the Student's t-criterion was calculated, for evaluating the same indicators with incorrect distribution the Mann-Whitney (U) criterion was calculated. The average value (M) and the error of the average value (m) were calculated.

Results and discussion. In males in all age groups, relatively high indicators characterizing the stiffness of liver tissue were recorded, without significant dynamics (1st – 8.2 ± 1.2 kPa; 2nd – 9.5 ± 0.8 kPa; 3rd – 11.4 ± 0.8 kPa; 4th – 11.8 ± 1.0 kPa; 5th – 11.0 ± ± 1.1 kPa, $p>0.05$). Almost all of them corresponded to the compensated stage of liver cirrhosis. Among females in the presence of HCV, the indicator characterizing the degree of liver tissue fibrosis showed a statistically significant increase from the minimum value in the 1st age group to the maximum in the 5th (1st – 5.9 ± 0.5 kPa; 2nd – 7.6 ± 0 kPa; 3rd – 8.2 ± ± 0.7 kPa; 4th – 10.9 ± 0.8 kPa; 5th – 12.9 ± 0.9 kPa, $p<0.001$) and everywhere it was higher than the standard indicator (5.0 kPa). It is quite obvious that the presence of HCV is characterized by a pronounced progressive development of fibrous tissue. The peculiarity lies in the fact that this trend is observed in men starting from 40, and in women – from 50 years. In all age groups, it was higher in males. After establishing some features characteristic of viral hepatitis C in the population we examined, we will move on to the regions we have identified.

In persons with HCV living in Baku, the indicators characterizing the stiffness of the liver tissue in males were higher (5.0 kPa) than the norm in all age groups by 1.5–2.5 times. After 50 years, it corresponded to the compensated stage of liver cirrhosis. But the dynamics of this indicator in the age groups was very insignificant and unreliable (1st – 8.6 ± 1.6 kPa; 2nd – 9.0 ± 0.8 kPa; 3rd – 9.4 ± 0.1 kPa; 4th – 12.1 ± 1.3 kPa; 5th – 11.3 ± 1.3 kPa, $p>0.1$). Among females under 50 years, the studied indicator showed its growth, which was not statistically significant, after 50 – its value corresponded to the compensated stage of liver cirrhosis (1st – 5.9 ± 0.5 kPa; 2nd – 7.6 ± 0.1 kPa; 3rd – 8.2 ± ± 0.7 kPa; 4th – 10.9 ± 0.8 kPa; 5th – 12.9 ± 0.9 kPa, $p<0.01$). The peculiarity was that the values of this indicator were higher among men under 50, and then this advantage was leveled. This fact requires further research in order to verify it, as well as the formation of primary and secondary prevention measures on this basis.

In patients from Sumgait, the indicator reflecting the stiffness of the liver tissue showed the maximum growth rate between the 1st and 2nd age groups, and then the dynamics was unreliable. In addition to the 1st, in the other groups this indicator was higher than the standard (1st – 5.0 ± 0.3 kPa; 2nd – 8.4 ± 1.6 kPa, $p<0.05$; 3rd – 7.3 ± 1.2 kPa; 4th – 8.9 ± 2.3 kPa; 5th – 10.0 ± 0.7 kPa, $p>0.05$). Among women, the age dynamics was identical to the one presented above (1st – 4.1 ± 0.4 kPa; 2nd – 9.9 ± 3.8 kPa, $p\leq0.001$; 3rd – 8.7 ± 2.1 kPa; 4th – 8.9 ± 1.9 kPa; 5th – 9.8 ± 3.6 kPa, $p>0.05$). No significant gender difference was recorded. The 50-year milestone played a minor role in male and female individuals.

Among men living in the regions of the Republic of Azerbaijan with diagnosed HCV, positive age dynamics was recorded from 18 to 49 years, then the values of this indicator decreased, but not significantly. In all age groups in men, its average value was higher than the standard (1st – 7.2 ± 1.5 kPa; 2nd – 12.7 ± 2.3 kPa; 3rd – 15.5 ± 1.9 kPa, $p<0.01$; 4th – 11.7 ± 1.7 kPa; 5th – 13.05 ± 1.9 kPa). Among females, in the presence of HCV, positive age dynamics of the indicator under discussion was recorded and it was statistically significant from the minimum value in 18–29 years to the maximum in 60 years and older and its values exceeded the norm (1st – 5.9 ± 0.7 kPa; 2nd – 7.5 ± ± 1.2 kPa; 3rd – 7.4 ± 1.0 kPa; 4th – 13.7 ± 1.6; 5th – 15.2 ± 1.5 kPa, $p\leq0.001$). In all age groups, the discussed indicator was higher among males compared to females.

Discussing the results of the study, it should be noted that the method we used to determine fibrotic liver damage in people with chronic HCV, today fully meets the needs of specialists, because it is highly informative, with high specificity and effectiveness, not traumatic, not invasive. All these make the methodology we used accessible, allowing us to conduct research repeatedly, which is very important for dynamic observation of patients, evaluation of treatment tactics and prognosis [10]. The results obtained by us allow us to assess the state of the problem and outline the main directions for providing qualified medical care to the population of our republic. Based on the results obtained, we found out that HCV as a whole, without dividing patients into regions of residence, has a significant effect on the increase in the indicator characterizing the stiffness of liver tissue, which does not differ from the opinion of other authors [9]. Moreover, this process begins much earlier in men than in women. The presence of HCV dramatically changes the situation, because men were again in the lead in terms of stiffness. Our analysis of individual regions of residence showed that among the population of Baku, in the presence of HCV, the rate of liver tissue fibrosis in males compared to females was significantly higher, but again up to 50 years, after which the difference was leveled. In Sumgait, the situation was not much different from the one we presented above: gender differences were not registered here, but all indicators were higher than the norm, for men starting from 18, and for women – from 30 years. Only among men, the age of 50 was a turning point in terms of the rate of development of fibrous tissue. As for the districts of the Republic of Azerbaijan, in them in the presence of an established HCV, the studied indicator in its absolute value was higher among men compared to women and again up to 50 years, after which the indicators stabilized, but in any case they were higher than the standard.

Conclusion

1. Chronic HCV has a significant negative effect on indicators reflecting the degree of formation of fibrous tissue in the liver.
2. Age and male sex in HCV patients are risk factors for the formation of fibrous tissue in the liver, which significantly worsens its functional state.
3. In HCV patients, the age of 50 years without a gender factor significantly increases the volume of fibrotic liver damage.

Perspectives of further research. It is planned to further study and publish as for comorbid conditions, including metabolic syndrome, type 2 diabetes mellitus, arterial hypertension, dyslipidemia, which fully cause the development of the atherosclerotic process, which may additionally cause the aggravating formation of fibrous tissue in the liver, with the help of which we would be able to explain its activation in patients after 50 years.

References

1. Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study European Union HCV Collaborators. *Lancet Gastroenterol Hepatol*. 2017 May;2(5):325-336. PMID: 28397696. doi: 10.1016/S2468-1253(17)30045-6
2. Bodawi MM, Atif MS, Mustafa YY. Systematic review and meta-analysis of HIV, HBV and HCV infection prevalence in Sudan. *Virol J*. 2018; 15(148):1–16. PMID: 30253805. PMCID: PMC6157049. doi: 10.1186/s12985-018-1060-1
3. Antonova TV, Romanova MA. Hronicheskaja HCV-infekcija i immunorezistentnost'. Jeffektivnaja farmakoterapija [Chronic HCV infection and immunoresistance. Effective pharmacotherapy]. *Gastrojenterol*. 2017;2:1–8. [Russian]

4. Tsvetkov VV, Tokin II, Pozdnyakov SA. Klinicheskaya ehpidemiologiya vnepechenochnykh proyavlenii khronicheskoi infektsii vyzvannoi virusom gepatita [Clinical epidemiology of extrahepatic manifestations of chronic infection caused by hepatitis virus]. *Med Sovet*. 2019;21:248–253. [Russian]. doi: 10.21518/2079-701X-2019-21-248-253
5. Tkachenko LI, Maleev VV. Steatoz pecheni u bol'nykh khronicheskim virusnym gepatitom B [Liver steatosis in patients with chronic viral hepatitis B]. *Kazan Med Zh*. 2014;1(95):35–41. [Russian]. doi: 10.17816/KMJ1452
6. Ivashkin VT, Maevskaya MV, Zharkova MS, Zhiganova SV. dr. Klinicheskie rekomendatsii Rossiiskogo obshchestva po izucheniyu pecheni i Rossiiskoi Gastroenterologicheskoi Assotsiatsii po diagnostike i lecheniyu fibroza i tsirroza pecheni i ikh oslozhnenii [Clinical recommendations of the Russian Society for the Study of the Liver and the Russian Gastroenterological Association for the diagnosis and treatment of fibrosis and cirrhosis of the liver and their complications]. *Ros Zh Gastroenterol Gepatol Kolonoproktol.* 2021;6:56–68. [Russian]
7. Zhdanov KV, Korjakin SS, Kozlov KV, Tusev DA. Hronicheskij gepatit S i nealkogol'naja zhirovaja bolezn' pecheni. Osnovnye aspekty patogeneza. [Chronic hepatitis C and non-alcoholic fatty liver disease. The main aspects of pathogenesis]. *Vestnik Ros Voen-Med Akad*. 2022;1(61):25–30. [Russian]
8. Klyaritskaya IL, Shelikhova EO, Moshko YUA, Semenikhina EV i dr. Ehlastografiya v diagnostike [Elastography in the diagnosis]. *Krym Ter Zh*. 2017;2:28–33. [Russian]
9. Pisaqlia F. The role of ultrasound elastographic techniques in chronic liver disease:current status and future perspektives. *Eur J Radiol*. 2014;83:450–455. PMID: 23891139. doi: 10.1016/j.ejrad.2013.06.009
10. Zhuravlev EV, Ogneva EV. Primenenie ehlastografii u bol'nykh s khronicheskimi zabolevaniyami pecheni [The use of elastography in patients with chronic liver diseases]. *Gastroenterol*. 2018;2(52):98-103. [Russian]. doi: 10.22141/2308-2097.52.2.2018.132616

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ОСОБЛИВОСТІ УРАЖЕННЯ ПЕЧІНКИ ЗА ДАНИМИ УЛЬТРАЗВУКОВОЇ ЕЛАСТОМЕТРІЇ У ХВОРИХ НА ХРОНІЧНИЙ ВІРУСНИЙ ГЕПАТИТ СЕРЕД НАСЕЛЕННЯ РІЗНИХ РЕГІОНІВ АЗЕРБАЙДЖАНУ (ЗА РЕЗУЛЬТАТАМИ ЗВЕРТАННЯ)

Махмудова К. Дж.

Резюме. *Мета* – встановити частоту реєстрації різного ступеня ураження печінкової тканини при хронічній HCV-інфекції.

Об'єкт та методи дослідження. У дослідженні взяли участь 1611 осіб, які звернулися до Медичного центру Medikus clinic, Баку, Азербайджан. З них осіб чоловічої статі 830, жіночої – 771. Частка осіб з HCV склала 972 особи, з яких чоловіків було 432, а жінок – 540. Серед обстежених було виділено вікові групи: 1 -18-29 років, 2 -30-39, 3 - 40-49, 4 - 50-59 та 5 - 60 років і старше. З метою верифікації наявності HCV застосовували специфічні лабораторні методи та критерії їхньої оцінки, яким був HCV [ifa]. Дослідження проводилися на апараті Bekman Coulter Accese 2 згідно з методикою ELISA. Для вірусу гепатиту С аналітична чутливість становила 15/m МО/мл. ПЛР/PZR використовувалася для підтвердження наявності у обстежуваних HCV, дослідження проводилося на апараті Rotor Gene Q (Німеччина). Еластометрію проводили на апараті 2D-Supersonic Aixplorer SWE (Франція). Обстеження хворих проводилося згідно з шкалою Cut - offs, а фіброз печінки визначався за шкалою METAVIR. Проведення ультразвукової еластометрії печінки дозволило оцінювати ступінь фіброзу печінкової тканини у хворих на хронічний HCV, що важливо при прогнозуванні ускладнень хвороби та їх наслідків.

Результати та висновки. В осіб чоловічої статі у всіх вікових групах реєструвалися відносно високі показники, що характеризують жорсткість печінкової тканини, без достовірної динаміки (1 група – 8,2±1,2кРа; 2 – 9,5±0,8 кРа; 3 – 11,4±0,8кРа, 4 – 11,8±1,0 кРа; 5 – 11,0±1,1 кРа, p>0,05), майже всі вони відповідали компенсованій стадії цирозу печінки. Серед осіб жіночої статі за наявності HCV показник, що характеризує ступінь фіброзу печінкової тканини, демонстрував статистично достовірне зростання від мінімального значення в 1-ій віковій групі до максимального в 5-ій (1 група – 5,9±0,5 кРа;2 – 7,6± 0 кРа; 3 – 8,2±0,7 кРа; 4 – 10,9±0,8 кРа; 5 – 12,9±0,9 кРа, p<0,001), і скрізь він був вищим за нормативний показник (5, 0 kPa). Наявність HCV характеризується вираженим прогресивним розвитком фіброзної тканини. Особливість полягає в тому, що у чоловіків ця тенденція відзначається, починаючи з 40 років, а у жінок з 50 років. У всіх вікових групах він був вищим у осіб чоловічої статі. Здебільшого фіброз прогресував після 50 років. Значний вплив на розвиток фіброзної тканини в печінці мали чоловіча стать та вік пацієнтів. Найбільш високі значення показника, що вивчається, відзначалися в районах Азербайджанської Республіки. Зростання ступеня ураження печінкової тканини після 50 років, ймовірно, зумовлене розвитком атеросклеротичного процесу та наявністю коморбідних захворювань.

Ключові слова: хронічний вірусний гепатит С, еластометрія печінки, фіброз.

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