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CHRONIC VIRAL HEPATITIS B AND C IN PEDIATRIC PATIENTS: POSSIBILITIES OF ULTRASOUND TECHNIQUES FOR PATIENTS' MANAGEMENT

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Chronic viral hepatitis B and C have already become one of the medical and social problems of modern hepatology and paediatrics due to their high prevalence and ability to transform liver parenchyma and form additional complications. Nowadays, it is important to assess and examine patients by ultrasound techniques to estimate changes in morphometric, hemodynamic, and echoacoustic characteristics of the liver in patients with viral hepatitis B and C.

The aim: to estimate ultrasound morphometric parameters and hemodynamic indexes, morphological deviations of the liver and spleen in pediatric patients with chronic viral hepatitis B and C by implementing of the system as Y. Davoudi diagnostic scale (2015) and analysis of echo-acoustic patterns.

Materials and methods. 34 children were examined. 19 children with chronic viral hepatitis B and C formed group I, while 15 almost healthy children formed group II. All examined patients underwent collecting of anamnesis, general clinical examination, determination of the degree of liver fibrosis by non-invasive method (Fibrotest or fibroelastometry) and ultrasound examination of the abdominal cavity organs with the possibility of Doppler scanning. Differences at $p < 0.05$ were considered statistically significant.

Results. Obtained data showed that in patients of group I index of Y. Davoudi grayscale was higher ($2,6 \pm 0,26$ U) compared with patients of group II ($1,4 \pm 0,32$ U) ($p < 0,01$). Systolic blood flow velocities in the portal vein and the splenic vein were decreased in patients of group I ($15,59 \pm 0,4$ cm/s; $15,7 \pm 0,8$ cm/s) compared with group II ($17,68 \pm 0,8$ cm/s; $17,54 \pm 0,42$ cm/s) ($p < 0,05$), resistance index in the hepatic artery was increased in patients of group I ($0,78 \pm 0,02$ IU) compared with patients of II group ($0,68 \pm 0,04$ IU) ($p < 0,05$). Histogram indexes of the liver and liver-kidney region were higher in patients of group I ($p < 0,001$).

Conclusions. Y. Davoudi diagnostic scale, hemodynamics parameters of the portal, splenic and hepatic vessels, echoacoustic patterns and other indexes could be prognostic factors which will indicate liver fibrosis progression in patients with chronic viral hepatitis B and C. The analysis of the obtained data showed that deviations in morphometric, echoacoustic and Doppler indexes of liver and spleen in paediatric patients with chronic viral hepatitis B and C were more clinically significant compared with almost healthy children and could be taken into account as liver fibrosis predictors

Keywords: Children, viral hepatitis B and C, liver fibrosis prognosis, ultrasound investigation, follow-up

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1. Introduction

Chronic viral hepatitis B and C are one of the important and urgent medical and social problems of hepatology due to their high prevalence, ability to progress to transform liver parenchyma with forming of liver cirrhosis and hepatocellular carcinoma, which often leads to form medical disability of the pediatric population [1–3]. Early diagnosis and assessment of the dynamics of the progression of liver tissue transformation with fibrosis formation in children with chronic viral hepatitis C (CVHC) and chronic viral hepatitis B (CVHB) will allow timely initiation of therapy and will reduce the risk of complications' appearance [1, 4–6]. Nowadays, the system of non-invasive laboratory markers, indexes and

instrumental methods and modern techniques of examination is widely implemented in clinical practice in order to optimize the process of liver fibrogenesis monitoring and assess its morpho-functional state in dynamics [4, 7–10]. The «gold» standard in the modern world for the diagnosis of liver fibrosis and estimation of its aetiology is puncture biopsy, but due to a number of significant shortcomings and possible outcomes, the procedure is significantly limited in use in pediatric practice. The most accessible and cheapest method of instrumental examination of patients with CVHC and CVHB in pediatric practice is the system of ultrasound techniques of liver examination, which is routinely used in clinical practice by specialists. In addition, Yasmin Davoudi et

al. implemented and published the US Grayscale, which allows assessing of the morphometric parameters of the abdominal organs (liver, spleen, gall bladder, portal vein,

hepatic veins, splenic vein) in patients with CVHC and CVHB with an estimation of possible degree of changes (Table 1) [8, 11].

Table 1

Adopted ultrasound Grayscale for assessing sonographic parameters of the hepatobiliary region in patients (Y. Davoudi et al., 2015) [11]

Points	The size of the liver	Echo pattern	Echogenicity	The surface of the liver	The size of the spleen	The wall thickness of gall bladder	Diameter of portal vein	Diameter of hepatic veins	Diameter of splenic vein
0	≥150mm	Homogeneous	Normal	Smooth	≤130mm	≤3mm	≤13mm	4-10 mm	≤10 mm
1	<150mm	Heterogeneous	Slightly elevated	Rough	> 130mm	> 3 mm	> 13 mm	<4 or> 10 mm or not determined	> 10 mm
2			Moderately elevated						
3			Very high						

It was reported that using this scale in pediatric practice is a new and helpful, clinically estimated method. To sum up, all data which are presented above, we see that today it is important to assess the dynamics of changes in morphometric, hemodynamic, and echoacoustic characteristics of the liver in pediatric patients with CVHB and CVHC as possible instrumental predictors of liver fibrosis progression. Also, these indexes could further be used for the determination of liver fibrosis prognosis.

The aim: to estimate ultrasound morphometric parameters and hemodynamic indexes, morphological deviations of the liver and spleen in pediatric patients with chronic viral hepatitis B and C by implementing in monitoring system Y. Davoudi diagnostic scale (2015) and analysis of echo-acoustic patterns of selected organs for these patients.

2. Materials and methods

In the clinical course of the research, we examined 19 patients with confirmed diagnoses of chronic viral hepatitis B and C, aged from 5 up to 17 years (mean – 12,7±5,5 years), which had formed the main group (group I), and 15 healthy children, aged from 4 up to 16 years (mean – 13,8±4,7 years), which had formed group II, in the period from October 2020 up to May 2023. All patients with CVHB and CVHC were under dynamic observation on the basis of the communal non-profit enterprise «Vinnytsia Regional Clinical Children's Infectious Diseases Hospital Vinnytsia Regional Council» and the Department of Pediatric Infectious Diseases of National Pirogov Memorial Medical University, Vinnytsya. The diagnoses of chronic viral hepatitis B and C were confirmed by qualitative and quantitative methods of PCR testing and ELISA with the determination of specific diagnostic markers. Management of patients with chronic viral hepatitis B and C was performed according to international and local regulatory documents. Patients underwent collecting of anamnesis, general clinical examination, determination of the degree of liver fibrosis by non-invasive method (Fibrotest or fibroelastometry) and ultrasound examination of the abdominal cavity organs with the possibility of Doppler scanning.

The analysis and evaluation of ultrasound protocols were performed with morphometric stratification according to the Y. Davoudi scale (2015) US Grayscale, analysis of blood flow in the portal vein, splenic vein and hepatic artery also was performed. Systolic blood flows (V_{qS}), diastolic blood flows (V_{qD}), resistance indexes (RI), and diameters (d) of selected vessels were estimated. An ultrasound investigation of patients was performed on an ultrasound device Samsung HM70A. The control group was formed by almost healthy children who did not have in clinical evaluation and anamnesis any signs of liver lesions, viral hepatitis B and C, drug-induced hepatitis, toxic hepatitis, metabolic diseases, obesity and hereditary hepatobiliary lesions. Data analysis was performed using the software package "R-Studio" and "Statistica 10.0" by using the methods of descriptive statistics for parametric quantities. Data were presented as mean (M) and mean error (m) for quantitative values. The reliability of the data difference was established using a paired Student's t-test. The difference was considered clinically significant at p<0,05.

The study was performed and planned in accordance with the principles, standards and norms of local ethics regulatory documents (Local ethics committee, Communal non-profit enterprise «Vinnytsia Regional Clinical Children's Infectious Diseases Hospital Vinnytsia Regional Council», order №23 published on 14th of January 2022) and Principles of the Declaration of Helsinki. All patients and their parents were informed and had signed ICF to participate in the clinical study.

3. Results

Among the examined patients of the first group – 57,89 % (n=11) patients were diagnosed with CVHB, and 42,11 % (n=8) patients were diagnosed with CVHC. In addition, among patients with diagnosed CVHB, 7 patients received antiviral therapy with entecavir, and among patients with CVHC, 3 patients received antiviral therapy (sofosbuvir-ledipasvir) according to the approved clinical guidelines in Ukraine. It should be noted that in the group of patients with CVHB and CVHC 47,4 % (n=9) patients had a F0 degree of liver fibrosis according to Metavir diagnostic scale, F0-1 – 26,3 % (n=5), F1 –

15,8 % (n=3), F1-F2 – 5,25 % (n=1), F2 – 5,25 % (n=1), which were confirmed by fibroelastometry or Fibrotest.

After analyzing the protocols of ultrasound examination of abdominal organs and evaluation of morphometry of the abdominal cavity organs according to the Davoudi diagnostic grayscale (2015), it was found that in patients of group I, the score was 2,6±0,26 U, and in children of group II – 1,4±0,32 U (p<0,05).

It was estimated that after analysis of systolic blood flow velocity (VqS) in the portal vein, it was found that in patients of group I, this parameter was lower – 15,59±0,4 cm/s, compared with group II – 17,68±0,8

cm/s (p<0,05). The systolic blood flow velocity (VqS) in the splenic vein in patients of group I was lower than 15,7±0,8 cm/s, and in turn to patients of group II – 17,54±0,42 cm/s (p<0,05). A clinically significant difference in resistance index (RI) was detected in the hepatic artery of comparison groups – in patients of group I, RI was higher 0,78±0,02 IU versus patients of group II – 0,68±0,04 IU (p<0,05) (Table 2). Clinically significant differences in diastolic blood flow velocity (VqD), resistance index (RI) in portal and splenic veins, and diameter of vessels in comparison groups were not detected (p>0,05).

Table 2

Estimation of blood flow velocities, RI and diameter of the vessels of the liver and spleen (M±m)

Groups of patients	Portal vein				Splenic vein				Hepatic artery			
	d	VqS	VqD	RI	d	VqS	VqD	RI	d	VqS	VqD	RI
Group I (n=19)	7.5± ±0.32	15.59± ±0.4*	7.04± ±0.46	0.54± ±0.02	5.9± ±0.25	15.7± ±0.8*	6.89± ±0.63	0.56± ±0.02	5.1± ±0.11	19.03± ±0.76	4.0± ±0.4	0.78± ±0.02*
Group II (n=15)	7.3± ±0.28	17.68± ±0.8	7.75±0.8	0.58± ±0.034	5.7± ±0.23	17.54± ±0.42	7.1± ±0.4	0.6± ±0.022	5.02± ±0.08	20.26± ±0.9	6.52± ±0.9	0.68± ±0.04

Note: * – established clinically significant difference of the data using the paired Student's t-test with p<0.05

Echoacoustic changes of the liver, kidney and liver-kidney region in examined patients were established after analysis of histogram indexes of selected regions (Table 3). It was estimated that the histogram index of liver in patients of group I was higher (76.1±1.9 U) compared with patients with group II (65.25±1.2 U) (p<0.001). Almost the same trend was fixed and registered in the liver-kidney region in the comparison group: in patients of group I, and this parameter was increased (77.8±1.6 U) compared with patients of group II (67.85±1.2 U) (p<0.001). There is no difference in histo-

gram index of kidney region in examined patients (p>0.05).

Echoacoustic changes of the liver by the type of increased liver echogenicity were detected in 73.68 % (n=14) of examined patients of group I and 20.00 % (n=3) of children of group II, changes in the vascular component of the liver were detected in 47.36 % (n=9) of pediatric patients of group I and 26.66 % (n=4) of children of group II. Lymphadenopathy syndrome of the liver hilum was founded in 15.79 % (n=3) of the I group (Table 4).

Table 3

Estimation of histogram indexes of liver, kidney and “liver-kidney” region in children during ultrasound examination (M±m)

Histogram indexes	Group I (n=19)	Group II (n=15)
Liver parameter, U	76.1±1.9***	65.25±1.2
Kidney parameter, U	57.08±1.45	55.1±1.4
“Liver-kidney” region, U	77.8±1.6***	67.85±1.2

Note: *** – established clinically significant difference of the data using the paired Student's t-test with p<0.001

Table 4

Evaluation of the echoacoustic patterns of the liver (according to the ultrasound examination protocols of the abdominal cavity organs) (%)

Detected echoacoustic pattern	Group I (n=19)		Group II (n=15)	
	Abs.	%	Abs.	%
Enhanced echogenicity of liver tissue	14	73.68 %	3	20.00 %
Changing in the vascular component of the liver	9	47.36 %	4	26.66 %
Lymphadenopathy syndrome of the liver hilum	3	15.79 %	–	–

4. Discussion

In scientific literature, we have found similar investigations in adult patients with liver fibrosis and cirrhosis. Similar to Y. Davoudi et al. (2015), we have shown that in pediatric patients with chronic viral hepatitis B and C using of selected diagnostic ultrasound grayscale should be used for clinical evaluation of morphometric and echoacoustic changes in the abdominal cavity organs, but age-related deviation in the size of organs should be taken into account [11]. In scientific research which was performed by Mirjana Perisic et al., it was published that high diastolic velocity in the splenic artery was a basic specific and sensitive phenomenon which could help to characterize venous blood flow in the portal system in patients with liver cirrhosis and splenomegaly [12]. The same trend was presented by Lutz H. et al. as reducing of portal vein flow and elevation of hepatic artery resistance index in patients with liver fibrosis due to chronic hepatopathy [13]. The same data with increasing resistance index in the hepatic artery and reducing blood flow velocity in the system of the portal vein were founded in our examined paediatric patients. In the scientific research which were published by Kanji Y. et al., were found data about sensitivity and correlation between reducing of right portal vein blood flow velocity to identify liver fibrosis progression in patients with chronic liver diseases (non-alcohol fatty liver disease, CVHB, CVHC, alcohol fatty liver disease) [14]. Compared to our obtained data, we came across that a similar trend was found in our examined patients – reduction of blood flow velocity in the portal vein was found in patients with chronic viral hepatitis B and C with an increasing index of liver fibrosis stage. To sum up, it seemed to be estimated that using of selected parameters by doctors in routine practice, such as hemodynamics indexes in complex with collected data of Y. Davoudi diagnostic grayscale (2015), further could be used to form liver fibrosis prognostic model in patients with viral hepatitis B and C [11, 14].

Study limitations: small sample size.

Perspectives for further research. In further investigation, it will be necessary to examine more cohorts of pediatric patients with chronic viral hepatitis B and C with an estimation of additional ultrasound indexes and

ratios and conduction of these results with modern laboratory markers of liver fibrosis progression.

5. Conclusions

1. Ultrasound techniques could be used in routine practice in the management of pediatric patients with chronic viral hepatitis B and C. Yasmin Davoudi's diagnostic grayscale (2015) should be used by US specialists to estimate deviations in the morphometric structure of abdominal cavity organs in pediatric patients with chronic viral hepatitis B and C.

2. Having analyzed obtained data, we came across that in patients with chronic viral hepatitis B and C index of Y. Davoudi grayscale was higher ($2,6 \pm 0,26$ U) compared with healthy children ($1,4 \pm 0,32$ U) ($p < 0,01$).

3. It was estimated that systolic blood flow velocities in the portal vein and splenic vein were decreased in patients with viral hepatitis B and C compared with healthy children ($p < 0,05$), but the resistance index in the hepatic artery was increased in patients with viral hepatitis ($p < 0,05$).

4. Presented data showed that histogram indexes of the liver and liver-kidney region were higher in patients with viral hepatitis ($p < 0,001$).

Y. Davoudi diagnostic scale, hemodynamics parameters of the portal, splenic and hepatic vessels, detected echoacoustic patterns, and other additional indexes could be used as additional the non-invasive diagnostic work-up and follow-up parameters in paediatric patients with chronic viral hepatitis B and C.

Conflict of interest

The authors declare that there is no conflict of interest in relation to this paper, as well as the published research results, including the financial aspects of conducting the research, obtaining and using its results, as well as any non-financial personal relationships.

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Data availability

Data will be made available on reasonable request.

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