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Microscopic Composition of Bile in Convalescent Children of Viral Hepatitis "A", "B" and "C"

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Abstract: In children undergoing VHA, VHB and VHC observed opposite changes microscopic indicators that due to various pathologic and pathophysiologic changes initiated various hepatitis viruses. Thus, children with cVHA cholesterol crystals are not detected in the composition of bile, and the children with cVHB and cVHC cholesterol crystals detected in all portions of bile. This figure shows that cholelithiasis are detected more among children cVHB and cVHC. Non-drug combination and medication interventions contributes almost complete normalization of microscopic parameters for all the children. This allows to recommend this complex interventions as the best approach in the rehabilitation of children who had viral hepatitis.

Keywords: viral hepatitis, bile, cholesterol crystals, biliary microlithiasis, microscopic composition of bile.

Relevance: Currently, an increase in the prevalence of liver diseases is noted all over the world.

In the Republic of Uzbekistan, the incidence of viral hepatitis tends to decrease dynamically. In 2010, compared with 1990, the incidence of viral hepatitis decreased by 8.2 times and amounted to 107.7 versus 882.0 per 100,000 population. In 2010, compared with 2009, the incidence of viral hepatitis decreased by 18.6% [1].

Modern methods of diagnostics and treatment of patients with viral hepatitis are being introduced into practice. However, despite this, measures to combat viral hepatitis need to be further improved, especially in terms of early detection of patients, laboratory differential diagnosis, treatment of patients with acute forms of hepatitis, also with residual manifestations. [2].

Often dysfunctions of the biliary tract occur in children with multiple foci of secondary infections, also after viral hepatitis [3, 5].

Considering the above mentioned, the differentiated therapy of biliary dysfunctions is of great difficulty. It is known that the conditions for the normal functioning of liver cells, and thus the entire hepatobiliary system, is the absolute integrity of the membranes and the physiological structure of the cell organelles. Stabilization of cell membranes ensures the physiological secretion of bile, and the restoration of intercellular connections - the normalization of its outflow [4].

The purpose of the work: To study changes in the microscopic composition of bile in children - convalescents of viral hepatitis A (cVHA), B (cVHB) and C (cVHC) and optimize therapeutic treatment

Materials and methods of research

The clinical part of the study was carried out in the period 2019-2020 years. In the children's association of the Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation of the Ministry of Health of the Republic of Uzbekistan; the children's infectious diseases department of the 3-clinic of TMA; the "City consultative and diagnostic hepatological" center on the basis of 1st City Infectious disease hospital; the hepatology department on the basis of the Research Institute of Virology and the children's hepatitis department of the Uzbekistan Research Institute of Epidemiology, microbiology and infectious diseases. The study included 60 cVHA children, 36 cVHB children, and 32 cVHC children with biliary tract pathology (BT).

The comparison group included indicators of 20 children with cVHA, cVHB and cVHC without biliary tract pathology; similar indicators of 10 practically healthy children were taken as a control group.

The pathology of the bile duct was confirmed by the results of general clinical studies, biochemical blood tests, instrumental methods (ultrasound of the abdominal organs, duodenal sounding), microscopic examination of the composition of bile, and statistical data.

In children convalescents of viral hepatitis with biliary tract pathology, biliary tract was more common at the age of 7–14 years (65.6%), and in children with cVHA and cHCV, girls predominated (51.7% and 59.4%, respectively), and vice versa, in children, cVHB predominated boys (63.8%).

Depending on the treatment, patients with biliary tract pathology were divided into 3 groups: group 1 consisted of 20 patients with cVHA, 10 patients with cVHB and 10 patients with cVHC who received only dietary nutrition (Pevsner's diet No.); Group 2 - 20 patients with cVHA, 10 patients with cVHB and 10 patients with cVHC, who received physiotherapy (electrophoresis with magnesium sulfate solution) against the background of diet therapy; group 3 - 20 patients with cVHA, 16 patients with cVHB and 12 patients with cVHC who received combined therapy (physiotherapy and Phosphogliv).

Phosphogliv was prescribed according to the following scheme: for 10 days - intravenously by stream, then orally from the following calculation: children under 3 years old - ½ capsule 3 times a day, from 3 to 7 years old - 1 capsule 3 times a day, older than 7 years - 2 capsules 2-3 times a day. The duration of the course of treatment with the capsule form averaged 14 days.

Results of the study and discussion: The results of the study of the microscopic composition of bile before treatment are shown in Table 1.

Table 1 Microscopic picture of all portions of bile in children convalescents of viral hepatitis with impaired biliary system before treatment

Composition		Microscopic picture of bile, %						
		cVHA (n=60)		cVHB (n=36)		cHCV (n=32)		Norm
		abs	%	abs	%	abs	%	
Portion A	Mucus	13	21,6	5	13,8	2	6,3	No
	Columnar epithelium	8	13,3	4	11,1	32	100	units
	Leukocytoids <10 per f/v	21	35	8	22,2	32	100	units
	Leukocytoids >10 per f/v	9	15	4	11,1	-	-	No
	Cholesterol crystals	-	-	9	24,9	11	34,4	No
	Bilirubinate Ca	2	3,3	11	30,5	7	21,8	No
	Biliary microlithiasis	4	6,6	19	52,7	12	37,5	No

Portion B	Mucus	7	11,6	3	8,3	-	-	No
	Columnar epithelium	6	9,9	3	8,2	32	100	units
	Leukocytoids <10 per f/v	20	33,4	13	36,1	32	100	units
	Leukocytoids >10 per f/v	7	11,6	2	5,5		-	No
	Cholesterol crystals	-	-	12	33,2	17	53,1	No
	Bilirubinate Ca	2	3,3	12	33,2	17	53,1	No
	Biliary microlithiasis	5	8,3	16	44,4	18	56,3	No
Portion C	Mucus	5	8,3	2	5,5	-	-	No
	Columnar epithelium	8	13,3	3	8,2	32	100	units
	Leukocytoids <10 per f/v	17	28,3	7	19,4	32	100	units
	Leukocytoids >10 per f/v	3	5	3	8,3	-	-	No
	Cholesterol crystals	-	-	13	36	22	68,7	No
	Bilirubinate Ca	2	3,3	9	24,9	14	43,7	No
	Biliary microlithiasis	2	3,3	20	55,5	14	43,7	No

As can be seen from Table 1, in children with cVHA and cVHB (21.6%, 11.6%, 8.3% and 13.8%, 8.3%, 5.5%, respectively) mucus occurs in all portions of bile (A, B, C). In children with cVHB mucus was detected only in A portions of bile (6.3%). 100% of cVHC children VHAe columnar epithelium and leukocytoids up to 10 per field of view. They are determined in all portions of bile. In children with cVHA and cVHB, columnar epithelium is detected in more than 8.2-13.3% of cases in all portions of bile. Children with cVHA and cVHB VHAe leukocytoids up to 10 per field of view, in all portions of bile (35%, 33.4%, 28.3% and 22.2%, 36.1%, 19.4%, respectively), and more than 10 per field of view 15%, 11.6%, 5% and 11.1%, 5.5%, 8.3% respectively.

Cholesterol crystals are not detected in children with cVHA, and in children with cVHB and cVHC, cholesterol crystals are detected in all portions of bile (34.4%, 53.1%, 68.7% and 24.9%, 33.2%, 36%, respectively). This indicator proves that children with cVHB and cVHB VHAe more gallstone disease.

In children with cVHB and cVHC, biliary microlithiasis are detected in more than 21.8-68.7% of cases in all portions of bile (normally, biliary microlithiasis are not detected), which indicates the lithogenic properties of bile in children with parenteral hepatitis. On the contrary, in children with cVHA biliary microlithiasis were found less in all portions of bile (A - 5.6%, B - 5.9% and C - 2.7%).

In this regard, based on the data obtained, we used various treatment methods in children with impaired microscopic parameters who had VHA, HBV, and HCV. The research results are shown in Tables 2, 3 and 4.

We evaluated the effectiveness of prescribed diet therapy in children with cVHA, cVHB, and cVHC. Our studies VHAe shown that in children who had HBV and HCV, diet therapy did not lead to normalization of microscopic parameters. This may be due to deeper and more severe pathomorphological and pathophysiological disorders caused by VHB and VHC. Therefore, in children with cVH, it is necessary to supplement dietary therapy with other pharmacological and non-pharmacological interventions.

In group 1, cVHA had a certain effect in some cases. So, in 3.3% of patients, columnar epithelium was not detected in the "A" portions of bile. However, diet therapy in isolation did not VHAe a noticeable effect on other microscopic parameters.

The next stage of the study was to study the effect of prescribing dietary therapy in combination with physiotherapy interventions.

The effectiveness of this combination turned out to be somewhat higher. So, in 5% of children with cVHA mucus and leukocytoids normalized - more than 10 in f/v, in 10% of children with cVHA columnar epithelium and leukocytoids - less then 10 in f/v in the "A" portions of bile. In

the composition of the "B" portions of bile, only leukocytoids normalized - less then 10 in f/v - in 5% of cases, in the composition of the "C" portions of bile, mucus normalized, and columnar epithelium returned to normal, the amount of leukocytoids is little - up to 10 in f/v, and leukocytoids in p / s over 10 - in 5% of cases. Other microscopic parameters did not change.

The effectiveness of therapy in group 2 cVHB was somewhat lower. In the composition of the "A" portions of bile mucus, columnar epithelium, leukocytoids in p / sp. low to 10 and leukocytoids in p / s over 10 - normalized in 10% of cases, in the "B" portions of bile, mucus (10%) and columnar epithelium (10%) significantly decreased compared to the results before treatment, and in 30% in children, leukocytoids in p/p over 10 normalized. In 10% of cases, mucus, columnar epithelium, leukocytoids in p/p over 10, cholesterol crystals, and biliary microlithiasis were normalized in the composition of "C" portions of bile.

In the 2-group cVHB the number of the columnar epithelium and leukocytoids (less then 10 in f/v) significantly decreased in all portions of bile compared with the results before treatment and the 1st group. In 20% of children, cholesterol crystals in the composition of "C" portions of bile significantly decreased compared to the results before treatment.

The best results were obtained in the 3rd group.

As can be seen from these tables, in children with VHA, in the composition of "B" portions of bile, an absolute effect was obtained in all respects, in the composition of "A" and "C" portions of bile, mucus, leukocytoids less then 10 in f/v and columnar epithelium significantly decreased compared with the results before treatment, 1- and 2-groups.

In children with cVHB in the composition of "A" portions of bile columnar epithelium (6.3%) significantly decreased compared with the results before treatment, and leukocytoids little to less then 10 in the f/v (6.3%) significantly decreased compared with the results before treatment and group 1. In the composition of the "B" portions of bile, leukocytoids (less then 10 in f/v10 - 12.5%), calcium bilirubinate (6.3%) and biliary microlithiasis (12.5%) significantly decreased compared to the results before treatment, 1 - and 2-groups. As part of the "C" portions of bile, leukocytoids in the f/v were less then 10 (6.3%), cholesterol crystals (6.3%) and biliary microlithiasis (12.5%) significantly decreased compared with the results before treatment, 1- and 2-groups.

In 75-83,4% of children with cVHC, the columnar epithelium and leukocytoids (less then 10 in the f/v) normalized in all portions of bile. In 8.3% of children, calcium bilirubinate and cholesterol crystals were found in the "B" and "C" portions of bile. These indicators significantly decreased compared with the results before treatment, 1- and 2-groups.

Biliary microlithiasis (microscopic stones) are usually composed of lime, mucus and a small amount of cholesterol. Biliary microlithiasis are normally found more often in portions "B" and "C" in flakes of mucus. "Sand" or the accumulation of all sedimentary elements of bile in the form of microscopic grains also indicates the presence of gallstone disease.

Thus, the results of the above studies show that children with cVHB and cVHC have more gallstone disease than children with cVHC.

Table 2 - microscopic picture of bile in children with cVHA

Type	practical healthy (n=10)		Group before treatment (n=60)		1 Group (n=20)		2 Group (n=20)		P1	3 Group (n=20)		P2	P3
	abs	%	abs	%	abs	%	abs	%		abs	%		
Portion A													
Mucus	-	-	13	21,6±5,3	4	20±9,1	3	15±8,1		1	5±5,0**	< 0,003	<0,003
Columnar epithelium	1	10±9,4	8	13,3±4,3	2	10±6,8	-	-		-	-		
Leukocytoids <10 per f/v	1	10±9,4	21	35±6,1	7	35±10,9	5	25±9,6		1	5±5,0**	< 0,05	< 0,003
Leukocytoids >10 per f/v	-	-	9	15±4,6	3	15±8,1	2	10±6,8		-	-		
Cholesterol crystals	-	-	-	-	-	-	-	-		-	-		
Bilirubinate Ca	-	-	4	6,6±3,2	1	5±5,0	1	5±5,0		-	-		
Biliary microlithiasis	-	-	4	6,6±3,2	1	5±5,0	1	5±5,0		-	-		
Portion B													
Mucus	-	-	7	11,6±4,1	2	10±6,8	2	10±6,8		-	-		
Columnar epithelium	1	10±9,4	6	9,9±3,8	2	10±6,8	2	10±6,8		-	-		
Leukocytoids <10 per f/v	1	10±9,4	21	35±6,1	7	35±10,9	6	30±10,5		-	-		
Leukocytoids >10 per f/v	-	-	7	11,6±4,1	2	10±6,8	2	10±6,8		-	-		
Cholesterol crystals	-	-	-	-	-	-	-	-		-	-		
Bilirubinate Ca	-	-	4	6,6±3,2	1	5±5,0	1	5±5,0		-	-		
Biliary microlithiasis	-	-	6	10±3,8	2	10±6,8	2	10±6,8		-	-		
Portion C													
Mucus	-	-	7	11,6±4,1	2	10±6,8	1	5±5,0		-	-		
Columnar epithelium	1	10±9,4	9	15±4,6	3	15±8,1	2	10±6,8		1	5±5,0**	< 0,05	
Leukocytoids <10 per f/v	1	10±9,4	17	28,3±5,8	5	25±9,9	4	20±9,1		1	5±5,0**	< 0,05	< 0,05
Leukocytoids >10 per f/v	-	-	3	5±2,8	1	5±5,0	-	-		-	-		
Cholesterol crystals	-	-	-	-	-	-	-	-		-	-		
Bilirubinate Ca	-	-	4	6,6±3,2	1	5±5,0	1	5±5,0		-	-		
Biliary microlithiasis	-	-	4	6,6±3,2	1	5±5,0	1	5±5,0		-	-		

Note: * - reliability of differences compared with healthy children; ** - reliability of differences compared with the group of children before treatment; P1 - significance of differences between

groups 1 and 2; P2 - significance of differences between groups 1 and 3; P3 - significance of differences between groups 2 and 3

Table 3 - microscopic picture of bile in children with cVHB

Type	practical healthy (n=10)		Group before treatment (n=36)		1 Group (n=10)		2 Group (n=10)		P1	3 Group (n=16)		P2	P3
	abs	%	abs	%	abs	%	abs	%		abs	%		
Portion A													
Mucus	-	-	6	16,6±6,2	2	20±12,6	1	10±9,4		-	-		
Columnar epithelium	1	10±9,4	7	19,4±6,5	2	20±12,6	1	10±9,4		1	6,3±6,0**		
Leukocytoids <10 per f/v	1	10±9,4	8	22,2±6,9	2	20±12,6	1	10±9,4**		1	6,3±6,0**	<0,05	
Leukocytoids >10 per f/v	-	-	7	19,4±6,5	2	20±12,6	1	10±9,4		-	-		
Cholesterol crystals	-	-	11	30,5±7,6	3	30±14,4	2	30±14,4		-	-		
Bilirubinate Ca	-	-	11	30,5±7,6	3	30±14,4	3	30±14,4		-	-		
Biliary microlithiasis	-	-	19	52,7±8,3	5	50±15,8	4	50±15,8		-	-		
Portion B													
Mucus	-	-	8	22,2±6,9	2	20±12,6	1	10±9,4**		-	-		
Columnar epithelium	1	10±9,4	8	22,2±6,9	2	20±12,6	1	10±9,4**		-	-		
Leukocytoids <10 per f/v	1	10±9,4	16	44,4±8,2	5	50±15,8	3	30±14,4		2	12,5±8,2**	<0,05	<0,05
Leukocytoids >10 per f/v	-	-	7	19,4±6,5	2	20±12,6	2	20±12,6		-	-		
Cholesterol crystals	-	-	12	33,2±7,8	3	30±14,4	2	20±12,6		-	-		
Bilirubinate Ca	-	-	12	33,2±7,8	3	30±14,4	3	30±14,4		1	6,3±6,0**	<0,05	<0,05
Biliary microlithiasis	-	-	16	44,4±8,2	5	50±15,8	3	30±14,4		2	12,5±8,2**	<0,05	<0,05
Portion C													
Mucus	-	-	7	19,4±6,5	2	20±12,6	1	10±9,4		-	-		
Columnar epithelium	1	10±9,4	7	19,4±6,5	2	20±12,6	1	10±9,4		-	-		
Leukocytoids <10 per f/v	1	10±9,4	8	22,2±6,9	2	20±12,6	2	20±12,6		1	6,3±6,0**		
Leukocytoids >10 per f/v	-	-	7	19,4±6,5	2	20±12,6	1	10±9,4		-	-		
Cholesterol crystals	-	-	13	36,1±8,0	4	40±15,4	3	30±14,4		1	6,3±6,0**	<0,05	<0,05
Bilirubinate Ca	-	-	9	24,9±7,2	2	20±12,6	2	20±12,6		-	-		
Biliary microlithiasis	-	-	20	55,5±8,2	6	60±15,4	5	50±15,8		2	12,5±8,2**	<0,05	<0,05

Note: * - reliability of differences compared with healthy children; ** - reliability of differences compared with the group of children before treatment; P1 - significance of differences between groups 1 and 2; P2 - significance of differences between groups 1 and 3; P3 - significance of differences between groups 2 and 3

Table 4 - microscopic picture of bile in children with cVHB

Type	**practical healthy** (n=10)		**Group before treatment** (n=32)		1 **Group** (n=10)		2 **Group** (n=10)		P 1	3 **Group** (n=12)		P2	P3
	abs	%	**abs**	%	**abs**	%	**abs**	%		**abs**	%		
Portion A													
Mucus	-	-	7	21,8±7,2	2	20±12,6	2	20±12,6		-	-		
Columnar epithelium	1	10±9,4	32	100	10	100	9	90±9,4**	<0,05	2	16,6±10,7**	<0,001	<0,001
Leukocytoids <10 per f/v	1	10±9,4	32	100	10	100	9	90±9,4**	<0,05	2	16,6±10,7**	<0,001	<0,001
Leukocytoids >10 per f/v	-	-	-	-	-	-	-	-		-	-		
Cholesterol crystals	-	-	11	34,4±8,3	3	30±14,4	2	20±12,6		-	-		
Bilirubinate Ca	-	-	7	21,8±7,2	2	20±12,6	2	20±12,6		-	-		
Biliary microlithiasis	-	-	13	40,6±8,6	4	40±15,4	3	30±14,4		-	-		
Portion B													
Mucus	-	-	10	31,2±8,1	3	30±14,4	2	20±12,6		-	-		
Columnar epithelium	1	10±9,4	32	100	32	100	8	80±12,6**	<0,05	3	25±12,5	<0,001	<0,001
Leukocytoids <10 per f/v	1	10±9,4	32	100	32	100	8	80±12,6**	<0,05	2	16,6±10,7	<0,001	<0,001
Leukocytoids >10 per f/v	-	-	-	-	-	-	-	-		-	-		
Cholesterol crystals	-	-	17	53,1±5,6	5	50±15,8	4	40±15,4		-	-		
Bilirubinate Ca	-	-	17	53,1±5,6	5	50±15,8	5	50±15,8		1	8,3±7,9	<0,003	<0,003
Biliary microlithiasis	-	-	18	56,3±8,7	5	50±15,8	4	40±15,4		-	-		
Portion C													
Mucus	-	-	7	21,8±7,2	2	20±12,6	2	20±12,6		-	-		
Columnar	1	10±9,	32	100	32	100	8	80±12,6*	<0,0	2	16,6±10,7	<0,00	<0,00

epithelium		4						*	5			1	1
Leukocytoids <10 per f/v	1	10±9,4	32	100	32	100	9	90±9,4**	<0,05	2	16,6±10,7	<0,001	<0,001
Leukocytoids >10 per f/v	-	-	-	-	-	-	-	-		-	-		
Cholesterol crystals	-	-	22	68,7±8,1	7	70±14,4	5	50±15,8**		1	8,3±7,9	<0,003	<0,003
Bilirubinate Ca	-	-	14	43,7±8,7	4	40±15,4	4	40±15,4		-	-		
Biliary microlithiasis	-	-	14	43,7±8,7	4	40±15,4	4	40±15,4		-	-		

Note: * - reliability of differences compared with healthy children; ** - reliability of differences compared with the group of children before treatment; P1 - significance of differences between groups 1 and 2; P2 - significance of differences between groups 1 and 3; P3 - significance of differences between groups 2 and 3

Findings:

1. In children who had VHA, HBB and VHC, multidirectional changes in microscopic parameters are observed, which is due to various pathomorphological and pathophysiological changes initiated by various types of hepatitis viruses;
2. In children with cVHA, cholesterol crystals are not detected in the composition of bile, and in children with cVHB and cVHC, cholesterol crystals are detected in all portions of bile. This indicator proves that children with cVHB and cVHC have more gallstone disease.
3. The combination of non-drug (physiotherapy) and drug (Phosphogliv) interventions contributes to the almost complete normalization of microscopic parameters in all children who had VHA, as well as in the majority of children, with cVHB and cVHC. This allows us to recommend this complex of interventions as the optimal approach in the rehabilitation of children who VHA had viral hepatitis.

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