Serotonin Metabolism Parameters in Patients with Chronic Hepatitis and Liver Cirrhosis

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We studied disorders in serotonin metabolism in patients with chronic hepatitis and cirrhosis of the liver with and without inflammatory process (cytolysis syndrome) and their impact for the formation of depressive disorders. Blood serotonin content decreased in patients with cirrhosis of the liver with pronounced depressive disorders. Serum serotonin level was elevated in all patients with the cytolysis syndrome.

Key Words: *chronic hepatitis; liver cirrhosis; serotonin; depressive disorders; cytolysis syndrome*

Changes in transmitter concentrations play an important role in the origin of psychosomatic and neurosomatic disorders in chronic diseases of the liver (CDL). Serotonin (CNS neurotransmitter) is involved in various physiological reactions as a factor of nerve pulse transmission. The involvement of the central serotoninergic system in the development of anxiety in humans, in the pathogenesis of phobias and fear, in the formation of such manifestations as anhedonia (inability to experience pleasure), helplessness, loss of motivation, and depressions is clearly proven [1,3,7,8].

The liver plays an important part in serotonin metabolism. Hepatocytes contain enzymes maintaining the specific metabolism of some amino acids, serotonin precursors. The liver is also involved in all processes of biogenic amine inactivation. Disorders in normal functioning of the liver are paralleled by significant changes in serotonin content in the blood and hepatocytes. Due to its vasoconstrictor effect and increase of vascular wall permeability, serotonin promotes the increase in portal pressure, aggravates edema and inflammation in the liver, which complicates the course of chronic hepatitis (CH) and cirrhosis of the liver (CL).

Many authors observed increased blood serotonin level in patients with CDL, particularly at the stage of cirrhosis [5,6]. It is assumed to be caused by disorders in the detoxifying function of the liver and portosystemic shunting, promoting release of vasoconstriction agents (including serotonin) from damaged hepatocytes into the blood [2,4].

We studied serotonin metabolism in patients with CH and CL with and without inflammatory process (cytolysis syndrome) and evaluated its impact for the formation of depressive disorders.

MATERIALS AND METHODS

The study was carried out in 60 subjects, divided into 3 groups, 20 per group: 1) normal subjects (mean age 31.6±8.8 years); 2) patients with CH (mean age 29.6±10.4 years); and 3) patients with CL (mean age 49.2±7.7 years). The female to male proportion was virtually the same in all groups.

The diagnoses of CH and CL were verified by complaints, history of the disease, findings of general clinical examinations, including laboratory findings, virological and instrumental studies.

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Mental status of patients was evaluated using a brief multifactorial questionnaire for personality evaluation (BMQP) and Beck depression inventory for evaluation of the level of depressive disorders. Serum serotonin was measured by ELISA (normal value up to 200 ng/ml).

RESULTS

In all patients, viral etiology of CH and CL was confirmed (chronic HCV and HBV infection eventuating in CH and CL). Half of patients with CH and CL had the cytolysis syndrome.

Serotonin level was increased in CL patients and did not differ from normal (Table 1).

Healthy individuals differed from CDL patients by all characteristics of mental and personality profile (BMQP score); they had no mental disorders or disorders in the psychological status. Patients with CH and CL differed significantly by the levels of hypochondria, depression, and hysteria. These scores are classified as the so-called neurotic triad determining the psychological portrait of patients with CDL and the type of reaction to disease.

Beck score showed differences in the level of depressive disorders in all groups. This level was significantly higher in CL patients compared to CH patients and normal subjects.

Changes in the psychoemotional status of patients with CH and CL were shown mainly by the neurotic triad scores (BMQP test) and level of depressive disorders. Hence, we measured serum serotonin, depending on the values shown by scoring.

Serum serotonin concentrations in CH and CL patients with high neurotic triad scores (BMQP test) and levels of depression were lower than in patients with low score (Table 2). Significant differences were detected in CL patients by the second axis of BMQP inventory (p=0.05) and Beck score (p=0.001) reflecting the level of depressive disorders. A negative correlation (r=-0.460; p=0.04) between serotonin level and depression was detected. The more pronounced were depressive disorders, the lower were serum serotonin levels in CL patients.

TABLE 1. Parameters of Serotonin Metabolism, Individual Psychological BMQP Profiles, and Level of Depressive Disorders According to Beck Score ($M\pm m$)

Parameter	Normal subjects	CH	CL	p
	1	2	3	
Serotonin, ng/ml	185.5±20.9	189.5±12.1	216.2±13.0	
Hypochondria	37.7±2.1	48.3±2.6	57.9±1.9	p_{1-2}=0.006 p_{1-3}<0.001 p_{2-3}=0.01
Depression	41.4±1.9	48.9±2.6	63.5±3.3	p_{1-2}=0.03 p_{1-3}<0.001 p_{2-3}=0.003
Hysteria	43.7±1.9	50.9±1.7	58.8±2.2	p_{1-2}=0.02 p_{1-3}<0.001 p_{2-3}=0.01
Psychopathy	31.0±1.7	46.2±3.4	48.7±3.5	p_{1-2}<0.001 p_{1-3}<0.001
Paranoiac condition	40.0±1.4	51.3±2.1	52.3±3.1	p_{1-2}<0.001 p_{1-3}=0.003
Psychasthenia	16.4±4.6	39.5±4.9	41.5±4.6	p_{1-2}=0.003 p_{1-3}=0.002
Schizoid condition	22.6±3.7	43.2±3.9	43.8±3.8	p_{1-2}<0.001 p_{1-3}<0.001
Hypomania	36.4±2.5	50.5±2.9	48.9±3.0	p_{1-2}=0.001 p_{1-3}=0.003
Beck score	15.1±0.4	17.4±0.8	21.8±1.6	p_{1-3}<0.001 p_{2-3}=0.05

TABLE 2. Serotonin Metabolism Parameters in CDL Patients with High (HS) and Low (LS) Neurotic Triad Scores (BMQP Profiles) and Levels of Depressive Disorders (Me; Q_1:Q_3)

Parameter	CH				CL				*p*
	LS		HS		LS		HS		
	1		2		3		4		
	n	Me	*n*	Me	*n*	Me	*n*	Me	
BMQP score 1: hypochondria	11	200.7 163.5:242.2	9	175.9 148.4:232.6	9	218.1 157.3:250.5	11	214.7 157.3:254.9	
BMQP score 2: depression	11	190.7 166.6:217.1	9	187.8 150.1:238.1	9	256.8 249.7:275.6	11	201.0 157.3:249.7	p_{3-4}=0.05
BMQP score 3: hysteria	13	202.0 173.9:242.2	7	166.4 148.4:198.7	6	240.6 209.7:255.6	14	205.6 157.3:249.7	
Beck's score: level of depression	13	184.4 169.7:201.6	7	199.0 151.7:242.2	8	255.0 228.3:285.3	12	190.4 156.3:227.3	p_{3-4}=0.01

Hence, blood serotonin level decreases in patients with CL with pronounced depressive disorders, presumably due to exhaustion of the serotonin system. This can indicate involvement of this system in the formation of depression in CL patients. Brain structures contain just 1-2% serotonin, which impedes the use of serotonin metabolism parameters for evaluation of the state of the nervous system.

The liver plays an important role in serotonin metabolism, being involved in its formation and inactivation. We studied the effect of the inflammatory process (cytolysis syndrome) on serotonin metabolism in CDL patients. It was found that serum serotonin level increased significantly in patients with the cytolysis syndrome in CH and CL (Table 3). In addition, the inflammatory process was associated with significantly higher levels of serotonin in patients with CL than in those with CH. A direct correlation between inflammatory process and serotonin level was detected in patients with CH (r=0.760; p=0.0001) and CL (r=0.594; p=0.006), in other words, the more severe was the cytolysis syndrome in patients with CDL, the higher was serum serotonin level.

TABLE 3. Relationship between Inflammatory Process (Cytolysis Syndrome) and Serotonin Metabolism in Patients with CDL ($M\pm m$)

CDL	No cytolysis syndrome	Cytolysis syndrome
CH	140.1±13.5 (*n*=8)	222.5±10.0* (*n*=12)
CL	169.6±8.9 (*n*=10)	262.9±12.2*+ (*n*=10)

Note. *p=0.003 compared to cases without cytolysis syndrome; +p<0.02 compared to CH.

Hence, inflammatory process (cytolysis syndrome) is essential for serotonin metabolism, increasing its serum level in patients with CH and CL. The severity of the cytolysis syndrome directly correlates with serotonin level. The more severe is inflammatory process in CH and CL, the higher is blood serotonin level. This can be explained by disorders in the detoxifying function of the liver, promoting release of serotonin from damaged hepatocytes into the blood.

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