VIROLOGY

LPO and Free-Radical Oxidation Parameters in Patients with Acute Viral Hepatitis

B. S. Nagoev, M. T. Abidov, and M. R. Ivanova

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 134, No. 12, pp. 645-646, December, 2002
Original article submitted December 3, 2002

Serum MDA level and concentration of superoxide anion in leukocytes were measured in patients with acute hepatitis B and C at the peak of the disease, during regression, and during early convalescence. The concentration of active oxygen forms in leukocytes was maximum at the peak of the disease and decreased before discharge from the hospital.

Key Words: *acute viral hepatitis B and C; active oxygen forms; lipid peroxidation*

Hepatocyte cytolysis and progressive necrobiosis of liver cells are determinant morphological changes in the liver in viral hepatitis [1,2,7]. A universal mechanism of cell damage and death in various organs, particularly in the liver, is excessive peroxidation of membrane structures caused by hyperproduction of reactive oxygen species (ROS) [4,6,9,13].

ROS damage cell proteins and nucleic acids, trigger lipid peroxidation (LPO) processes, which, in turn, damage cells and induce autoimmune reactions, allergy, alteration of extracellular substances, and chronic inflammation [5,10]. The mechanism of damaging effect of viruses on hepatocytes is not completely understood, but the role of tissue hypoxia [3,8,11,13] and impaired oxidative phosphorylation in mitochondria was proved.

Evaluation of immunoreactivity in the course of infectious process is important for evaluation of its severity and prognosis. The intensity of LPO processes in the serum is an integral characteristic of immunoreactivity. ROS generation can be evaluated by the concentration of superoxide anions damaging cell membranes. Mitochondrial and microsomal chains of electron transfer are the most potent sources of superoxide anions.

Kh. M. Berbekov Kabardino-Balkarsk State University, Nalchik

MATERIALS AND METHODS

The study was carried out in 167 patients aged 16-68 years, 77 of these with viral hepatitis B (VHB) and 90 with viral hepatitis C (VHC). The diagnosis was confirmed by clinical epidemiological data, laboratory findings, and detection of specific markers. HBsAg, anti-coreAg, HBeAg, anti-HBeAg, HBV DNA were detected in the blood of patients with VHB and anti-HCV IgM, NS4, and HCV RNA in the blood of VHC patients. Control group consisted of 30 donors. The patients were examined at the peak of the disease when clinical symptoms were most pronounced (intoxication and jaundice), later when jaundice regressed, and before discharge from the hospital.

The intensity of LPO was evaluated as described elsewhere [14] by serum levels of TBA-reactive substances, primarily MDA, an intermediate product of lipid peroxidation of membrane structures. The concentration of superoxide anion was measured spectrophotometrically by the rate of cytochrome *c* reduction [12].

RESULTS

The level of MDA increased significantly at the peak of the disease (Table 1). During the 2nd week of jaundice (regression of disease) the concentration of MDA

0007-4888/02/1346-0557$27.00

TABLE 1. Serum Concentration of MDA and Content of Reduced Cytochrome *c* in Leukocytes in VHB and VHC ($X \pm m$)

Parameter	VHB			VHC		
	peak	regression	early convalescence	peak	regression	early convalescence
MDA, μM	3.9±0.2* (77)	10.2±0.6* (74)	2.7±0.2* (68)	3.5±0.2* (90)	8.1±0.4*+ (88)	2.9±0.2* (84)
Cytochrome *c*, μmol/min	6.3±0.1* (77)	—	3.7±0.1* (68)	6.7±0.1*++ (95)	—	4.5±0.1*+ (88)

Note. *$p<0.001$ compared to the control (1.30±0.07 μM for MDA, 1.30±0.002 μmol/min for cytochrome *c*); +$p<001$, ++$p<0.01$ compared to VHC. "—": not determined.

continued to increase and considerably surpassed the level observed at the peak of the disease. This parameter in VHB was significantly higher than in VHC, probably due to more pronounced accumulation of LPO products in the serum. The higher level of MDA in VHB patients attests to higher intensity of the pathological process.

The level of MDA decreased significantly during the early convalescence, but remained above the normal. This parameter was similar in VHB and VHC patients (Table 1).

The concentration of superoxide anions in leukocytes in VHB and especially in VHC patients increased significantly at the peak of the disease (Table 1). During early convalescence the level of cytochrome *c* decreased, but remained above the control, especially in patients with VHC (Table 1).

Hence, the concentrations of ROS in leukocytes and LPO products in the serum increased in patients with viral hepatitis and this increase was most pronounced at the peak of the disease. Before discharge from the hospital the changes were less pronounced, but the parameters did not returned to normal. During early convalescence the concentrations of superoxide anions and hence, of all ROS were higher in VHC patients, which suggested more profound immunobiochemical damage to hepatocytes and chronic transformation of the process. These data prompt purposeful immunocorrection, including, among other drugs, tamerit, a new antiinflammatory and immunomodulating drug, which should be added to combined therapy for acute viral hepatitis.

REFERENCES

1. A. F. Blyuger, A. Ya. Maiore, and V. K. Zal'tsmane, *Biomembranes: Structures, Functions, Medical Aspects* [in Russian], Riga (1981).
2. A. F. Blyuger and A. Ya. Maiore, *Uspekhi Gepatol.*, No. 7, 22-54 (1978).
3. N. A. Boldyrev, A. V. Zmyzgova, A. V. Kozlov, and O. A. Azizova, *Sov. Med.*, No. 4, 93-95 (1989).
4. O. N. Voskresenskii and V. N. Bobyrev, *Vopr. Med. Khim.*, No. 4, 21-26 (1992).
5. L. G. Korkina and B. T. Velichkovskii, *Oxygen Radicals in Chemistry, Biology, and Medicine* [in Russian], Riga (1988), pp. 153-163.
6. V. V. Sokolovskii, *Vopr. Med. Khim.*, No. 6, 1-11 (1988).
7. S. N. Sorinson, *Viral Hepatitis* [in Russian], St. Petersburg (1997).
8. G. Ambrosio, M. L. Weisfeldt, W. E. Jacobus, and J. T. Flaherty, *Circulation*, **75**, 282-291 (1987).
9. K. P. Burton, *Free Radic. Biol. Med.*, **4**, No. 1, 15-24 (1988).
10. B. Halliwell and J. M. C. Gutteridge, *Free Radicals in Biology and Medicine*, Oxford, New York (1989), pp. 58-188, 366-494.
11. D. Jamierson, B. Chance, and E. Cadenas, *Ann. Rev. Physiol.*, **48**, 703-710 (1986).
12. J. M. McCord and I. Fridovich, *J. Biol. Chem.*, **243**, 5753-5763 (1968).
13. M. Tien, B. Svingen, and D. Aust, *Fed. Proc.*, **40**, No. 2, 179-182 (1981).
14. M. Uchiama and M. Michara, *Anal. Biochem.*, **86**, No. 1, 271-278 (1978).