EFFECT OF INTRAGASTRIC INJECTION OF OXYGEN ON SOME METABOLIC INDICES IN ACUTE EXPERIMENTAL TOXIC HEPATITIS

V. I. Uspenskii

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It is not yet known to what extent local circulatory and histotoxic hypoxia developing in the liver in acute toxic hepatitis may be a pathogenetic factor in the development of the pathochemical changes in this organ.

Mölbert [8] and Christie and Judah [5] have shown that the hepatotoxic action of carbon tetrachloride is manifested mainly by damage to the mitochondrial apparatus of the liver cells, thereby disturbing the oxidation-reduction processes in the Krebs cycle.

Duspiva and Franken [6] concluded from their experimental investigations that hydropic degeneration in the liver in acute hypoxia is the result of disturbances of oxidation-reduction processes in the liver.

Because of the facts described above, it was decided to investigate the content of lipids and glycogen in the liver and of β-lipoproteins in the blood, together with a parallel study of the tissue respiration of the liver, in acute toxic hepatitis caused by administration of carbon tetrachloride.

If a disturbance of tissue respiration plays an important role in the development of fatty infiltration of the liver and disappearance of the liver glycogen, stimulation of the respiration of the liver tissue by introducing oxygen into the portal system (by injecting it into the stomach) must influence the character of the pathochemical changes found in fatty degeneration of the liver. To investigate this problem, in parallel experiments intragastric oxygen therapy was given to rats poisoned with carbon tetrachloride.

EXPERIMENTAL METHOD

Experiments were carried out on 94 male albino rats weighing 200-250 g and kept on an ordinary laboratory diet. The animals as a whole were divided into four groups: group 1 included healthy rats (control); group 2—rats poisoned with carbon tetrachloride (CCl_4), with acute hepatitis; group 3—animals poisoned with CCl_4 and receiving intragastric oxygen injection at the same time; group 4—healthy animals receiving intragastric injections of oxygen.

Carbon tetrachloride was injected subcutaneously in three doses, each of 0.3 ml/100 g body weight, on alternate days. The animals of group 2, besides the injections of CCl_4, were given oxygen by intragastric injection daily in a dose of 5 ml/100 g body weight, through a thin elastic polyethylene catheter (time of injection about 1 min). Oxygen was given in the same way to healthy rats (group 4). The control animals received no treatment. On the 7th day from the beginning of the experiment and on the 2nd day from the last injection of CCl_4 into the rats of groups 2 and 3, all the animals were decapitated and determinations were made of the tissue respiration and lipid and glycogen content of the liver, and the concentration of β-lipoproteins in the blood serum.

The tissue respiration was investigated in a Warburg's apparatus at 37.5° in pure oxygen. The liquid medium was a 0.85% solution of sodium chloride. The thickness of the slices was 0.4-0.5 mm. The values of Q_{O_2} and Q_{CO_2} were calculated in microliters of O_2 and CO_2 per milligram of the residual dry weight of the slices per hour.

The liver glycogen was determined by a modification of the method of Seifter and co-workers [9].

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Tissue Respiration and Content of Total Lipids and Glycogen in the Liver and β-lipoproteins in the Serum of Control and Experimental Rats (M ± m, n—number of experiments)

Index	Control (group 1)	poisoned with CCl_4 (group 2)	poisoned with CCl_4 receiving intragastric oxygen (group 3)	Healthy animal receiving intragastric oxygen (group 4)
Q_{O_2}	4,9±0,12 (n=8)	3,8±0,11 (n=10) P<0,001	6,1±0,21 (n=11) P<0,001	8,0±0,13 (n=8)
Q_{CO_2}	3,8±0,08 (n=8)	3,2±0,13 (n=10) P<0,001	5,2±0,22 (n=11) P<0,001	6,9±0,12 (n=8)
Total lipids of liver (in g%)	16,0±0,61 (n=12)	30,1±0,74 (n=12)	22,2±0,61 (n=12)	17,5±0,7 (n=8)
Glycogen of liver (in g%)	2,54±0,15 (n=12)	0,58±0,04 (n=12) P<0,001	1,78±0,11 (n=12) P<0,001	2,6±0,15 (n=8)
β-Lipoproteins of blood serum (in mg%)	39,5±1,6 (n=22)	29,0±1,03 (n=23) P<0,001	49,5±1,1 (n=21) P<0,001	39,7±1,0 (n=8)

The total content of lipids in the liver was determined by the method usually adopted in the author's laboratory: the lipids from a 200-mg liver sample, dried to constant weight, were extracted with dichloreothane in a Soxhlet apparatus; the result was expressed as a percentage of the dry weight.

The concentration of β-lipoproteins in the blood serum was determined by the turbidimetric method [7].

EXPERIMENTAL RESULTS

The results obtained are shown below in the table.

It follows from the table that acute toxic hepatitis, caused by administration of CCl_4 to rats was accompanied by a decrease in the tissue respiration of the liver. The rate of utilization of oxygen and elimination of carbon dioxide by liver slices was reduced, indicating a disturbance of the combined activity of the oxidation-reduction enzymes in the liver tissue and the decarboxylation enzymes linked with them.

Parallel with the decrease in tissue respiration, in the animals of group 2 the total content of lipids in the liver rose while the glycogen content fell. The β-lipoprotein level in the blood serum was lowered.

Intragastric injection of oxygen into the rats with acute toxic hepatitis was accompanied by a marked increase in the rate of oxygen utilization and carbon dioxide elimination by the liver tissue compared with these indices in the animals of group 2. In these animals the glycogen content of the liver increased while the lipid content decreased. The concentration of β-lipoproteins in the blood serum not only did not fall but, on the contrary, was above the normal level.

Intragastric injection of oxygen into healthy rats (group 4) had no effect on the content of these substances in the liver and blood serum, but the tissue respiration in the liver slices was considerably increased.

These experiments thus demonstrated the beneficial effect of intragastric injection of oxygen in acute toxic hepatitis in relation to the tissue respiration, the content of lipids and glycogen in the liver, and the concentration of β-lipoproteins in the blood serum. These results correspond to clinical evidence of the value of intragastric oxygen therapy in infectious hepatitis [1-4].

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