Modifying Effect of Hypokinezia on Reparative Regeneration in the Liver

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Restriction of motor activity in partially hepatectomized animals causes regressive changes in the remaining part of the liver and complementary hypertrophy due to ablation of the largest part of the liver. The extent of reparative regeneration of the liver under these conditions is determined by modifying influence of hypokinesia.

Key Words: *hypokinesia, liver regeneration, regulation*

Long-lasting hypokinesia is known to delay liver growth during ontogenesis. This phenomenon is caused by inhibition of physiological regeneration of the liver [1,3,7]. We investigated reparative regeneration of the liver in animals kept during postoperational period under conditions of restricted motor activity.

MATERIALS AND METHODS

Pubertae Wistar rats (body weight 150-160 g) were used. In 80 animals two thirds of liver mass were surgically removed [10]. Forty rats were kept under hypokinetic conditions (HC) [2] and forty other rats were under ordinary conditions of motor activity (OMA). Nonoperated age-matching rats (n=80) served as control. One half of them was kept under hypokinetic conditions and the other half lived under normal conditions. At the beginning of experiments, 12 intact animals were taken as the initial control, and on day 7, 10, 20, and 30 in the morning the 9-11 rats in each group were taken for investigations. Rats were killed by decapitation. Pieces of liver were fixed in Carnoy's fluid. Regenerative process was assessed by analysis of histological preparations [4,6].

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RESULTS

During a 30-day period, the liver mass in intact rats increased 1.27-fold. On the 7th day the mass of regenerated liver in operated rats under OMA-conditions reached 91% of that in control rats and on the 10th day had normal values. On days 7, 10, 20, and 30, the mass of regenerating liver in partially hepatectomized (PHE) rats under HC was smaller by 28.2, 32.1, 45.2, and 51.9% compared with intact control and by 57.7, 67.1, 48.5, 43.9% compared with OMA rats, respectively. At the same time, the increase of the regenerated mass in PHE rats under HC was higher than that in nonoperated rats under HC (Table 1).

In PHE rats kept under OMA conditions, the mitotic index of hepatocytes increased on days 7 and 10 by 7.68 and 4.88 times, respectively, and returned to normal on days 20 and 30. At these terms, no mitoses were observed in nonoperated rats under HC. In PHE rats under HC, the number of mitoses increased on days 7, 10, and 20, while on day 30 mitoses were not observed (Table 2).

The number of binuclear hepatocytes in the liver of intact rats was 8.6-13.9%. In PHE rats, the number of binuclear hepatocytes decreased by 2.97, 2.04, 2.21, and 1.87 times at the studied terms. In nonoperated rats under HC, this parameter increased by 1.53, 1.78, 1.75, and 1.93 times, whereas in the PHE rats under the same conditions it decreased com-

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TABLE 1. Weight of the Liver in PHE Rats under Ordinary and Hypokinetic Conditions (*M*±*m*)

Terms, days	Groups	Weight of liver	
		g	%
0	Initial control	6.2±0.29	4.4±0.27
7	Intact	7.8±0.18	4.4±0.16
	PHE	7.1±0.19*	4.1±0.13
	HC	5.6±0.42*+	4.2±0.26
	PHE+HC	4.1±0.13*+°	3.3±0.17*+°
10	Intact	8.1±0.26	4.1±0.13
	PHE	7.6±0.35	3.9±0.09
	HC	5.5±0.2*+	3.6±0.17*+
	PHE+HC	5.1±0.32*+	3.5±0.18*
20	Intact	9.6±0.68	3.8±0.06
	PHE	10.1±0.83	4.2±0.24
	HC	5.3±0.29*+	3.6±0.21
	PHE+HC	4.9±0.54*+	3.3±0.47
30	Intact	7.9±0.15	3.5±0.06
	PHE	8.2±0.63	3.7±0.12
	HC	3.8±0.19*+	3.4±0.06*
	PHE+HC	3.6±0.28*+	3.3±0.19

Note: Here and in Tables 2 and 3 $p<0.05$ compared with: *intact, +PHE, °HC groups.

paring with both intact and nonoperated rats under HC (Table 2).

In the PHE rats under OMA conditions hypertrophy of hepatocytes was observed at all studied terms with the maximum on the 10th day. In nonoperated rats under HC we observed decrease in the size of hepatocytes and their nuclei compared with the initial control group. At the same time, in the PHE rats under HC the size of hepatocytes and their nuclei increased compared with nonoperated rats under HC (Table 3).

Our results indicate that hypokinesia affects reparative regeneration of the liver. Although its influence does not abolish mass increase in operated liver and does not modify cellular processes of typical regeneration, neither extent of liver regeneration nor cellular indices under HC achieve the values of regenerative hypertrophy observed in operated animals under OMA at any terms. The level of regeneration was the same for both experimental procedures. Such a conclusion is possible only if nonoperated rats under HC are taken as controls. Using the same approach, other researchers discovered compensatory hypertrophy in kidney under combined action of the unilateral nephrectomy with other factors [5,8,9].

Thus, hypokinesia modifies reparative regeneration in the liver.

TABLE 2. Proliferative Activity of Hepatocytes in PHE Rats under Normal and Hypokinetic Conditions (*M*±*m*)

Terms, days	Groups	Mitotic index, ‰	Binuclear cells, %
0	Initial control	0.43±0.044	10.9±0.87
7	Intact	0.31±0.075	11.9±0.64
	PHE	2.38±0.428*	4.0±0.46*
	HC	0.00*+	18.2±1.75*+
	PHE+HC	0.18±0.039+°	11.9±0.56+°
10	Intact	0.18±0.049	9.4±0.58
	PHE	0.88±0.021*	4.6±0.21*
	HC	0.00*+	16.7±1.60*+
	PHE+HC	0.30±0.073+°	4.3±0.69*°
20	Intact	0.23±0.073	13.9±1.33
	PHE	0.28±0.059	6.3±0.69*
	HC	0.00*+	24.3±2.52*+
	PHE+HC	0.47±0.167°	6.0±0.82*°
30	Intact	0.84±0.181	8.6±0.64
	PHE	0.69±0.273	4.6±0.32*
	HC	0.00*+	16.6±2.94*+
	PHE+HC	0.00*+	5.3±0.51*°

TABLE 3. Size of Hepatocytes in PHE Rats under Normal and Hypokinetic Conditions (*M*±*m*)

Terms, days	Groups	Area, μm^2	
		nucleus	cytoplasm
0	Initial control	25.9±0.26	163.9±3.85
7	Intact	26.0±1.02	168.3±2.47
	PHE	31.8±0.93*	204.9±1.94*
	HC	20.7±0.84*+	129.5±2.08*+
	PHE+HC	24.3±0.37+°	150.2±3.01*+°
10	Intact	25.6±0.55	162.6±4.21
	PHE	38.7±0.67*	248.6±4.21*
	HC	23.4±0.51*+	146.6±3.13*+
	PHE+HC	25.3±0.62+°	166.6±3.82+°
20	Intact	26.6±0.25	175.9±1.79
	PHE	32.4±0.66*	220.6±4.88*
	HC	19.3±0.59*+	125.1±4.19*+
	PHE +HC	23.4±0.25*+°	152.2±1.66*+°
30	Intact	27.3±0.32	182.9±3.57
	PHE	34.5±1.04*	238.1±5.24*
	HC	21.9±0.47*+	141.7±1.99*+
	PHE+HC	24.9±0.63*+°	161.8±4.63*+°

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