Vagal Regulation of Microhemodynamics and Oxygen Supply to the Small Intestine Muscles

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Three days after subdiaphragmal vagotomy, the rate of local blood flow in the muscular layer of rat jejunum increases, decreases on the 7th-30th day, and is normalized on the 60th-220th day. Po_2 is lowered within 3-30 days, but not after 14 days. Microhemodynamic disturbances are accompanied by changes in the configuration of the microvessels, increased permeability of their walls, and modification of the aggregation status of the blood. Correlations between the dynamics of blood flow rate, its kinetic parameters, and Po_2 on the one hand, and morphological reorganization of the microcirculatory bed, on the other, suggest that hypoxia of the small intestine muscles developing after vagotomy has a circulatory nature.

Key Words: *small intestine; microhemodynamics; microcirculatory bed; oxygen; vagotomy*

Vagal nerves play a role in the regulation of microcirculation and blood supply to the muscular layer of the small intestine. Vagotomy has been widely used in the treatment of peptic ulcer [1,10,11]. Generally, only one aspect of blood supply (physiological, morphological, biophysical etc.) was investigated in the majority of studies [3,12,13]. This approach does not allow one to evaluate objectively the role of the nervous system in the regulation of intestinal blood flow. In the present study we determined local blood flow rate (LBFR) in the small intestine muscular layer at various intervals after vagotomy, analyzed the kinetics of local blood flow, estimated blood supply, examined the changes occurring in the microcirculatory bed (MCB), and studied the correlations between some of these parameters.

MATERIALS AND METHODS

Experiments were carried out on 69 outbred male albino rats weighing 180-210 g. Bilateral subdiaphragmal vagotomy was performed in 38 rats under sodium γ-oxybutyrate-Seduxen anesthesia (150 and 0.6 mg/100 g body weight, respectively). Other rats, including 6 animals, were sham operated on the 3rd day after vagotomy and served as the control. Laparotomy was performed under urethane anesthesia (150 mg/100 g body weight) 16-18 h after the last feeding on days 3, 7, 14, 30, 60, and 220 days after vagotomy, and LBFR was measured by hydrogen clearance [9]. Po_2 [2] in the muscular layer of the proximal portion of the jejunum was determined using an LP-7 polarograph with an indicator platinum needle electrode and a reference calomel electrode. For leveling spatial and functional variations LBFR and Po_2 were measured in 3-5 sites of the intestine. The kinetic curves characterizing hydrogen absorption and release were processed [8] with subsequent development of an adequate mathematical model of microhemodynamics.

Parameter p2 was used in the mathematical model. This parameter describes the kinetics of local blood flow: $f_i(t_i,p1,p2,p3)=p1\times\exp(t/p2)+p3$, where t is the time, t_i is the time at the ith measurement

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of amplitude, f_i is the amplitude at the ith moment of time, p1, p2 and p3 are the parameters of exponential function.

At the end of the study, jejunal segments adjacent to the sites of measurements were excised and fixed in 12% neutral formalin. Microcirculatory bed was visualized by silver nitrate impregnation [4]. Statistical significance of the differences was evaluated using Strelkov's tables [5] and Student's t test. The integrating parameter of local blood flow was calculated from the following formula:

$$IP=\sqrt{\frac{X_e-X_c}{X_c}+\frac{U_e-U_c}{U_c}+\frac{Z_e-Z_c}{Z_c}},$$

where X is the LBFR, U and Z are p2 parameters of mathematical model of microhemodynamics for hydrogen absorption and release, respectively. e is the experimental value, and c is the control value. The relationships between the studied parameters were estimated by correlation analysis [6].

RESULTS

An increase in LBFR and a decrease in Po_2 (Table 1) were observed 3 days after vagotomy. Similar changes were occurred in sham operated rats. There were no appreciable changes in p2 kinetic parameter. Morphological analysis of the muscular layer MCB revealed local curvatures and undulations of resistive microvessels, constriction of some arterioles and precapillaries, decreased number of functioning capillaries, and plethora of some capacitance elements. The signs of blood circulation were observed in a considerable number of arteriole-venule anastomoses at the submucosa-muscular layer interface. Presumably, they reflect shunting of terminal circulation and account for increased LBFR and decreased Po_2. After 7 days, LBFR did not differ from the control, while the kinetic characteristics of blood flow changed considerably: p2 parameter for the hydrogen release phase significantly decreased. Po_2 remained lowered. The MCB reorganization during this period of postvagotomy syndrome was of another nature. The configuration of arterioles and some capillaries changed considerably: they became more convoluted and the number of arteriolar angularization increased (Fig. 1). Dilation of microvessels (Fig. 2) and erythrocyte aggregates in the capillaries and venules indicated venous stagnation. Small henorrhages along microvessels attested to increased permeability of their walls. After 14 days, the intensity of these changes decreased considerably, and the studied physiological parameters were similar to the control values. After 30 days, functional and structural characteristics were changed:

TABLE 1. Changes in MCB and Po_2 Occurring in the Muscular Layer of the Jejunum at Various Intervals after Vagotomy ($M\pm m$)

Parameter		Control	Sham operated, 3 days	Vagotomy, days					
				3	7	14	30	60	220
LBFR, ml/min/100 g tissue		238.1±21.6	318.4±19.9*	327.6±18.5*	232.8±15.6	268.3±17.9	153.3±13.5*	308.7±26.8	230.7±15.9
Po_2, mm Hg		62.6±5.9	43.0±2.9*	35.9±2.0*	37.4±2.2*	62.0±3.4	34.5±3.5*	49.2±1.1	58.7±4.2
p2	absorption	1.51±0.12	1.99±0.40	1.72±0.40	1.27±0.19	1.57±0.25	2.31±0.21*	1.96±0.31	1.48±0.28
	release	2.77±0.09	3.10±0.19	2.02±0.11	2.17±0.14*	2.65±0.07	3.82±0.15*	4.20±0.17*	2.82±0.19
IP		—	0.725	0.648	0.728	0.458	1.173	0.985	0.226

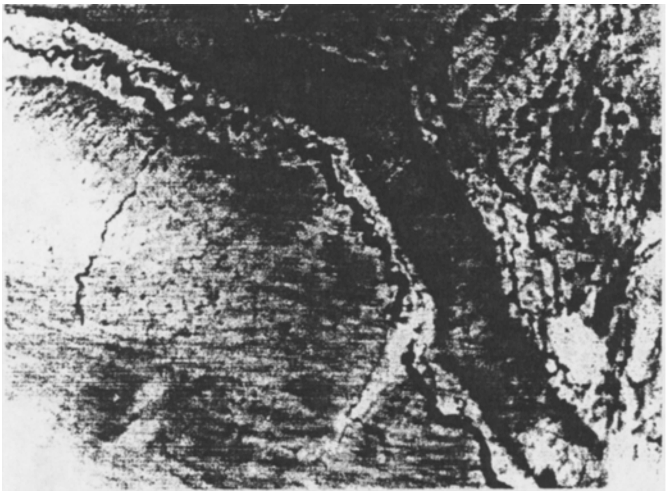

Fig. 1. Angularization of arterioles in the muscular layer of the jejunum, 7 days after vagotomy. Here in Figs. 2-4: silver nitrate impregnation, ×240.

Fig. 2. Dilation of microvessels of the capacitance component of the microcirculatory bed; convoluted arterioles in the muscular layer; 7 days after vagotomy.

LBFR and Po_2 decreased, p2 parameter increased both for hydrogen absorption and release phases, and morphological changes in MCB became more pronounced and similar to those observed after 7 days (Fig. 3). After 60 days, LBFR and Po_2 did not differ significantly from the control, while changes in the kinetic characteristics of local circulation were preserved: p2 parameter for the hydrogen absorption phase was higher than in the control. There were no changes of the CB morphology. After 220 days, we observed no significant modifications of the microhemodynamics parameters: Po_2, and MCB (Fig. 4). A correlation was established in vagotomized animals between the integral parameter of local blood flow and Po_2 (r=0.73, p<0.05), indicating that oxygen deficiency developing in the muscular layer of the small intestine is a circulatory hypoxia.

Our results show that the disturbances in parasympathetic innervation of small thin intestine coincide with phasic modifications of microhemocirculation and oxygen supply to the muscular layer (with maxima 3-7 and 30 days after vagotomy): LBFR increases after 3 days and decreases after 7 and 30 days, Po_2 decreases after 3-7 days, and normalizes after 14 days and decreases again after 30 days. Morphological analysis of MCB in the muscular layer revealed phasic reorganization of its structure. Three days after vagotomy spasm of some arterioles and precapillaries is observed, resistive vessels become convoluted, the amount of arteriovenular anastomoses increases, and some vessels become plethoric. These changes in structural organization of MCB account for the seemingly paradoxic phenomenon: a decrease in Po_2 in the muscular layer with a concomitant increase in LBFR. At a remote period (7-30 days and to a lesser extent after 14 days), MCB rearrangements are of another nature. The reaction becomes generalized, the configuration of arterioles and some capillaries changes, some microvessels become dilated as a consequence

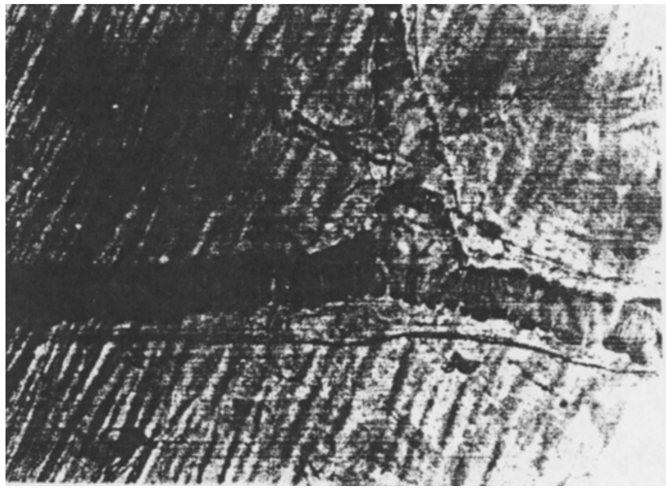

Fig. 3. Change of in the vascular wall structure and local dilation of precapillary arteriole in the muscular layer, 30 days after vagotomy.

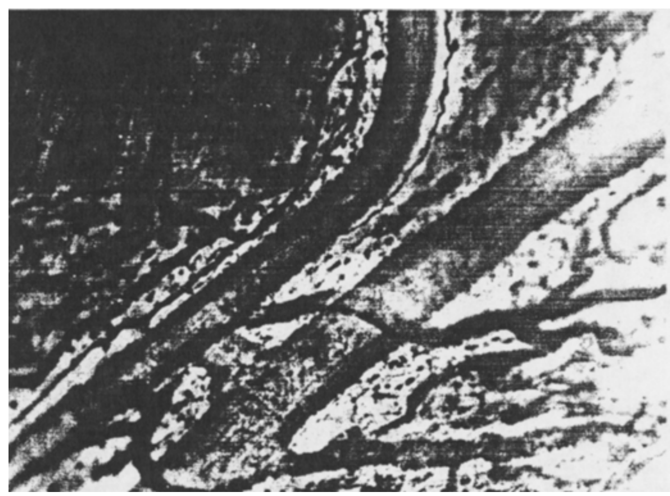

Fig. 4. Normalization of the microcirculatory bed structure in the muscular layer, 220 days after vagotomy.

of venous stagnation), and erythrocyte stasis and aggregation are observed in capillaries and venules. Small hemorrhages appear along microvessels, indicating changes in the vascular wall permeability. These morphological modifications of the MCB agree with physiological data (LBFR and Po_2) and confirm the assumption that vagotomy impairs the perfusion of the small intestine wall and leads to its hypoxia. The correlation of the dynamics of vascular reaction and Po_2 with phasic neurodystrophic process occurring in the small intestine [7] suggests that the circulatory factor is an important determinant of the time course of this process.

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