

# Homeostasis Change in the Small Intestine with Disturbed Regional Blood Flow in Early Postnatal Ontogenesis

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## ABSTRACT

**Objective:** A study of the ischemic damage course and regeneration in the small intestine with disturbed regional blood flow in early postnatal ontogenesis. **Materials and Methods:** The experiments were carried out on 30 puppies at the age from 1 to 4 weeks. The state of regional blood flow in the ischemic area of the small intestine was investigated by blood filling of tissues, metabolism - by redox potential, oxygen pressure and diffusion oxygen coefficient, lipid peroxidation activity and catalase activity. Database formation and statistical calculations were performed using the applied programmes "Microsoft Excel", "ANOVA" for "Windows". **Results:** The performed research showed that in animals of early age pronounced microcirculatory disorders were observed. About this evidenced significant tissue bloodfilling in the ischemic region of the small intestine. Essential disorder of the blood supply in the organ naturally led to a pronounced fall in the redox potential, the oxygen pressure, and the diffusion oxygen coefficient in the tissues. On a level with the disturbances in the electrogenesis and tissue oxygenation, we found a significant diminution in their antioxidant capacity, as evidenced by a pronounced increase in lipid peroxidation and a decrease in catalytic activity. Insufficient oxygen supply of tissues caused the development of irreversible changes in the intestinal wall, the disorder of the organ motility with frequent appearance of small intestinal intussusception. **Conclusions:** A significant disturbance of the small intestine blood supply at the early age, caused by an operating trauma, leads to a pronounced decrease in electrical activity and oxygenation of the organ tissues, accompanied by marked metabolic disorders. Oxygen starvation of tissues in the ischemic region of the small intestine at the early age contributes to the development of irreversible changes in the intestinal wall, and frequent disruption of the regeneration process in this area.

**Keywords:** Small Intestine; Local Ischemia; Early Age

## 1. Introduction

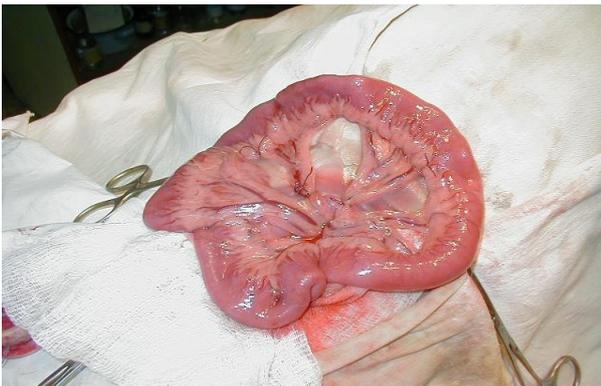
At present, the study of the mechanisms underlying the development of the compensatory reaction of the organism in response to an operating trauma is of great interest. This is due to the fact, that any surgical intervention in the intestine is associated with a disorder of its blood supply<sup>[1, 2]</sup>. One of the important factors in the pathogenesis of damage is ischemia, result in a disruption of the structural and functional tissues organization, especially at an early age<sup>[3-5]</sup>. Numerous studies established quite a variety of functional and morphological changes in ischemia, causing, mainly, the complex relationships of neuro-reflex, hemodynamic, metabolic and biological reactions<sup>[6, 7]</sup>.

## 2. Purpose

A study of the ischemic damage course and regeneration in the small intestine with disturbed regional blood flow in early postnatal ontogenesis.

## 3. Materials and methods

The experiments were carried out on 30 puppies at the age from 1 to 4 weeks. Experimental studies were performed in compliance with the rules and the International Recommendations of the European Convention for the Protection of Animals (1997). Under intravenous thiopental sodium narcosis (40-45 mg/kg body weight) in the same areas of the vessels of the organ were excluded from the blood flow (Fig. 1).



**Figure 1;** Region of the small intestine with ligated mesenteric vessels.

The state of regional blood flow in the ischemic area of the small intestine was investigated by blood filling of tissues, metabolism - by redox potential, oxygen pressure and diffusion oxygen coefficient, lipid peroxidation activity and catalase activity.

Stained slide preparation was performed with generally accepted method. Sections with thickness 10 mkm were stained by hematoxylin and eosin.

Database formation and statistical calculations were performed using the applied programmes "Microsoft Excel", "ANOVA" for "Windows".

#### 4. Results

In the first 2 days after the operation 6 puppies perished. On pathoanatomical autopsy was diagnosed diffuse purulent peritonitis, which developed as a result of hemorrhagic infarction of all layers of the intestinal

wall. In 10 cases was revealed small intestinal intussusception, which indicated a significant discoordination of peristaltic organ contractions. In most cases, the ischemic portion of the small intestine served as an invaginate.

The puppies came through the early postoperative period very difficult. During the exit of animals from the state of narcotic sleep, repeated vomiting was observed. In the first day after the operation they lied the most of the time, practically did not move. On the second day the puppies began to rise, take the water. In animals up to 3 weeks old probe feeding was performed. Owing to the postoperative intestine paresis a prolonged delay in stool and gases was noted. After 3 days the puppies took in a small amount of milk and liquid food. In the group of animals with uncomplicated course of the early postoperative period a complete recovery of the primary organism status occurred.

Investigations established that in 20 minutes after the vasoligation in the body a pronounced disturbance of electrical activity and oxygen supply of tissues was recorded. The redox potential fell by 97.69% ( $P \leq 0.001$ ). Oxygen pressure and diffusion oxygen coefficient decreased correspondingly by 57.67 ( $P \leq 0.001$ ) and 94.57% ( $P \leq 0.001$ ). In 60 minutes after the vasoligation these parameters diminished by 145.26% ( $P \leq 0.001$ ), 60.24% ( $P \leq 0.001$ ) and 95.52% ( $P \leq 0.001$ ) (Table. 1).

Parameter	Initial data	Test data, 20 minutes	Test data, 60 minutes
Redox potential, mV	-52,83 ±1,11	-104,44 ±8,34 <sup>xxx</sup>	-129,57 ±12,38 <sup>xxx</sup>
Oxygen pressure, kPa	7,37 ±0,29	3,12 ±0,21 <sup>xxx</sup>	2,93 ±0,3 <sup>xxx</sup>
Diffusion oxygen coefficient, cm <sup>2</sup> /s	(2,23 ±0,34) ·10 <sup>-2</sup>	(1,21 ±0,16) ·10 <sup>-2xxx</sup>	(1,0 ±0,22) ·10 <sup>-2xxx</sup>

**Table 1.** Change parameters of tissues oxygen supply in ischemic region of small intestine ( $M \pm m$ ), n=10

<sup>x</sup> -  $P \leq 0.05$ . <sup>xx</sup> -  $P \leq 0.01$ . <sup>xxx</sup> -  $P \leq 0.001$ . In other cases  $P > 0.05$  with respect to the initial data.

One day later after the operation in the ischemic part of the small intestine were noted pronounced hyperemia, multiple hemorrhages, alternating with single necrosis area. In the organ lumen conglomerates of desquamated necrotic tissues were found. At microscopic examination plethora and edema of all layers of the small intestine wall were observed, especially in the mucosa and submucosa, necrosis of the villi tips

with desquamation.

Significant changes in tissue homeostasis were recorded in the investigated region of the organ. The activity of lipid peroxidation increased essentially. The malonic dialdehyde content rose by 88.37% ( $P \leq 0.01$ ). The catalase activity decreased by 25.55% ( $P \leq 0.001$ ). There was a significant increase in bloodfilling of tissues. This indicator increased by 466.14% ( $P \leq 0.001$ ) (Tabl.

2). The redox potential was reduced by 64.28% ( $P \leq 0.01$ , test data -  $-86.79 \pm 6.26$  mV). The oxygen pressure and diffusion oxygen coefficient diminished

by 56.17 ( $P \leq 0.001$ , test data -  $3.23 \pm 0.31$  kPa) and 83.81% ( $P \leq 0.01$ , test data -  $(3.61 \pm 0.25) \cdot 10^{-2}$  cm<sup>2</sup>/s) (Fig. 2).

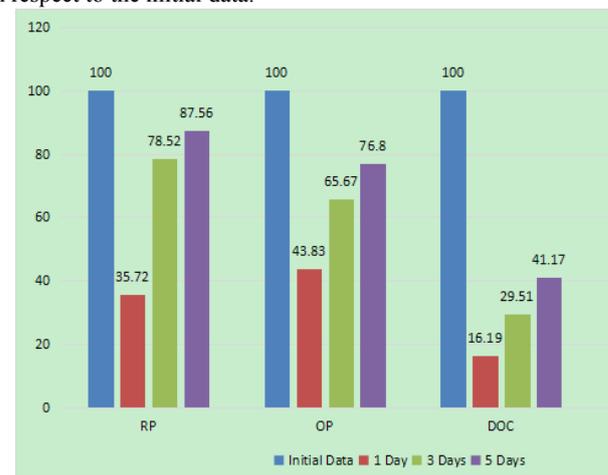
Parameter	One day	Three days	Five days
Malonic dialdehyde, nmol/g tissue	1,29 ± 0,14	1,3 ± 0,26	1,29 ± 0,16
Initial data	2,43 ± 0,18 <sup>xx</sup>	2,32 ± 0,22	2,25 ± 0,26 <sup>x</sup>
Test data			
Catalase, mg H <sub>2</sub> O <sub>2</sub> /min per 1 g of tissue	3,64 ± 0,13	3,43 ± 0,28	3,77 ± 0,2
Initial data	2,71 ± 0,07 <sup>xxx</sup>	3,04 ± 0,17	3,86 ± 0,29
Test data			
Bloodfilling, mkl/g tissue			
Initial data	240,25 ± 40,92	192,29 ± 26,94	265,78 ± 32,55
Test data	1360,14 ± 140,79 <sup>xxx</sup>	859,4 ± 86,23 <sup>xxx</sup>	752,95 ± 52,02 <sup>xxx</sup>

**Table 2.** Change parameters of tissues homeostasis in ischemic region of small intestine ( $M \pm m$ ), n=10

<sup>x</sup> -  $P \leq 0.05$ . <sup>xx</sup> -  $P \leq 0.01$ . <sup>xxx</sup> -  $P \leq 0.001$ . In other cases  $P > 0.05$  with respect to the initial data.

In the group of animals, that did not have necrosis, significant morphological changes were noted 3 days later after surgery. In the ischemic area of the organ extensive hemorrhages were detected. Microscopic examination of tissue small intestine wall sections showed the presence of a pronounced inflammatory process. There was edema with significant polynuclear infiltration, especially in the submucous, expressed venous plethora of the hemocirculatory circulation vessels, presence of multiple thrombus, mainly in capillaries and venules.

The activity of lipid peroxidation was high. The level of malonic dialdehyde exceeded the control value by 78.46% ( $P \leq 0.05$ ). Bloodfilling tissues remained raised by 346.93% ( $P \leq 0.001$ ). The redox potential and oxygen pressure gradually returned to normal. The first one was reduced by 21.48% ( $P \leq 0.05$ , test data -  $-64.18 \pm 4.18$  mV), the second one - by 34.33% ( $P \leq 0.01$ , test data  $4.84 \pm 0.62$  kPa). Diffusion oxygen coefficient was decreased by 70.49% ( $P \leq 0.01$ , test data  $(6.58 \pm 0.19) \cdot 10^{-2}$  cm<sup>2</sup>/s). Other indicators did not differ reliably from the initial data.



**Figure 2;** Change in Redox Potential (RP, mv), Oxygen Pressure (OP, kPa) and Diffusion Oxygen Coefficient (DOC, cm<sup>2</sup>/s) in ischemic region of small intestine (in percentage to initial data).

Five days later after the operation a decrease in inflammatory effects were detected in ischemic region of small intestine. However, in the mucous membrane, especially in its villi, there was still a pronounced inflammatory reaction. Here were clearly defined micronecrosis zones in the apical parts of most villi, in some of them were recorded dystrophic and necrobiotic changes in enterocytes.

In the study of homeostasis in these terms the following was noted: the content of malonic dialdehyde and bloodfilling remained increased by 74.42 ( $P \leq 0.05$ )

and 183.3% ( $P \leq 0.001$ ). A moderate decrease of redox potential and oxygen pressure in the tissues was determined by 12.44 ( $P \leq 0.05$ , test data -  $-59.4 \pm 2.29$  mV) and 23.2% ( $P \leq 0.05$ , test data -  $5.66 \pm 0.48$  kPa). Diffusion oxygen coefficient was reduced by 58.83% ( $P \leq 0.05$ , test data -  $(9.18 \pm 1.32) \cdot 10^{-2}$  cm<sup>2</sup>/s).

Seven days later after the operation, a significant subsiding of the inflammatory process was noted. There were no hemorrhages in the wall of the small intestine. In the study of the functional organ parameters were found the its approach to control data that testified of the restoration of tissue homeostasis in the ischemic zone.

## 5. Discussion

The performed research showed that in animals of early age pronounced microcirculatory disorders were observed. About this evidenced significant tissue bloodfilling in the ischemic region of the small intestine. Essential disorder of the blood supply in the organ naturally led to a pronounced fall in the redox potential, the oxygen pressure, and the diffusion oxygen coefficient in the tissues.

On a level with the disturbances in the electrogenesis and tissue oxygenation, we found a significant diminution in their antioxidant capacity, as evidenced by a pronounced increase in lipid peroxidation and a decrease in catalytic activity.

Insufficient oxygen supply of tissues caused the development of irreversible changes in the intestinal wall, the disorder of the organ motility with frequent appearance of small intestinal intussusception.

## 6. Conclusions

A significant disturbance of the small intestine blood supply at the early age, caused by an operating trauma, leads to a pronounced decrease in electrical activity and oxygenation of the organ tissues, accompanied by marked metabolic disorders.

Oxygen starvation of tissues in the ischemic region of the small intestine at the early age contributes to the development of irreversible changes in the intestinal wall, and frequent disruption of the regeneration process in this area.

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