Effect of the Hydra Peptide Morphogene at the Early Stages of Rat Postnatal Ontogenesis

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The effect of the hydra peptide morphogene, its structural fragment, and antagonist 5N pentapeptide on DNA production in the myocardium, tongue, gastric and tracheal epithelium was studied in 7-day-old rats. The hydra peptide morphogene stimulated proliferative activity of the myocardium and epithelium of different organs. 5N fragment did not affect the production of DNA in the myocardium and suppressed it in the epithelium.

Key Words: *myocardium; epithelium; DNA production; ontogenesis*

The hydra peptide morphogene (HPM) is a bioactive undecapeptide pGlu-Pro-Pro-Gly-Gly-Ser-Lys-Val-Ile-Leu-Phe. The morphogenetic properties of HPM have been studied in various invertebrates [11,12]. HPM stimulates epitheliocyte proliferation [7] and myocardial hypertrophy [6] in adult albino rats. HPM starts functioning at the early stages of mammalian ontogenesis: tissue content of HPM is higher during the embryonal and early postnatal periods of life [8]. HPM is probably involved in the development of structural homeostasis of mammals.

We examined the effect of HPM on proliferative processes during the early postnatal period and analyzed some biochemical mechanisms of the peptide effect.

MATERIALS AND METHODS

HPM and its structural analog 5N pentapeptide (Lys-Val-Ile-Leu-Phe), a functional antagonist of HPM, were used. Experiments were carried out on 107 outbred albino rat pups from 14 litters. Control and experimental groups were formed by dividing the litters. The peptides were injected intraperitoneally in a dose of 0.1 μmol/kg from the second to the sixth days of life daily. The controls were injected with an equal volume (0.05 ml) of sterile isotonic NaCl. Twenty-four hours after the last injection, the intensity of DNA synthesis was evaluated by the autoradiographic method in the left and right atrium, subendocardial zone of the ventricular septum, left and right ventricles, and lingual, gastric, and tracheal epithelium [3]. ^{3}H-Thymidine was injected intraperitoneally in a dose of 1 μCi/g 1 h before euthanasia. Cells in the S phase were counted (the labeled nuclei index, LNI, %) and the mean number of tracks above the labeled nucleus (label intensity, LI). For analyzing the mechanisms of the effect of HPM and its antagonist on tissue homeostasis, the lipid peroxidation and the antioxidant defense system (LPO-AOD) were studied. The contents of total lipids, α-tocopherol [9], lipid peroxides [2], and malonic dialdehyde [5] were measured in the blood and in lung homogenates using Lachema kits. The results were processed by the parametrical statistics methods using Student's *t* test.

RESULTS

During the early postnatal period HPM stimulated DNA production in the myocardium (Table 1), as evidenced by a 15.4-27.2% increase in LI in all examined myocardial zones. The shortening of the S phase, judging from a significant increase in the LI, stimulated the proliferation of cardiomyocytes at early stages of postnatal development [10]. In addition, in the right atrium with initially lower LNI, this parameter in-

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TABLE 1. Effects of HPM and 5N Fragment on the Production of DNA in the Myocardium and Epithelium of Albino Rats at Early Stages of Postnatal Ontogenesis ($M \pm m$)

Object of examination	Control		HPM		5N fragment	
	LNI, %	LI	LNI, %	LI	LNI, %	LI
Myocardial zones						
Atrium left	9.21±1.09	22.98±0.95	11.45±0.81	27.48±1.30*	9.95±0.50	23.00±1.18
right	7.16±0.82	21.87±0.72	10.45±0.94*	25.59±1.39*	8.20±0.75	22.01±1.26
Ventricle left	9.01±1.01	23.33±0.93	11.20±0.41	29.68±1.49*	10.40±0.58	24.11±1.18
right	8.58±1.09	22.94±0.75	9.21±0.83	26.48±1.23*	9.20±0.58	22.09±1.10
Interventricular septum	9.89±1.15	25.12±1.02	12.22±0.63	30.45±1.44*	9.84±0.44	24.25±1.20
Epithelial tissues						
Tongue	11.87±0.18	18.51±0.58	13.17±0.29**	24.66±0.97**	9.25±0.44**	13.39±0.49**
Stomach	4.18±0.16	22.78±1.48	5.14±0.16**	21.21±0.10	2.43±0.35**	14.76±1.08**
Trachea	1.88±0.10	24.12±0.65	2.20±0.11**	23.21±0.97	1.59±0.09**	20.98±1.00**

Note. *$p<0.05$, **$p<0.01$ compared with the control.

creased by 45% under the effect of HPM. HPM activated proliferation processes in the epithelium of different localization (Table 1). A significant increase in LNI and LI was observed in the multilamellar partially keratosic lingual epithelium of ectodermal origin. In unilayer epidermal epithelium of the pyloric part of the stomach, LNI was significantly higher than in the control and LI was stable. The number of DNA producing epitheliocytes increased in multilayer entodermal epithelium of the trachea but the LI was the same as in the control. In albino rats, HPM stimulated proliferative activity in the myocardium and epithelium during the early postnatal period.

The involvement of HPM in the regulation of proliferative processes at the early stages of postnatal development was confirmed by experiments with the functional antagonist of HPM (Table 1). 5N fragment significantly suppressed DNA production in lingual, gastric, and tracheal epithelium, but not in the myocardium. In general, 5N pentapeptide suppressed the proliferative processes in the early postnatal period. Presumably, 5N fragment affects epitheliocytes. A probable indirect mechanism of this effect is as follows: being an HPM antagonist, 5N fragment blocks the effect of endogenous morphogene. In this case the suppressive effect of 5N fragment in the epithelium and its absence in the myocardium are due to different size of the pool of endogenous HPM in tissues.

Lipid peroxidation is an integral component of tissue homeostasis. Accumulation of free radicals in tissues during LPO activation and/or suppression of AOD result in slower proliferation [1]. Analysis of the effect of HPM and 5N fragment on the LPO-AOD system in the blood and lungs (Table 2) showed that

TABLE 2. Effects of HPM and 5N Fragment on the LPO-AOD System of the Blood and Lungs of Albino Rats at Early Stages of Postnatal Ontogenesis ($M \pm m$)

Parameters	Control	HPM	5N fragment
Blood			
total lipids, g/liter	7.73±0.63	9.42±0.48*	7.82±0.34
hydroperoxides, μmol/g lipids	52.78±3.37	44.15±7.03	52.15±7.04
malonic dialdehyde, U fluorescence/g lipids	152.9±30.4	109.5±15.4	170.3±24.4
α-tocopherol, μmol/liter	19.43±2.41	18.81±1.80	12.41±1.10*
Lungs			
total lipids, mg/g tissue	1.65±0.12	1.57±0.16	1.23±0.12*
hydroperoxides, mmol/g lipids	1.11±0.21	0.66±0.08*	0.83±0.14
malonic dialdehyde, U fluorescence/g lipids	1571±173	1699±257	2209±176*
α-tocopherol, μg/g lipids	20.70±3.44	22.77±3.11	15.87±2.05

Note. *$p<0.01$ compared with the control.

HPM suppresses LPO in the lungs, which is manifested in decreased lung content of lipid peroxides and increased blood content of total lipids. Previously, it was shown that HPM activates the enzymate component of AOD [4]. 5N fragment caused opposite changes in the LPO-AOD system: lung content of malonic dialdehyde increased, while blood contents of total lipids and α-tocopherol significantly decreased.

These results suggest that HPM plays an important role in the development of tissue homeostasis at early stages of postnatal development in mammals. A mechanism regulating the rate of proliferation under the effect of HPM and its 5N fragment may include changes in the LPO-AOD system.

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