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STUDY OF THE CONDITION OF THE ORAL MUCOSA OF RATS WITH LONG-TERM ADMINISTRATION OF NIFEDIPINE

Abstract. The article examines the effect of long-term oral nifedipine on biochemical and cytomorphological changes in the oral mucosa of rats. 1 group intact (5 individuals). The 2nd group (7) received per os nifedipine in a dose of 5 mg / kg body weight of rats for 70 days. Nifedipine in the oral mucosa caused an increase in peroxidation processes, inadequate functioning of antioxidant enzymes, an increase in the activity of the pro-inflammatory enzyme - acid phosphatase. According to morphometric studies revealed violations in the epithelial layer and the lamina propria of the oral mucosa.

Key words: lipid peroxidation, antioxidant enzymes, acid phosphatase, nifedipine, epithelial layer, oral mucosa, rats.

The basis for the preservation of the normal physiological state of the oral mucosa is the constant desquamation of epithelial cells damaged and microbes-colonized. Only with the breakdown of the cell cycle and the synthesis of protective proteins [1] do the processes of a "second line of defense" develop - inflammation.

Some xenobiotics of medicinal nature cause side effects in the tissues of the oral cavity. These substances include antianginal agent nifedipine, which with prolonged use can cause inflammation in the oral mucosa.

The aim of the work is to study the effect of long-term use of nifedipine on the state of the oral mucosa of rats.

Materials and methods

In the experiment taken 12 white rats males 1,5-months. age, which were kept on a full diet of vivarium: 1st group (5 individuals) intact, in the 2nd group (7) rats received a suspension of nifedipine (manufactured by Pharmaceutical Company LLC Zdorovye, Ukraine) in a dose of 5 mg / kg body weight of rats for 70 days.

After slaughter, the blood serum and oral mucosa (oral mucosa) were taken from the animals. The level of POL was assessed by the content of malonic dialdehyde (MDA) [2]. The activity of antioxidant enzymes was determined: glutathione peroxidase (GPO) [3], glutathione reductase (GR) [4], catalase [5]. Acid phosphatase activity was determined by the method of [6].

For cytomorphological studies, fragments of the buccal mucosa were dissected out in rats, fixed in formalin and embedded in paraffin. Sections 10 μm thick were processed according to Einarson [7] and used for review morphological and morphometric studies. With a small magnification of the microscope, the coefficient of erosion of the epithelium (CEE) was measured, what

proportion is the zone of damaged epithelium to the area of the investigated (in units). The percentage ratio of the zone of the cellular layers of the epithelium (ZKS) and the zone of the stratum corneum (ZRS) was determined [8]. To assess the reaction of the connective tissue of the lamina propria of the mucous membrane, the coefficient of vascular stenosis (CVS) was calculated. For this, it was determined what part of the area of the wall of the vessel of the microcirculatory bed (ICR) to the area of its lumen (in units).

The results of the experiments were processed by standard methods with the definition of criteria for the reliability of differences in student.

Research results

Chronic oral administration of nifedipine in the serum of rats caused an increase in peroxidation processes - the MDA content increased 3.9 times as compared with the intact group (p = 0.06; Table 1). At the same time, the activity of antioxidant enzymes significantly decreased in serum: glutathione reductase 1.4 times (p = 0.09); catalase - 1.9 times (p <0.001; table 1).

Table 1

The content of MDA and the activity of enzymes in the serum and oral mucosa of rats under the influence of nifedipine (M ± m; p)

Animal groups	MDA content (μmol / ml; μmol / g)		Activity					
			GPO (мкат/г)	GR (нкат/мл; нкат /г)		Catalase (мкат/мл; мкат/г)		AP (мкмоль/г)
	blood serum	oral mucosa	oral mucosa	blood serum	oral mucosa	blood serum	oral mucosa	oral mucosa
Intact	0,49±0,030	13,7±0,32	55,0±10,9	0,040±0,0063	4,38±0,023	2,93±0,051	58,2±1,32	0,99±0,50
Nifedipine	1,91±0,67 p=0,06	16,8±0,43 p=0,001	16,7±3,22 p=0,005	0,028±0,0020 p=0,09	2,68±0,0020 p=0,002	1,58±0,19 p<0,001	53,2±0,61 p=0,005	2,85±0,61 p=0,04

Note. In tab. 1-3 indicator of reliability p calculated compared with the intact group

Enhancement of lipid peroxidation processes was also observed in the oral mucosa. Thus, the level of MDA under the action of nifedipine increased by 23% (p = 0.001) compared with the intact group. Under the influence of nifedipine, catalase activity in DPR decreased by 9% (p = 0.005); GPO - 3.3 times (p = 0.005); GH - 1.6 times (p = 0.002; table 1), which indicates their insufficient functioning. In the oral mucosa of rats under the action of nifedipine 2.9 times (p = 0.04; Table 1), acid phosphatase activity increased, indicating an increase in inflammatory events in this object of study.

In the group of rats who received nifedipine, on the background of the vivarium diet, peculiarities of the morphological picture of the oral mucosa were noted. The mucous membrane in general looked more thickened than in the intact group. The epithelial layer was more heterogeneous. There were areas of separation and even the absence of the stratum corneum. The coefficient of erosion of the epithelium (CEE) increased threefold compared with the intact group: 0.18 ± 0.04 u. against 0.06 ± 0.001 u. (p = 0.03).

In the basal layer, a part of the cells had signs of initial hydropic dystrophy in the cytoplasm. Basically, the patterns of mitosis are typical. In the spinous layer, the cells looked altered in places: larger cells with partially cellular cytoplasm were encountered, the nuclei of which were somewhat enlarged. In some places, the cells were moved apart due to pericellular edema. Zones of cell layers (ZKS) in the group of rats treated with nifedipine did not significantly change, the zone of the stratum corneum (GEM) decreased by 26% (p = 0.03) as compared with the intact group (Table 2).

Table 2

Morphometry of the epithelial layer of the rat cheek mucosa. Volume fractions of cellular and stratum corneum (%) (M ± m; p)

Animal groups	Cell layer (ZKS), (%)	Zone of the stratum corneum (ZRS) (%)
Intact	39,3±1,4	17,6±0,8
Nifedipine	40,2±1,5	13,1±1,2 p=0,03

In general, the lamina propria of the mucosa looked thickened. Connective papillae narrow, go deep into the layer of epithelium and have branching. Observed swelling of the connective tissue both around the vessels and at a distance from them. Bunches of fibers are separated and thickened.

The walls of the blood vessels of the ICR were somewhat thickened due to the swelling of the cells present here. The internal lumen of the vessels looked dilated. The coefficient of stenosis of blood vessels (KVV) was reduced by half compared with the intact group (p = 0.02; Table 3).

Table 3

The coefficient of stenosis of the vessels of the ICR of the mucous membrane of the cheek of rats (M ± m; p)

Animal groups	Coefficient of vascular stenosis (KVV) (conventional units)
Intact	3,1±0,32
Nifedipine	1,5±0,36 p=0,02

Conclusion

Studies have shown that in selected experimental conditions - the long-term administration of an inducer of gingival cell hyperplasia, nifedipine, its pathogenic effect on the condition of the oral mucosa of rats was revealed. Thus, under the action of the drug, the enhancement of lipid peroxidation processes, dysregulation and partial inactivation of enzyme proteins was revealed. Similar biochemical changes were observed at the level of the body - in the serum of animals. In addition, acid phosphatase, which is known to be a pro-inflammatory enzyme, was significantly activated in the PRS.

Based on the data of general microscopy and comparison of morphometric parameters, it was established that under the action of nifedipine, abnormalities in the SOPR epithelial layer were revealed: heterogeneity of its structure, areas of exfoliation and partial absence of the stratum corneum, increase in the epithelium erosion coefficient. Nifedipine caused focal vacuolar degeneration in the epithelium. Own plate SOPR thickened connective tissue - edemato.

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