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THE INFLUENCE OF THE THIOTRIAZOLINE OINTMENT WITH SILVER NANOPARTICLES ON MORPHOLOGICAL LESIONS OF GUINEA PIGS' SKIN DUE TO THE LOCAL EFFECTS OF ULTRAVIOLET RAYS AT THE REMOTE TERMS AFTER IRRADIATION

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Abstract

Local ultraviolet irradiation of guinea pigs was performed and the morphofunctional state of the skin was investigated in terms of the delayed after irradiation under the conditions of using of the thiotriazolin ointment with SNP. It was established that under the influence of the ointment of thiotriazoline with SNP, a faster return to the norm of the structure of the skin and its morphometric parameters is noted: reduction of thickness and restoration of the normal structure of the epidermis in the period from the 15th to the 21st day, decrease of the index of density of fibroblasts to the value of norm by 28th day.

Key words: local UVI of guinea pigs, morphofunctional skin condition, Thiotriazoline ointment with silver nanoparticles.

Introduction. The effect of ultraviolet irradiation (UV) on the skin has both positive and negative values [16, p. 1818, 12, p. 112]. UVI with suberythematous and small erythematous doses have a beneficial effect on the body [10, p. 164, 14, p. 147]. However, most of the malignant neoplasms are caused by excessive exposure of UVI [13, p. 149] and is

the result of many years of excessive exposure of this radiation to a person with a long latent period between the effect and occurrence of the disease [1, p. 82]. This determines the need to study the mechanisms of negative consequences [15, p. 53], especially remote (photoinduced aging, actinic keratosis, elastosis, sunny lentigo, melanoma and non-melanoma skin tumors [8, p. 178, 7, p. 752]), the effect of ultraviolet radiation on the body, in particular on the skin, and the creation of measures for prevention of their occurrence [11, p. 1320]. The high activity of the tiotriazoline ointment with silver nanoparticles (SNP) with burn wound [4, c. 128, 9, c. 922], ultraviolet (UV) erythema in the early post-erythematous period [6, c. 398, 3, c. 12] was established. This suggests that this ointment will be effective in ultraviolet irradiation at the remote terms, in particular, prevent the development of negative effects in the skin.

The purpose of the work. To investigate the effect of tiotriazolin ointment with SNP on morphological lesions of guinea pigs' skin due to the local action of ultraviolet rays in the distant after irradiation of the term.

Materials and methods. The research was carried out on 54 albino guinea pigs weighing 300-350 g, which were divided into 3 groups: I - animals subjected to local UV (without treatment, control, $n = 24$), II - UVI + Thiotriazoline ointment with SNP (main group, $n = 24$), III - intact animals ($n = 6$). Animals of the first two groups were irradiated with ultraviolet light pre-shaded areas of the skin using a mercury-quartz irradiator OKN-11-M (UV A and B). Guinea pigs of group II were applied a thin layer of Thiotriazoline ointment with SNP to the skin in the treatment and prophylactic mode. All procedures with animals, as well as their withdrawal from the experiment on the 8th, 15th, 21st and 28th day, were conducted in compliance with the principles of bioethics. The material for morphological study was the carved complex of tissues (skin, subcutaneous tissue, muscles) from the irradiation zone. The material was fixed in 10% neutral formalin, pieces of tissue were subjected to standard alcoholic treatment, paraffin sections were stained with hematoxylin and eosin, using the Van Gizon method [3, p. 296]. For the objectivization of the results of the study, a morphometric method was used to determine the thickness of the epidermis in the skin, the density of fibroblasts in 1 mm² papillary layer of the dermis. The thickness of the epidermis in the skin was expressed in μm , the density of fibroblasts was expressed in sample per mm². The study of preparations painted by histological and histochemical methods, as well as morphometric studies were performed on a microscope of Olympus BX-41. The obtained data were processed by the method of variational statistics [2, p. 34].

Research results. Microscopically, **on the 8th day** of the experiment in the main group, the thickness of the epidermis is 42.02 ± 2.81 , which is significantly higher than in intact animals (34.12 ± 1.73), but less than in the control group (114.64 ± 3.23) ($p < 0.05$). Among the basal cells there are Langerhans cells. There is horny layer with moderate hyperkeratosis. The dermis, unlike the control group, has a normal configuration of collagen and elastic fibers, between which fibroblasts and other cellular elements of the dermis are located. The density of fibroblasts is 933.92 ± 36.55 , which exceeds the corresponding index in intact animals (493.90 ± 12.60) in 1.9 times and lower than in the control group (1861.11 ± 74.32) in 2 times. Vascular basement membrane is thin and continuous. **On 15th day** the thickness of the epidermis (41.03 ± 2.72) in the second group is significantly lower than in group I (90.59 ± 3.17). In the papillary layer of the dermis under the loci of hyperplasia of the epidermis, the content of elastic fibers decreases, thickened collagen fibers are determined, and an increase in the number of fibroblasts is observed, but their density decreases to 914.05 ± 40.15 , which is lower than the corresponding indicator in the control group in 1.9 times, but it is higher than in intact guinea pigs ($p < 0.05$). Vascular basement membrane is thin and continuous. **On the 21st day** of the experiment in the main group of all laboratory animals, the structure and thickness of the epidermis in general do not differ from those in the group of intact animals (40.51 ± 2.89) (Fig. 1) and significantly lower than in the group without treatment. In the projection of areas of hyperplasia of the epidermis in the papillary layer of the dermis, the content of elastic fibers is reduced, the density of fibroblasts and fibrocytes is elevated. The density of fibroblasts is 890.34 ± 45.31 , which is lower than in the control group in 1.4 times but it is higher than in the intact group ($p < 0.05$). Flattened endothelial cells are located on the thin, continuous vascular basement membrane. In the untreated group, the papillary layer of the dermis is enlarged, represented by thickened beams of moderately fuchsinophilic collagen fibers, with the disappearance of elastic fibers (Fig. 2), in some places with perifocal lymphocytic infiltration. **On 28th day** the structure of the skin and the thickness of the epidermis (38.80 ± 2.05) of 100% of the animals of the main group do not differ from intact guinea pigs and they are less than in the control group (69.16 ± 3.00) ($p < 0.05$). As part of the epidermis, the basal, spiky, granular and horny layers are clearly differentiated. The horn is compact and represented by eosinophilic, non-nuclear scales. The papillary and mesh layers of the dermis are with the usual histological configuration of collagen and elastic fibers. Vascular basement membrane is thin and continuous. The endothelial cells located on it are flattened. In one observation isolated small loci of the deficiency of elastic fibers and compaction of collagen fibers with a slight increase

in the content of fibroblasts and fibrocytes are detected subepidermally in the papillary layer. However, the density of fibroblasts in the main group (544.00 ± 28.56) is less than in the control group in 1.9 times and does not significantly differ from the corresponding indicator in intact animals.

Thus, the tiotriazolin ointment with SNP reduces the negative effect of ultraviolet radiation on the development of morphological disorders of skin, which is confirmed by morphometric data (on the **8th, 15th, 21st and 28th** days of the experiment, the thickness of the epidermis in the main group is significantly less than the same one in the control group in 2.7 times, 2.2 times, 1.9 times, 1.8 times corresponding; the density of fibroblasts in the corresponding times is lower in the group with the use of ointment of thiotriazoline with SNP than in the group without treatment in 2 times, 1.9 times, 1,4 times, 1,9 times ($p < 0,05$) corresponding) and further study opens its prospects for the prevention and reduction of the negative influence of ultraviolet radiation.



Fig. 1. Equal thickness of the epidermis. Distributed location of cellular elements of the dermis. The main group (tiotriazolin ointment with SNP), 21th day. Coloring with hematoxylin and eosin, x200.

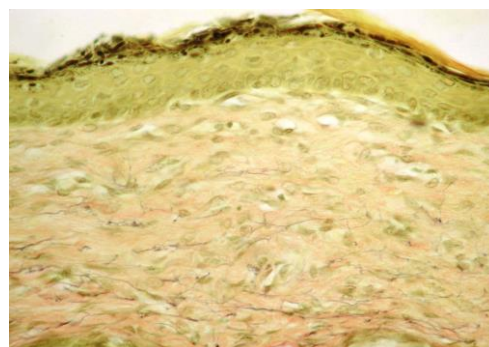


Fig. 2. Reduction of the content of elastic fibers and collagenization of the papillary layer of the dermis. Control group (without treatment), 21th day. Fukselin coloring by Weigert with picrofucsin painting by Van Gison, x400.

Conclusions

1. Local UVI of guinea pigs' skin in a minimal erythema dose causes marked changes in the morphofunctional state of the skin in the distant post-eritum period (within 28 days) - thickness of the epidermal layer, dystrophic changes in epidermocytes and dyskeratosis, increasing the thickness of fibroblasts, increasing dermis collagenization, changes in the

content and structure elastic fibers, increasing uneven derma fibrosis with the subsequent development of sclerotic changes.

Under the influence of tiotriazolin ointment with SNP, a faster return to the norm of the structure of the skin and its morphometric parameters is noted: reduction of the thickness of the epidermis and approaching the level of intact animals from the 15th day, restoration of the normal structure of the epidermis on the 21st day of the experiment, reduction of the density index fibroblasts to the value of the norm by the 28th day.

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