CYCLIC NUCLEOTIDE BREAKDOWN ENZYMES IN THE EYE TISSUES IN EXPERIMENTAL HERPETIC KERATITIS

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It is now known that the cyclase system is not only a powerful universal regulator of various physiological processes, but it also participates in the development of some pathological states [5, 6]. A decrease in the cAMP concentration in the organs and blood has been demonstrated in many diseases of widely different etiology [3, 4]. Investigation of the cyclic nucleotide level in the rabbit cornea in experimental herpetic keratitis revealed a decrease in the cAMP concentration and an increase in the cGMP concentration [2]. However, the mechanism of this disturbance in the cyclase system of the organ of vision is not clear.

To elucidate some aspects of this mechanism an attempt was made to study activity of enzymes breaking down cyclic nucleotides in the eye tissues of rabbits during the development of experimental herpetic keratitis.

EXPERIMENTAL METHOD

Chinchilla rabbits weighing 2-2.5 kg were used. Activity of cAMP phosphodiesterase (PDE) and of cGMP PDE in the cornea, sclera, and ciliary body of the eye was investigated. The tissues were isolated as described previously [1]. Activity of the enzymes was determined by a radioindicator method [7]. Four groups of animals were used: intact rabbits and three groups of rabbits with different stages of development of experimental keratitis (3, 10, and 17 days, respectively, after infection). The animals were infected by application of 0.2 ml of virus-containing material (HSV-II, strain MS with a virus titer of 10^{-7} CPD_{50}/0.2 ml) to the scarified cornea. A 1% solution of amethocaine was used for local anesthesia. For the calculations of tissue enzyme activity, protein was determined as in [8].

EXPERIMENTAL RESULTS

Levels of activity of both enzymes under normal conditions were established in the eye tissues chosen for study (Table 1). The highest PDE activity was observed in the ciliary body, the lowest in the sclera.

In the initial stage of development of herpetic keratitis (3rd day after infection) activity of cGMP PDE was reduced in all tissues studied, whereas activity of cAMP PDE, on the contrary, was increased.

On the 10th day of development of experimental herpetic keratitis (the height of the clinical picture of the disease) changes in activity of these enzymes observed on the 3rd day after infection were even more marked. In the period of the beginning of clinical recovery (17th day) activity of the enzymes showed a return toward the initial level.

Correlation between activity of the cyclic nucleotide breakdown enzymes and the clinical stage of development of experimental herpetic keratitis revealed by these experiments demonstrate involvement of the cyclase system in the pathogenesis of this disease.

The fact that statistically significant changes in PDE activity were found only in the cornea, in which the principal clinical and biochemical manifestations of herpetic keratitis are located, also is evidence of the pathogenetic role of changes in these enzymes in the de-

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TABLE 1. Activity of Enzymes of Cyclase System (in moles PI/g protein) in Eye Tissues in Herpetic Keratitis (M ± m, n = 5-15)

PDE	Tissue	Normal	Keratitis		
			3 days	10 days	17 days
cAMP	Cornea	3,2±0,1	3,7±0,1	4,0±0,1	3,8±0,1
	Sclera	2,4±0,2	2,7±0,1	2,9±0,1	2,4±0,1
	Ciliary body	3,4±0,1	3,6±0,1	4,0±0,1	3,2±0,1
cGMP	Cornea	3,2±0,2	2,5±0,1	2,3±0,1	2,8±0,2
	Sclera	2,5±0,2	2,4±0,4	2,2±0,1	2,4±0,2
	Ciliary body	3,5±0,3	3,0±0,2	2,9±0,2	3,2±0,3

velopment of herpetic keratitis. The character of the changes in PDE activity, which were not restored to their original level on the 17th day of the disease (Table 1), also is noteworthy. Frequent recurrences of this disease of the organ of vision may perhaps be attributable to this fact.

It can be concluded on the basis of the facts described above that in herpetic keratitis PDE inhibitors or substances increasing the cAMP concentration in the cells probably ought to be used. The optimal conditions for undertaking this type of correction and also the side effects which may perhaps arise under these circumstances require further investigation.

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