EFFECT OF L-CARNOSINE ON THE INTRAOCULAR PRESSURE

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KEY WORDS: carnosine; intraocular pressure; prostaglandin-induced hypertension.

L-carnosine (β-alanyl-L-histidine) [9] has a stabilizing action on the system of the sarcoplasmic reticulum [5]. Carnosine also has the property of reducing the permeability of blood vessels, thereby limiting the local inflammatory reaction, and also of neutralizing the action of biologically active substances such as bradykinin and histamine [10, 13].

No data could be found in the literature on the influence of carnosine on effects produced by prostaglandins (PG). On instillation into the conjunctival sac or by subconjunctival injection, PG of the E_1, E_2, and $F_{2\alpha}$ groups cause an acute rise of intraocular pressure (IOP) in laboratory animals; this prostaglandin-induced ocular hypertension arises as a result of increased formation of intraocular fluid. This is the result of disturbance of the permeability of the blood–aqueous humor barrier. The increase in microvascular permeability is greatest in the anterior part of the uveal tract of the eye [1, 4, 6, 14].

Since PG participate in the pathogenesis of acute increases in IOP in man in response to various influences on the eyes [7, 12], the aim of the investigation described below was to study the effect of carnosine on the ophthalmotonus of intact eyes and on the course of prostaglandin-induced ocular hypertension in rabbits.

EXPERIMENTAL METHOD

Experiments were carried out on 12 series of chinchilla rabbits weighing 2.8-3.5 kg; the animals' right eye was experimental, the left eye – control. IOP was measured by Maklakov's tonometer (weight 10 g) under local anesthesia (instillation of 0.5% amethocaine solution into the conjuctival sac). After measurement of the initial pressure, 0.2 ml of 10 mM carnosine was injected beneath the conjunctiva of the experiental (right) eye and 0.2 ml of physiological saline was injected beneath the conjunctiva of the control (left) eye. After injection of these solutions IOP was measured every 20 min for 1 h. The PG were dissolved in distilled water in the ratio of 1:2 and 4 drops (15-20 μg) were installed into both eyes 1 h after the subconjunctival injection of the above-mentioned solutions. IOP was measured in both eyes every 15 min for 90 min. Altogether 15 experiments were carried out on 12 rabbits. The carnosine was obtained from Fluka (Switzerland) and the PGE_2 from Upjohn (USA).

EXPERIMENTAL RESULTS

Subconjunctival injection of carnosine into the intact rabbit eye did not cause irritation of the anterior segment of the eye, did not affect the width of the pupil, and reduced IOP by 1.3-2.0 mm Hg compared with the ophthalmotonus of the control eye (Fig. 1). As Fig. 1 shows, IOP of the experimental eye was significantly lower than IOP of the control eye throughout the experiment (1 h). The greatest difference in the levels of IOP of the right and left eyes was observed 20 min after injection of carnosine. It will be seen that the ophthalmotonus of the experimental eye was lowered by 1.1 ± 0.1 mm Hg compared with the initial level, whereas that of the control eye was increased by 1.4 ± 0.1 mm Hg.

Instillation of PGE_2 solution into the conjunctival sac caused elevation of IOP in all experiments by 5-16 mm Hg. However, preliminary injection of carnosine led to a significant decrease in the rise of IOP induced by subsequent instillation of PG. As Table 1 shows, the difference between IOP in the experimental (preliminary injection of carnosine) and con-

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TABLE 1. Effect of Carnosine on Course of Prostaglandin-Induced Ocular Hypertension (in mm Hg; M ± m)

Time of testing, min	n	Experimental eye	Control eye	p
Initially	15	17,7±0,3 Carnosine	17,4±0,4 Physiological saline	>0,3
60	15	16,5±0,4 + PGE_2	17,8±0,5 + PGE_2	<0,05
15	15	23,4±0,9	27,9±1,4	<0,01
30	15	24,7±0,9	27,5±1,1	<0,05
45	15	22,5±0,8	25,9±1,0	<0,02
60	15	20,7±1,1	23,2±1,2	>0,2
75	15	19,3±0,8	22,1±1,0	>0,1
90	9	18,8±1,3	21,8±1,5	>0,2

Legend. n) Number of measurements.

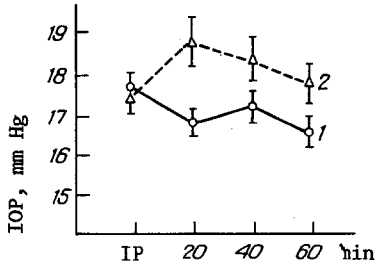

Fig. 1. Time course of change in IOP of rabbits after subconjunctival injection of carnosine (1) into one eye and of physiological saline (2) into other eye. IP) initial pressure.

trol (preliminary injection of physiological saline) eyes during 45 min after PGE_2 instillation was 2.8-4.5 mm Hg ($p < 0.02$).

In these experiments subconjunctival injection of carnosine thus led to a significant fall of IOP in the intact rabbit eye. Meanwhile subconjunctival injection of physiological saline caused elevation of ophthalmotonus – transient reactive hypertension, in whose pathogenesis a definite role is played by PG release. The absence of any corresponding changes in the experimental eye is indirect evidence of the antiprostaglandin effect of carnosine. This hypothesis was confirmed by direct experiments in which PG were injected into the eye.

The rapid fall of IOP of rabbits after injection of carnosine, while no change took place in the width of the pupil, differs from the slower fall of IOP after injection of sympathomimetics, namely phenylephrine and adrenalin, which also give an antiprostaglandin effect [3, 11], into the eye. The use of phenylephrine in clinical practice as an antiprostaglandin preparation to prevent ocular hypertension during laser coagulation of intraocular tumors has given positive results [2]. However, the mydriatic effect of phenylephrine restricts its use in other eye diseases and, in particular, in glaucoma, for dilatation of the pupil in glaucoma patients is a complicating factor. The fact that carnosine has an antiprostaglandin effect, but has no effect on the pupil, thus indicates that it may be used to reduce the level of IOP observed after laser therapy in glaucoma.

The effect of carnosine on the course of prostaglandin-induced ocular hypertension may perhaps be associated with its normalizing effect on permeability of the ocular microvessels and its ability to limit the local inflammatory reaction to injection of PG. Another possible explanation of the effect of carnosine may be its stabilizing action on membranes of ciliary epithelial cells which are involved in the formation of the aqueous humor.

Since PGE_2 formation in the aqueous humor, a subsequent rise of IOP, and the development of an inflammatory reaction are observed in clinical practice in connection with operations and the use of lasers [7, 8], the results of this investigation may provide an experimental basis for the clinical study of carnosine as a means of reducing the development of reactive hypertension associated with laser therpay and ophthalmic surgical operations.

LITERATURE CITED

1. A. Ya. Bunin, A. A. Yakovlev, L. A. Kondé, and N. A. Komlev, Vestn. Oftal'mol., No. 3, 24 (1975).
2. A. Ya. Bunin, A. F. Brovkina, V. N. Ermakova, and N. V. Makarskaya, Vestn. Oftal'mol., No. 3, 55 (1983).
3. V. N. Ermakova, Uch. Zap. Mosk. Nauchno-Issled. Inst. Glaznym Bolezn., No. 13, 208 (1967
4. V. N. Ermakova, Vestn. Oftal'mol., No. 1, 11 (1981).
5. S. E. Severin, A. A. Boldyrev, and A. M. Dupin, Vopr. Med. Khim., 30, No. 3, 32 (1984).
6. L. Z. Bito, R. R. Nichols, and R. A. Baroody, Exp. Eye Res., 34, No. 3, 325 (1982).
7. D. F. Cole and W. G. Unger, Exp. Eye Res., 17, No. 4, 357 (1973).
8. R. Gailitis, G. A. Peyman, J. Pulido, et al., Ophthal. Surg., 17, No. 8, 467 (1986).
9. V. S. Gulevitsch and S. Amiradzhibi, Ber. Dtsch. Chem. Ges., 33, 1902 (1900).
10. N. Kineshiro, J. Nihon. Univ. Sch. Dent., 13, No. 1, 1 (1971).
11. Y. Kitazawa and M. E. Langham, Nature, 219, 1376 (1968).
12. A. H. Neufeld and M. L. Sears, Exp. Eye Res., 17, 445 (1973).
13. S. Tsuneo and N. Kineshiro, J. Nihon Univ. Sch. Dent., 16, No. 1, 18 (1974).
14. M. B. Waitzman and C. D. King, Am. J. Physiol., 212, 329 (1967).

FUNCTIONAL CHANGES IN THE MYOCARDIUM AND MEDULLARY RETICULAR FORMATION IN CARDIOGENIC STRESS TREATED WITH LITHIUM NICOTINATE

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Acute ischemic heart damage causes pain and emotional-painful stress, which aggravates the course of infarction and may not only potentiate progression of ischemic damage, but may also cause damage to nonischemic areas of the myocardium [2].

The aim of this investigation was to study the character of damage to the myocardium and medullary reticular formation during experimental myocardial infarction (MI) and also to investigate the possibility of pharmacologic correction of the lesions with the aid of the atypical tranquilizer lithium nicotinate (Litonit), discovered at the N. I. Pirogov Odessa Medical Institute.

EXPERIMENTAL METHODS

Experiments were carried out on 35 dogs with experimental MI. Before induction of MI, the ECG of all the dogs was recorded in the usual 12 derivatiions on the 1st, 3rd, and 6th days. To judge immunologic reactivity, the passive hemagglutination test [11, 12] and the lymphocyte blast transformation test (LBTT) [13] were used. At the end of the investigations MI was produced surgically (by ligation of the descending branch of the left coronary artery). The operation was performed under intravenous pentobarbital anesthesia (5% solution

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