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CONTROL OF LYMPH DRAINAGE PATHWAYS OF THE EYE BY DALARGIN

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Methods of conservative treatment, aimed at stimulating the lymphatic component of the microcirulatory bed of the eye have not so far been used to treat pathological processes in ophthalmology, including in order to reduce the intraocular pressure (IO) in glaucoma, even though recently a new trend has developed, namely elinical lymphology, based on regulating the lymph drainage of the tissues [1-4].

The aim of this investigation was an experimental study of the effect of dalargin on the drainage channels of the eye under normal conditions and in experimental hypertension, used as a model of secondary glaucoma.

EXPERIMENTAL METHOD

Altogether three series of experiments were carried out on 82 eyes of chinchilla and white giant rabbits. Of this number, 52 rabbits acted as the control. In series I of the investigation, the aim of which was a morphological study of the drainage channels the anterior chamber of 16 eyes and the vitreous body (VB) of four eyes were perfused with ink containing gelatin, after subconjunctival (or electrophoretic) injection of dalargin (0.1%, 0.2-0.3 ml). The ink with gelatin was injected into the anterior chamber after preliminary paracentesis of the corena with a fine needle, and into VB by puncture of the sclera with a fine needle in the zone of the ciliary body, after preliminary paracentesis and release of the aqueous humor of the anterior chamber. Control experiments consisted of injecting ink into the anterior chamber (10 eyes) and into VB (10 eyes), followed by morphologic study of the drainage channels. One type of control in this series of investigations was subconjunctival injection of physiological saline (four eyes) followed by injection of India ink into the anterior chamber and into VB. The experiments of Series II were carried out to discover the effect of dalargin on the level of ophthalmotonus, in the presence of a normal IOP and in experimental ophthalmic hypertension. Before the experiments began, IOP was measured on a Maklakov tonometer with a weight of 10 g. Next, dalargin was injected subconjunctivally (0.1%, 0.2-0.3 ml), and 20-30 min later IOP was again measured (normal IOP 20-22 mm Hg), and control experiments were carried out on four eyes (Fig. 1b). After measurement of IOP a model of "secondary glaucoma" was created as follows: under general and local anesthesia (1 ml of morphine solution injected subcutaneously, 1 ml of procaine solution injected by the retrobulbar route) with a fine needle, sulfuric acid was applied to the zone of the limbus and to the perilimbic region, at a distance of 1 mm away from it around the whole perimeter of the cornea. The IOP was again measured after 20, 30, and 45 min. After creation of the experimental model of ophthalmic hypertension or "secondary glaucoma" due to the burn, dalargin was injected subconjunctivally (0.1%, 0.2-0.3 ml) into 10 eyes and IOP was again measured at various times (from 15 min to 3 h) after injection of the preparation (Fig. 1a).

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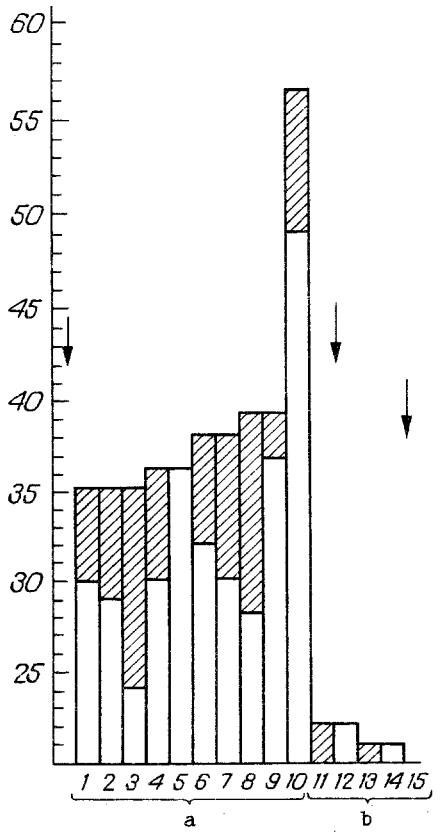

Fig. 1. Results of investigation of changes in IOP in response to injection of dalargin: a) hypotensive action of dalargin in experimental hypertension, b) absence of hypotensive effect of dalargin at normal IOP. Abscissa – columns – experiments on each of 14 eyes: 1-10) Group A (dalargin was injected after creation of model of ophthalmic hypertension), 11-14) Group B (dalargin administered when IOP was normal). Ordinate, IOP (in percent), where IOP of 25 mm Hg is taken as 100%. Shading indicates difference between levels of IOP after experiment before injection of dalargin, and after its injection.

EXPERIMENTAL RESULTS

In the experiments of Series I (control) results were obtained with respect to filling of the anterior drainage channels after injection of the marker into the anterior chamber, and on the presence of the marker in the posterior drainage channels after injection of the India ink into VB. The distribution of the India ink was perivascular, perineural, and intraseptal.

After injection of the marker into the anterior chamber and administration of dalargin subconjunctivally, the effect of filling with ink was observed in only three of 16 cases, and in 13 cases an unusual filling effect was obtained. This took the form of the appearance of dark round spots, not characteristic of the control experiments but reminiscent of extravasations around the limbus, the filling of vessels closely resembling in appearnace the lymphatic vessels of the capillary network, and the more frequent appearance of accompanying dark bands close to the vorticose and ciliary veins on the sclera.

After injection of india ink into VB the effect was unusual in all cases. Uncharacteristic dark areas appeared on the schlera and filling of the anterior drainage channels was found. Microscopic investigation in the experiments with dalargin revealed penetration of India ink from VB into the subciliary, suprachorioidal space. Just as in the control, vessels of the ciliary body and iris, vessels of the vascular membrane itself, and of the retina did not fill with ink in any single case, and the tissue of the membranes mentioned above likewise largely did not stain with ink. Intrascleral pathways filled with ink not only from

Fig. 2. Perivascular, intrascleral, and perineural distribution of India ink after injection of dalargin; micropreparation, 56 ×.

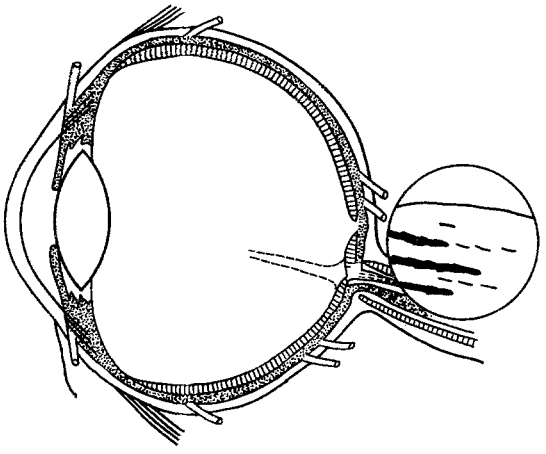

Fig. 3. Diagram showing dilatation of posterior drainage channels (perineural) under the influence of dalargin. 56 ×.

front, in the drainage zone, but also in the posterior part of the sclera. Microscpy showed that the "black bands" on the sclera were due, not to the diffuse spread of India ink in the scleral tissue, but to filling of the drainage channels – collectors and veins. The posterior perineural, perivascular, and intrascleral drainage channels were particularly distinctly dilated (by 3-4 times; Figs. 2 and 3).

Investigations of series II: with normal IOP (up to 25 mm Hg), 20-25 min after injection of dalargin it fell by 1-2 mm Hg or remained at its previous level (Fig. 1b: 11-14).

It will be clear from Fig. 1 that the increase in IOP after burning of the perilimbal zone with sulfuric acid amounted in five cases to 30-35 mm Hg, in four to 36-41 mm Hg, and in one to 54 mm Hg. After injection of dalargin, between 30 min and 2 h IOP fell from 2 to 4 mm Hg in two cases and from 5 to 10 mm Hg in seven cases. Consequently, the IOP level fell in nine of 10 cases after burning, accompanied by ophthalmic hypertension, as a result of administration of dalargin.

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AUTORADIOGRAPHIC AND IMMUNOHISTOCHEMICAL ANALYSIS OF ^{3}H-MELATONIN DISTRIBUTION IN ENDOCRINE AND NONENDOCRINE ORGANS

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In recent years particular attention has been paid by research workers to malatonin (5-methoxy-N-acetyltryptamine), a hormone of the APUD system [4]. It has been shown that the pineal gland is not the only source of melatonin formation in the body. The use of biological methods, radioimmunoassay, and thin-layer chromatography has shown that after removal of the pineal gland melatonin continues to appear in the plasma and uring of experimental animals [16]. The 24-hourly excretion of melatonin in rats after pinealectomy is about 20% of the control value. The use of methods of immunohistochemistry, with highly specific antibodies to melatonin, has established the identity of the melatonin-containing cells in certain regions of the brain, the retina, the gastrointestinal tract, and other organs [3, 4, 6, 7, 8]. Melatonin has a broad spectrum of physiological action [1, 4, 10, 13] and it is regarded nowadays as a universal regulator of biological rhythms. We know that exogenous methoxyindoles have a short half-life and that they are metabolized to a very considerable degree in the liver [11, 15, 17, 18]. Unmetabolized melatonin binds with plasma proteins, with albumin perhaps [11]. The physiological importance of binding of circulating melatonin with proteins has not yet been established. An hour after injection of tritium-labeled melatonin the concentration of the radioactive preparation in the pineal gland is 40 times higher, whereas in endocrine organs, peripheral nerves, and sympathetic ganglia, it is 3-5 times higher than in blood plasma [18]. Accumulation of radioactive label has been observed in the liver, kidneys, small intestine, and adrenals. Data indicating that tissues containg endogenous melatonin have high affinity for injected exogenous melatonin are of undoubted interest [9, 12, 18]. These facts are evidence of the urgent importance of the study of melatonin and the clarification of some problems connected with the transport, storage, and pathways of utilization of exogenous melatonin in the body.

This paper gives details of an autoradiographic and immunohistochemical investigation of the distribution of ^{3}H-melatonin in the early period after its administration, in certain endocrine and nonendocrine organs.

EXPERIMENTAL METHOD

Experiments were carried out on male BDF_1 mice. ^{3}H-Melatonin was injected intraperitoneally in a dose of 185 kBq/g. The animals were killed by decapitation 5 min and 1 and 3 h after injection of the labeled compound. The adrenals, and pieces of the duodenum, pancreas, and spleen were fixed in buffered Bouin's fluid and embedded in paraffin wax. Material for autoradiography was prepared and photographed by the standard method, using type "M" photographic emulsion. Melanotonin-containing were identified by the indirect immuno-

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