PEROXIDATION DAMAGE TO THE LENS AS A POSSIBLE CAUSE OF TRAUMATIC CATARACT

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The writers suggested previously that the primary cause of opacity of the lens during the development of senile cataract is lipid peroxidation (LPO) [1, 2]. Activation of LPO leads to oxidation of thiol compounds in the lens with the formation of light-scattering high-molecular-weight protein aggregates in it [3]. The question arises, may LPO also be the cause of other types of cataract, including traumatic? There is some indirect evidence in support of this hypothesis. For instance, penetration of foreign bodies containing copper and iron into the eye induces the development of opacity of the lens, fibrosis of the vitreous body, injury to the retina, and chronic inflammation of the uveal tract [7]. In all these cases the presence of free metallic ions of variable valency was observed in the aqueous and vitreous [8]. Experimental intravitrial injection of Cu^{++} ions leads to similar changes in the anterior part of the eye, manifested as opacity of the lens and the development of inflammation [6]. These metals with variable valence can induce the generation of active forms of oxygen and lipid peroxides *in vitro* [4]. In some types of trauma to the eye disturbance of permeability of the blood-eye barrier also is observed. This phenomenon is accompanied by acute ocular hypertension, due to the release of biologically acitve substances, hyperemia of the iris, and escape of protein and cells into the chamber fluid of the eye. Hypertension is then followed by a fall of the intraocular pressure. The reactions listed above are similar to that observed in response to injection of exogenous arachidonic or docosahexaenoic acids into the vitreous, which leads to activation of LPO and is accompanied by cataract development [5, 7]. The reaction observed under these circumstances is analogous to that to ocular trauma. These facts suggest that oxidation of polyunsaturated fatty acids may be a key stage in the acute response of the eye to trauma, and may lead to opacity of the lens.

The object of this investigation was to study activity of LPO in the lens tissue and aqueous humor of animals and man during the development of traumatic cataract.

EXPERIMENTAL METHOD

A model of traumatic cataract was reproduced in 20 male chinchilla rabbits (on 40 eyes) weighing on average 2.5 kg. The rabbits were anesthetized by injection of callipsol into the auricular vein in a dose of 30 mg/kg body weight. The development of traumatic cataract was induced by making a linear incision in the anterior capsule of the lens by means of a Sato's microscalpel with guard. The knife was introduced into the anterior chamber through the limbus; in the anterior chamber the knife was moved so that it did not touch the iris. Draining of the anterior chamber did not take place at the time of wounding. A 1% solution of atropine was instilled 3 times a day into the eyes of all the animals for 1 week before the beginning of the experiment, and the instillations continued throughout the experiment. Every 24 h the eyes of all the animals were examined by biophotomicroscopy, using an Opton SL-30 photoslit lamp. The degree of opacity of the lens was assessed objectively by quantitative morphometric analysis. The areas of zones of opacity of the lens in pictures on slides were measured on a Leitz TAS television analyzer (West Germany). The boundary between regions of opacity and transparent regions was drawn along the line of the highest gradient of optical density (OD) values on the image of the lens. Light-scattering zones of opacity were represented as pale areas (transparent areas) against a dark background in the region of the pupil with maximal mydriasis. At the end of the experiment (on average 2 weeks after injury to the eye) the an-

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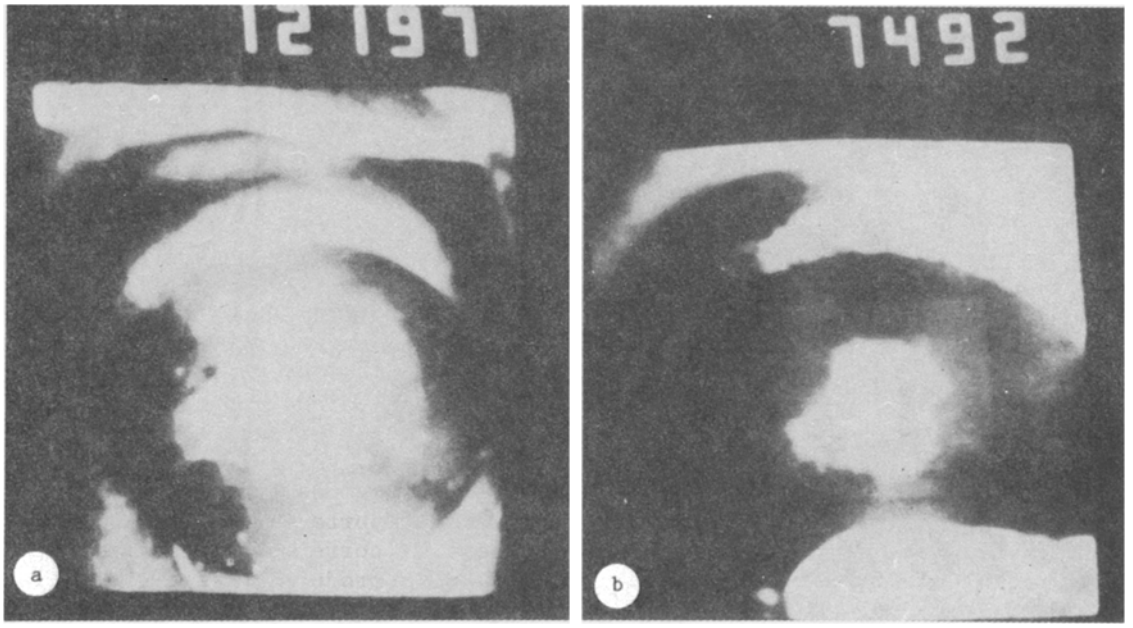

Fig. 1. Quantitative morphometric analysis of opacity of the rabbit lens in traumatic cataract. A, B) 1 and 7 days, respectively, after wounding. Photograph taken from television image analyzer. Magnification 10. Pupil maximally dilated. Zone of opacity of lens marked out by a mask. Scale of optical densities on left. Numbers indicate area of zone of opacity (in relative units).

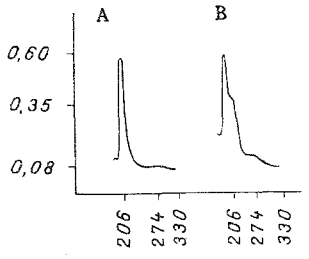

Fig. 2

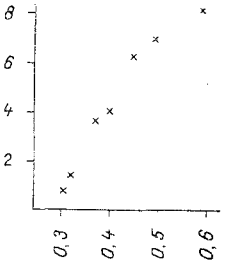

Fig. 3

Fig. 2. Characteristic UV absorption spectra of lipid extract from rabbit lenses in methanol—heptane system (5:1). Abscissa, wavelength (in nm); ordinate, optical density (in units). A) Transparent lens, B) traumatic cataract with opacity of lens localized in subcapsular layers and anterior cortex of the lens. Maximum of absorption in 230 nm region indicates accumulation of initial LPO products.

Fig. 3. Dependence of area of opacity in anterior cortical layers of rabbit lens in experimental traumatic cataract on degree of accumulation of primary LPO products in its tissue. Abscissa, concentration of LPO products (in relative units); ordinate, area of opacity (in relative units).

imals were killed. Lenses and aqueous humor were subjected to biochemical tests. In a separate series of experiments lenses taken from patients during operations of intracapsular cryoextraction of a traumatic cataract were studied. Altogether 43 human lenses with initial (25 cases) and total (18 cases) opacity as a result of the development of traumatic cataract, and also seven samples of aqueous humor obtained from the same eyes in the course of the operation, were studied. The control in this case consisted of transparent lenses and aqueous from donors' eyes (10 cases), supplied from a bank for corneal grafting. Concentrations of LPO products in lipid extracts from the lens and aqueous, namely diene and triene conjugates, ketodienes, and fluorescent LPO products, were determined by the method described previously [2].

EXPERIMENTAL RESULTS

In the model of traumatic cataract, 2-5 h after injury to the lens a delicate effusion of milky white fluid, localized in the zone of injury to the lens, was observed in the anterior chamber of all the eyes studied. The most intensive local opacity of the lens was observed actually in the region of the incision in the lens capsule. Along the periphery from the zone of injury, the opacity of the lens was less marked and was limited to its central part. Despite the fact that wounding of the lens was not accompanied by loss of lens material, the anterior subcapsular opacity of the lens developed very quickly in all eyes. However, total opacity of the lens was not observed. The character and size of the opacity differed somewhat in different experiments, but usually the dimensions of the opacity decreased with time, though they remained considerable for 10 weeks after wounding (Fig. 1). The development of traumatic cataract in the rabbits, during which, besides marked subcapsular opacity, a considerable area of diffuse opacity of the anterior cortex of the lens (occupying mainly its central part) also was observed, was accompanied by accumulation of diene and triene conjugates, and also of ketodienes in the lens and aqueous (Fig. 2). The concentration of primary LPO products in the aqueous exceeded their level in the opaque lens of the same eye. This fact is evidence that the primary change takes place in the composition of the aqueous during the development of traumatic cataract. Activation of LPO in the lens tissue may be an important pathogenetic stage in the development of its opacity. This is shown by the strong correlation existing between the degree of opacity of the lens and the concentration of LPO product in its tissue (Fig. 3). Investigation of LPO products in the lens and aqueous of patients with traumatic cataract showed that if initial opacities of the lens are present, primary LPO products predominate in them and in the aqueous. In cases when total opacity of the lens develops, fluorescent end-products of free-radical oxidation of lipids accumulate in its tissue.

This fact, together with the data described above, indicates the universal role of oxidative damage to the lens tissue in the genesis of cataract. The universal character of activation of LPO during the development of cataract suggests that the model of traumatic cataract which we used was adequate. As regards the mechanisms of development of opacity of the lens in traumatic cataract, it is worth noting that the opacity is formed primarily in the region of direct contact between the zone of injury to the lens and the aqueous humor. Cataract development is accompanied in this case by osmotic swelling of the lens fibers. Accumulation of lipid peroxides and of active forms of oxygen (H_2O_2 in particular) in the aqueous may disturb membrane permeability of the cellular fibers of the lens, thereby inhibiting activity of membrane-bound enzymes (Na,K-ATPase for example), and may thus lead directly to the changes noted above.

The level of lipid peroxides in the aqueous and lens may thus be an important regulator of the development of traumatic cataract.

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