

Beneficial effects of thioredoxin administration in experimental retinal degeneration

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Investigative Ophthalmology & Visual Science July 2018, Vol.59, 996

Abstract

Purpose : The term Retinitis Pigmentosa (RP) describes a large group of heterogeneous and hereditary retinopathies characterized by a progressive and quick rod degeneration followed of a later cone degeneration. RP has been related to oxidative stress, a process that can induce autophagy. In addition, RP can also induce gliosis and alterations in retinal microglia. To date, the role of autophagy and inflammation in this disease is still contradictory. The family of thioredoxins (Trx) includes more than 10 proteins that constitute one of the most important regulators of the cellular redox state and also modulates inflammation and microglia activation. The purpose of this work was to study if thioredoxin administration to rd1 mice, an experimental model of RP, is able to induce modifications in several markers of retinal autophagy and inflammation.

Methods : Animals were treated in accordance to the ARVO statement for the use of animals in ophthalmic and vision research. Rd1 and control mice were used in this study. In the rd1 retina, it is estimated that the peak of rod death occurs around post-natal day 11, and cones degeneration is evident around the third postnatal week. For this reason, mice were sacrificed at postnatal days 11, 17 and 28. The first two groups of mice were treated twice with Trx (3 mg/kg) and the third group received six doses of Trx. Retinas were dissected and cell death and several autophagy (LC3, Atg5 and Atg7) and inflammation (GFAP and Iba-1 staining) markers were studied by western blot and immunohistochemistry.

Results : Trx decreased retinal cell death, mainly at postnatal day 17. Though rd1 retinas showed alterations in Atg5 and Atg7 expression compared to control mice, Trx was not able to modulate these changes. Trx decreased retinal gliosis observed in rd1 mice; this effect was transient and could only be observed at postnatal day 11. Trx was also able to decrease the number of Iba-1 positive cells in rd1 mice, however, this effect was also transient and was not observed in 28 postnatal mice.

Conclusions : Herein, we demonstrate the possible beneficial effects of Trx in retinal degenerations, though these effects were not permanent. Furthermore, our results show a different treatment response between autophagy and inflammation suggesting different biological mechanism. To summarize, Trx could be used to ameliorate retinal inflammation boosting the effects of other treatments.

This is an abstract that was submitted for the 2018 ARVO Annual Meeting, held in Honolulu, Hawaii, April 29 - May 3, 2018.



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