COENZYME Q10 PREVENTS RETINAL DAMAGE CAUSED BY HIGH INTRAOCULAR PRESSURE (IOP)-INDUCED TRANSIENT ISCHEMIA IN RAT

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Coenzyme Q10 (CoQ10), an essential cofactor of the electron transport chain, has been reported to afford neuroprotection in neurodegenerative disorders (Matthews et al., 1998). We used an animal model of retinal ganglion cell (RGC) death induced by acute rise of intraocular pressure (IOP, Osborne et al., 2004) to gain more insight in the neuroprotective profile of CoQ10. Anaesthetized (urethane 1500 mg/kg i.p.) Sprague-Dawley rats, bearing a retinal microdialysis probe to measure extracellular glutamate (Richards et al., 2000), have been used. For test studies, animals received (30 min before ischemia) intravitreal administration (via the microdialysis probe; 2 µl/min rate, 5 min duration of treatment in all instance) of 1) CoQ10 (solution of CoQ10 0.1% + vitamin E 0.5%), 2) vitamin E (Vit-E, 0.5%) or 3) vehicle (saline + EDTA 0.1%). For neuropathological studies, animals have been treated topically also with CoQ10 , Vit-E or vehicle; in all instance, rats received eye application of 50µl of solution every 15 min during the 1 hour before and after ischemia had been induced. The number of RGC was counted as previously reported (Nucci et al., 2005). Topical treatment with Vit-E and CoQ10 significantly (p <0.001) reduce the percentage loss of RGC to 17.8 %, n=6 and 10.3%, n=7, respectively, as compared to 25.7 % observed in untreated ischemic retinas. DNA fragmentation is detected by TUNEL technique in RGC layer (5.3±0.9, n=3), inner nuclear layer (INL, 19.1±1.1, n=3); outer nuclear layer (ONL, 14.0±1.9, n=3). Vit-E (n=6) and CoQ10 (n=5) prevent DNA fragmentation in RGC (1.0±0.1, and 0.7±0.3, respectively), INL (5.6±0.8, and 3.1±0.5) and ONL (2.9±0.4 and 1.6±0.2). Microdialysis studies show that high IOP increases intraretinal glutamate levels sensitive to the reversal of CoQ10. The increase in glutamate (199.3± 43.7% vs. pre-ischemia levels set to 100%; pre-ischemia glutamate levels= 0.307±0.044 µM, n=6) peaks at 130 min after beginning of reperfusion. Focal administration, via the probe of CoQ10 (n=3, administered 30 min before ischemia), significantly reduces glutamate peak increase (26.06±12.1% vs 130 min reperfusion levels, p<0.001) whereas vehicle or Vit-E were without significant effect [141.4±56.5, (n=3) and 123.7±31.6 (n=5), respectively]. The present data demonstrate that Vit-E and CoQ10 are able to reduce the increase of glutamate levels induced in the retina by high IOP though CoQ10 only achieves statistical significance. This effect may contribute to the neuroprotection afforded by topical application of CoQ10 and Vit-E in rats undergone ischemia/reperfusion.

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