iovs investigative ophthalmology & visual science
an ARVO journal

July 2019
Volume 60, Issue 9

‹ ISSUE ›

OPEN ACCESS

ARVO Annual Meeting Abstract | July 2019

Recovery of retinal oxygenation after MEMS implant activation

Juan Carlos Martinez; Nicholas Scianmarello; Colin A. Cook; Alejandra Gonzalez-Calle; Yu-Chong Tai; Mark S Humayun

Author Affiliations & Notes

Investigative Ophthalmology & Visual Science July 2019, Vol.60, 3344. doi:

Abstract

Purpose :Retinal ischemia due to diabetic retinopathy or retinal vascular occlusions is the leading cause of blindness worldwide. Although, the underlying pathophysiology from each condition is different, the common end results are: inner retinal hypoxia and ischemia. Changes associated with retinal hypoxia include the simultaneous activation of different pathways including inflammatory, aerobic and anaerobic

metabolic response. Supplementing intravitreal oxygen has been demonstrated as a novel option in preliminary reports. Our implantable MEMS oxygenator drivesoxygen from the sub-conjunctival space to the proximity of the inner retina. The main objective of this study is to determine the efficacy of the oxygenation therapy in an ischemic animal model.

Methods : Nine eyes from six pigmented rabbits were included, split evenly between either healthy, implant-treated or non-treated groups. Retinal vein occlusion (RVO) was created in all animals from treated and non-treated groups 3 days prior to surgical implantation and activation of the oxygenator. Continuous measurements of pO_2 levels were performed next to the diffuser and retinal vessels using an oxygen probe controlled by a micromanipulator and monitored under indirect ophthalmoscopy. Eyes were then enucleated and the retina was peeled off and cryogenically preserved in liquid nitrogen for subsequent analysis of protein expression.

Results : RVO was confirmed in all animals immediately after the procedure and remained occluded over the experiment. Oxygenator devices were successfully implanted without complications. In the treated group, oxygen levels increased progressively after a couple of minutes of activation and remained over 15 mmHg and 100 mmHg respectively (Figure 1A). For the non-treated group, pO_2levels did not increase at the retina or nearby the device (below 5mmHg). Changes among protein expression and ratio (upregulation on NFkB and PDH; down-regulation of HIF1a, NFkB/IKKa ratio and P-PDH/PDH ratio) were observed in the treated group (Figure 1B-C).

Conclusions : The MEMS oxygenator device can be safely implanted into the eye. This study supports the feasibility of intravitreal oxygen delivery for treatment of ischemic retinal diseases through inflammatory response modulation. Future experiments will evaluate long-term efficacy.

This abstract was presented at the 2019 ARVO Annual Meeting, held in

Vancouver, Canada, April 28 - May 2, 2019.

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