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MEETING ABSTRACT

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Effect of orally administered, low-dose dronabinol on ocular hemodynamics in healthy subjects

Theresa LINDNER¹, Nikolaus HOMMER¹, Martin KALLAB¹, Stephan SZEGEDI¹, Stefan PUCHNER^{1,2}, Kristina STJEPANEK¹, Martin BAUER¹, René M. WERKMEISTER², Leopold SCHMETTERER^{1,2,3,4,5,6,7}, Marihan ABENSPERG-TRAUN⁸, Gerhard GARHÖFER¹, Doreen SCHMIDL^{1,*}

¹Department of Clinical Pharmacology, Medical University of Vienna, Austria; ²Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria; ³Singapore Eye Research Institute, Singapore National Eye Centre, Singapore; ⁴Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; ⁵Ophthalmology and Visual Sciences Academic Clinical Program, Duke-NUS Medical School, Singapore; ⁶SERI-NTU Advanced Ocular Engineering (STANCE), Singapore; ⁷Institute of Molecular and Clinical Ophthalmology, Basel, Switzerland; ⁸Department of Child and Adolescent Psychiatry, Medical University of Vienna, Austria

Background: It is hypothesized that besides its potential of lowering intraocular pressure (IOP) and neuroprotective effects, tetrahydrocannabinol (THC) may also improve ocular hemodynamics. In this study we investigated whether single orally administered dronabinol, a synthetic THC derivate, alters optic nerve head blood flow (ONHBF) and its autoregulation in healthy subjects. In addition, we investigated the effect of dronabinol on retinal blood flow and retinal oxygen metabolism.

Methods: The study was conducted in a randomized, double-masked, placebo-controlled, two-way crossover design. Measurements were taken on two study days before and 1 hour after drug intake. Participants received capsules containing 5 mg dronabinol on one study day and placebo on the other. ONHBF was assessed at rest and during isometric exercise using laser Doppler flowmetry. The isometric exercise was done for 6 minutes to increase mean arterial blood pressure (MAP). Ocular perfusion pressure (OPP) was calculated as $2/3 \times \text{MAP} - \text{IOP}$. We used a custom-built Doppler optical coherence tomography system to quantify total retinal blood flow (TRBF) and a commercially available Dynamic Vessel Analyzer to measure oxygen saturation of major retinal vessels. Based on these values, retinal oxygen extraction was calculated.

Results: A total of 12 female and 12 male healthy subjects (mean 26 ± 4 years) finished the study according to the protocol. The intake of dronabinol or placebo had no effect on IOP, MAP or OPP. During the study days, dronabinol was well tolerated and no cannabinoid-related psychoactive effects were reported. Dronabinol induced a significant increase in ONHBF at rest by $9.5 \pm 8.1\%$ ($p < 0.001$). Isometric exercise did not alter the ONHBF autoregulatory response. As for retinal blood flow, dronabinol resulted in a significant increase in TRBF from 38.9 ± 6.1 to 40.7 ± 6.7 $\mu\text{l}/\text{min}$ ($p < 0.001$), which was accompanied by a significant increase in retinal venous oxygen content (from 0.129 ± 0.008 to 0.132 ± 0.009 $\text{ml O}_2/\text{ml}$; $p = 0.02$). Retinal oxygen extraction remained stable (2.2 ± 0.4 vs. 2.2 ± 0.4 $\mu\text{l O}_2/\text{min}$; $p = 0.29$), as no change in retinal arterial oxygen content occurred ($p = 0.12$). Placebo had no effect on retinal arterial or venous oxygen content, retinal oxygen extraction, or TRBF ($p > 0.10$ each).

Discussion: Our data show that low-dose dronabinol increases ONHBF and TRBF in healthy subjects without altering the autoregulatory response of ONHBF or causing psychoactive side effects. Retinal oxygen extraction, IOP and OPP remained unchanged. Further studies are needed to investigate whether this drug may be a candidate for improving perfusion in patients with ocular vascular disease or glaucoma.

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Keywords: dronabinol – cannabinoids – hemodynamics – optic nerve head blood flow – retinal oxygen extraction – retinal blood flow – laser Doppler flowmetry – Doppler optical coherence tomography – randomized controlled clinical trial

*Corresponding author e-mail: doreen.schmidl@meduniwien.ac.at