Is there a Risk of Blindness With CBD?

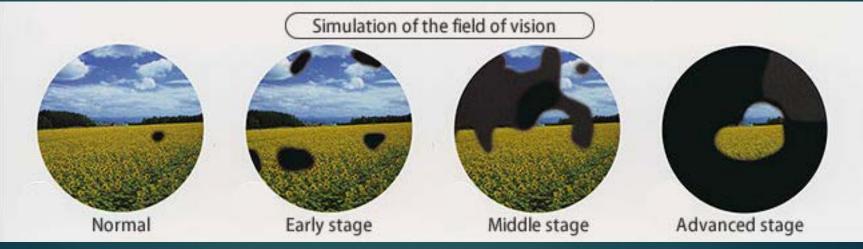
DR. DENISE A. VALENTI CEO/PRESIDENT IMMAD, LLC impairment measurement marijuana and driving OPTOMETRIST RESIDENCY TRAINED IN VISION LOSS, PARTIAL SIGHT

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Studies Show Increased Pressure In Eye With CBD

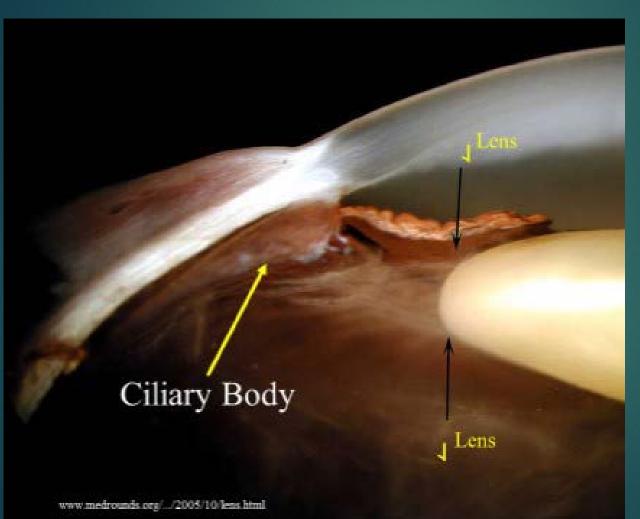


- While we often hear of marijuana being able to lower the pressure in the eye; this is only with THC, the psychoactive cannabinoid in marijuana.
- We never hear about CBD and its increasing of the intraocular pressure of the eye (IOP) and risk of glaucoma.
- The same study often cited to justify having glaucoma as one of the diseases allowed for the use of medicinal marijuana (THC) showed CBD spikes the pressure in the eye.



Cannabinoid Receptors In Human Ciliary Muscle of Eye





Ciliary muscle involved in the flow in and out off fluid, influencing pressure.

It is probable that THC and CBD act on ciliary body cannabinoid receptors.

But in an opposite manner for each.

2008 Human Study



Six participants with glaucoma

- ► 5 mg Delta-9-THC
- 20 mg CBD
- 40 mg CBD
- ▶ placebo

Lowered IOP No effect Raised IOP No effect



While effect of THC often cited, rarely hear the concerns with even moderate doses of CBD.

<u>J Glaucoma.</u> 2006 Oct;15(5):349-53. **Effect of sublingual application of cannabinoids on intraocular pressure: a pilot study.** <u>Tomida I¹, Azuara-Blanco A, House H, Flint M, Pertwee RG, Robson PJ</u>.S

Doses CBD That May Induce Risk of Vision Loss



- MS Cannabis plant extracts containing 2.5-120 milligrams of a THC-CBD combination have been taken by mouth daily for 2-15 weeks.
- Schizophrenia, 40-1,280 milligrams of CBD has been taken by mouth daily for up to four weeks.

http://www.mayoclinic.org/drugs-supplements/marijuana/dosing/hrb-20059701

- Epilepsy 200-300 mg of CBD by mouth daily for up to 4.5 months.
- Sleep disorders 40-160 mg CBD by mouth.

https://cbdoilreview.org/cbd-cannabidiol/cbd-dosage/

May not be necessary to stop CBD treatment, just treat the induced glaucoma.

CBD Studies of IOP Elevation

Miller, Leishman, Bradshaw and Straiker: Investigative Ophthalmology & Visual Science December 2018, Vol.59, 5904-5911. doi:10.1167/iovs.18-24838

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- Straiker and Miller: ARVO 2018
- Miller and Straiker: ICRS 2018
- CBD caused an elevation in IOP in a mouse model.



Blindness From Increased IOP Is Preventable



- Let's not create a new generation of children and adults with preventable vision loss.
- Before approving any further use of CBD, do the appropriate studies to determine the safety for the eye.
- No one anywhere has done the appropriate assessment in a human model to determine if CBD is safe for the visual system.
- No indication it was ever looked at prior to approving a CBD product for treatment of mult-ihandicapped children even though the company and FDA were aware of vision risk.
- Patients would not need to go off CBD, just treat the glaucoma.

Studies for this are not complex, time consuming or costly......

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Introduction: It is critical to have a comprehensive understanding of the health impact of cannabinoids on visual health. Twenty-Nine states allow the use of medicinal marijuana containing tetrahydrocannabinol. THC for the treatment of disease. Both THC and cannabidiol CBD have been shown to impact ocular structures, with THC lowering the pressure of the eye and CBD spiking the pressure of the eve in humans (Tomida) and rodent models (Straiker). Use of THC to Lower Eye Pressure: The dosing with THC required to have continuous lowering of eye pressure must occur every four hours regardless of the potency of the product. The average cost for conventional treatment of glaucoma is around \$60.00. Using a cost for marijuana of \$15 per gram and a marijuana cigarette being about .5 grams and in order to keep IOP appropriately low a patient would require three cigarettes per day. This makes the monthly expense of marijuana treatment for glaucoma at \$690 (Novak).

History of Glauoma Treatment With THC: A patient who had progressive, blinding, severe glaucoma won legal battles to have the right to use THC in the form of marijuana to treat his eye disease. Beginning in 1976 this patient was receiving marijuana from the National Institutes of Health. At that time there were few tools to diagnose early glaucoma and few options for treatment. Examples are shown below. The pharmaceutical interventions had discomforting side effects with limited efficacy. Surgery to increase drainage and lower the pressure of the eye was primitive compared to today's techniques and there was a substantial risk of vision loss. So, in the year 1976, THC to treat glaucoma could be considered a reasonable alternative. Eventually an acceptable drug that had been patented in 1968 would come onto the market in 1978. This drug, timolol, proved to be one of the first drugs that had efficacy with minimal disconcerting side effects. A more modern product, biamatoprost has been shown to be significantly more effective than endogenous cannabinoids in acting on the drainage structure, ciliary body and effectively treats glaucoma (Ramano). With more modern pharmaceutical and surgical options, there is no reason to use marijuana as a treatment to lower the pressure of the eye in glaucoma.

Use of CBD Without Ever Studying Impact on IOP: The US Food and Drug Administration has approved Epidiolex, a prescription product containing CBD in oral form. It is approved for the treatment of seizures associated with two rare and severe forms of epilepsy. Lennox-Gastaut syndrome and Dravet syndrome, in patients two years of age and older. A starting dose is suggested 2.5 mg/kg twice daily with a maintenance dose up to 10 mg/kg twice daily. This comes out to be between 250 and 998 mg for a person weighing 110 pounds. There have been no risk or toxicity studies looking at IOP related to CBD use.



CBD Elevates Eye Pressure

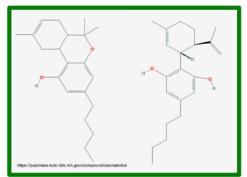
THC Action Likely At Ciliary

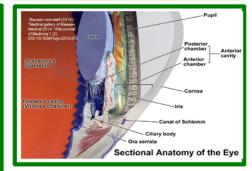
A dose of 40 mg CBD sublingual was shown to transiently elevate IOP in six humans (Tomida).

Normal mice when dosed with topical CBD showed an elevation of IOP. However, CBD lowered IOP in a genetic mouse model absent the cannabinoid receptors. The same research group found that there was gender difference related to THC, with females showing one/half the response of lowering IOP (Straiker). The mechanism for IOP change is not known but is thought to have action on ciliary.



THC and CBD Structures





Cannabis & IOP Studies

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Straiker A and Miller S, Delta 9-THC and CBD differentially regulate intraocular pressure. Invest. Ophthalmol. Vis. Sci.. 2018; 59(9):6040

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