

Medical Marijuana for Glaucoma Therapy

Despite the drug's potential IOP-lowering capabilities, toxicity to the ocular surface is a major concern.

BY KATHERINE SHEN, OD

Over the past year, media coverage and national awareness of the legalization of marijuana for medical and recreational use have increased. Twenty-one states plus Washington, DC, have enacted laws that allow the use of medical marijuana with a doctor's recommendation, and two of those states—Colorado and Washington—have legalized marijuana for recreational use.¹ It is therefore important that eye care providers learn about medical marijuana for glaucoma therapy. This article reviews some of marijuana's effects on the eye.

BACKGROUND

Marijuana (cannabis) is the drug most frequently used illicitly today. It is also one of the oldest drugs used for medical purposes. The drug's therapeutic use was first recorded in a classical Chinese medical book in 2737 BC,² and European doctors introduced marijuana to Western medicine in the 19th century. The cannabis plant has more than 480 chemical constituents and 60 compounds that only contain carbon, hydrogen, and oxygen known as cannabinoids.³ The main psychoactive constituent of cannabis is the cannabinoid delta-9-tetrahydrocannabinol (THC). In 1988, a specific protein receptor (CB1) for THC was discovered on mouse nerve cells. CB1 mediates most of the central nervous system (such as the brain and spinal cord) and certain peripheral tissues, including the lungs, heart, urogenital and gastrointestinal tracts, and the eye.⁴ In 1993, a second receptor (CB2) for THC was identified in cells and tissues associated with the immune system such as the tonsils, spleen, and leucocytes.⁴

INTRAOCULAR PRESSURE LOWERING

According to the American Glaucoma Society, the mainstay of treatment for glaucoma patients is to lower

“Different cannabinoid compounds have reduced IOP through oral, intravenous, sublingual, and topical administration pathways.”

intraocular pressure (IOP).⁵ Although, historically, three modalities (medication, laser treatment, and surgery) have been used to decrease IOP, it has been demonstrated that smoking marijuana lowers the IOP of both healthy and glaucomatous eyes.⁶

In 1971, Heplar and Frank reported that smoking marijuana reduced IOP by 25% to 30% in 11 youthful subjects.⁶ The duration of action after smoking the drug was 3 to 4 hours, and a dose-response relationship was present. Conjunctival hyperemia, reduced tear production, and a change in pupillary size were also observed. Acute systemic effects included the reduction of systemic blood pressure and tachycardia. Psychotropic effects included euphoria or dysphoria, disruption of short-term memory, cognitive impairment, a distorted sense of time, reduced coordination, and sleepiness. Dawson et al reported an equal reduction in IOP between nonusers and long-term (10 years or more) users of marijuana.⁷

Different cannabinoid compounds have reduced IOP through oral, intravenous, sublingual, and topical administration pathways.⁸ Although the exact mechanism by which cannabinoids regulate IOP is unknown, CB1 and CB2 have been identified in ocular tissues, with CB1 as the main cannabinoid receptor at the ocu-

DISCUSSING MEDICAL MARIJUANA WITH GLAUCOMA PATIENTS

By David Diaz, MD

With the adoption of medical marijuana laws by many states, glaucoma patients are naturally interested in whether marijuana can help preserve their vision. The conversation between the physician and patient can be tricky. After decades of political and cultural strife over the drug's use, deeply entrenched notions confuse the issue. At one extreme, marijuana is a nefarious "gateway drug." At the other, it is a "natural remedy" that is completely safe and useful for almost any malady.

Many glaucoma patients desperately desire new treatments, because they fear they are going blind. My goal is to discuss medical marijuana truthfully, succinctly, and in a manner that strengthens trust between the doctor and patient. I welcome the inquiry and respond, "I'm glad you asked. Many people are wondering whether marijuana might be helpful." I quickly describe the mechanics of glaucoma and explain that marijuana can lower eye pressure. Next, I give my professional opinion: "Unfortunately, in its current state, smoking marijuana is not useful for the vast majority of glaucoma patients. The pressure drop does not last long enough, and smoking marijuana has dangerous effects throughout the body." Finally, I offer hope: "The drug is being researched and has great potential. It is already used as a pill for anorexia and nausea in diseases like cancer. We may soon have a marijuana-based medicine for glaucoma, but we do not have it yet."

I ask patients whether they are already using marijuana, and if so, I ask them to avoid the practice in the hours before appointments, as it will confuse my evaluation of medical or surgical efficacy. When further discussion seems useful, I elaborate on marijuana's potential and why smoking it is a poor choice for glaucoma therapy:

- Inhaled tetrahydrocannabinol (THC) lowers IOP from 25% to 33% in two-thirds of subjects, an effect comparable to the best glaucoma eye drops. Clearly, THC may someday be a powerful treatment option for glaucoma.¹
- The IOP effect peaks at 2 hours and lasts only 3 to 4 hours, meaning continuous IOP control would require smoking marijuana six or more times daily.¹
- The psychoactive effects of continuous marijuana consumption would impair normal function.
- Both the volume of marijuana and the concentration of THC within cigarettes vary widely. As a result, the THC that a patient receives and its IOP effects will also vary unpredictably.
- THC can lower blood pressure, which may worsen glaucomatous neuropathy through hypoperfusion injury.²
- Smoke inhalation causes or exacerbates diseases such as asthma, emphysema, pneumonia, lung cancer, and heart disease.

When discussing with patients marijuana for glaucoma therapy, I strive to provide a multifaceted view. THC has enormous potential. Marijuana's status as a schedule I narcotic has discouraged research for decades, but someday, this drug may be a powerful addition to our glaucoma regimen as a topical, oral, or depot-type agent. Currently, however, inhaled medical marijuana is not indicated for the vast majority of glaucoma patients.

David Diaz, MD, is a glaucoma specialist at the University of Vermont in Burlington, Vermont. Dr. Diaz may be reached at daviddiaz100@yahoo.com.

1. Green K. Marijuana smoking versus cannabinoids for glaucoma therapy. *Arch Ophthalmol*. 1998;116:1433-1437.

2. Kaufman PL. Marijuana and glaucoma. *Arch Ophthalmol*. 1998;116:1512-1513.

lar level. The location of the CB1 cannabinoid receptors and their effect on cyclic adenosine monophosphate suggest that CB1 influences the production of aqueous. In 1999, ocular cannabinoid receptors were identified via immunohistochemistry, with the greatest density found in the trabecular meshwork, the nonpigmented ciliary epithelium, and the ciliary muscles; a lesser density of ocular cannabinoid receptors was found in Schlemm canal.⁹ The presence of CB1 receptors at the nonpigmented epithelium of the ciliary body and in the choroidal vessels could be one of the main mechanisms through which cannabinoid agonists lower IOP by diminishing the production of aqueous humor.¹⁰ How CB2 receptors reduce IOP has not been established.

NEUROPROTECTIVE PROPERTIES

Cannabinoids' full mechanism of action in the human eye is not fully understood. Numerous studies have demonstrated that cannabinoids increase neuron survival in neurodegenerative diseases.¹¹ In glaucoma, the final pathway leading to vision loss is the selective death of retinal ganglion cells through apoptosis, which is initiated by axonal injury at the optic disc by either compression or ischemia. In ischemia, the release of glutamate activates the N-methyl-D-aspartate receptor. Such activation is one of several pathways to apoptotic cell death. It causes an influx of calcium into the cells and generates free radicals.¹² THC can inhibit the release of glutamic acid by increasing potassium and decreasing

calcium permeability, and it can also block the activation of glutamate and N-methyl-D-aspartate.¹²

Cannabinoids also have antioxidant and vasorelaxant properties, and they may increase ocular blood flow.⁴ Patients with open-angle glaucoma may experience an abnormal increase in plasma endothelin-1 in response to vasospastic stimuli.⁴ Marsicano et al demonstrated that cannabinoids reduced endothelin-induced calcium mobilization, thus inhibiting vasoconstriction.¹¹ Cannabinoids may therefore be of benefit to eyes with ischemia-induced optic nerve damage. On the other hand, inhaled THC can cause systemic hypotension, which could harm optic nerve perfusion.¹³

CONCLUSION

Cannabinoids are a potential IOP-lowering treatment for glaucoma. They seem to have neuroprotective properties, which may or may not be applicable to retinal ganglion cells or other visual pathway neurons.⁴ The use of eye drops containing THC has been investigated, but it has not been possible to formulate sufficiently concentrated therapy due to the low water solubility of the active ingredients. Additionally, the formulations created have been toxic to the ocular surface and have not been tolerable due to local side effects.¹⁴ At this time, marijuana's side effects and short duration of action preclude recommending this drug in any form for the treatment of glaucoma. ■

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Katherine Shen, OD, is an associate at Specialty Eyecare Group in Seattle and Kirkland, Washington. Dr. Shen may be reached at drshen@specialtyeye.com.



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