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ORIGINAL ARTICLE

Medical Cannabis, a Beneficial High in Treatment of Blepharospasm? An Early Observation

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ABSTRACT

The objective of this study was to observe the effect of medical cannabis in benign essential blepharospasm (BEB) as an adjunct to botulinum toxin. A retrospective chart review was performed on patients certified for medical cannabis use for BEB from September 2015 to May 2016. Patient demographics and responses, cannabis history, and severity indices were collected. Ten patients were certified for medical cannabis use. Five met the inclusion criteria, which was any patient with a diagnosis of BEB receiving standard botulinum toxin treatment who had started medical cannabis treatment by a registered distributor within the state, and was contactable by phone. Four patients discontinued use. Three out of four patients (75%) reported symptomatic improvement. Medical cannabis is an accepted therapy for muscle spastic disorders. Its potential as an adjunctive therapy for BEB remains unknown, and further investigations would be of benefit.

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Blepharospasm; cannabis; marijuana; muscle spasm

Introduction

Benign essential blepharospasm (BEB) is a common craniofacial movement disorder. BEB can be a disabling process, as symptoms of excessive involuntary blinking, photophobia, and uncontrolled eyelid closure can cause functional blindness.[1,2] Its prevalence is estimated to be 32.2 per 1 million. Onset generally occurs after the fourth decade, with a higher frequency in women, and it can severely impact quality of life.[1,3,4] BEB is most often idiopathic; however, brainstem lesions have been reported.[1,2,5]

One standard treatment of BEB is life-long therapy with scheduled periocular botulinum toxin injections, which reduce symptoms of facial dystonia for BEB and other facial spasm disorders (hemifacial spasm and Meige syndrome).[1,2,6] Although not curative, botulinum toxin provides an effective, safe, successful long-term alleviation of facial dystonia symptoms such as BEB.[1,2,6] With routine treatment, symptom-free periods can be maintained.

Medical cannabis, a once-taboo subject, has gained much press over the years with its potential utility as being an adjunct treatment for many diseases. Studies have shown benefit in symptomatic improvement for muscle spasms related to multiple sclerosis, and also in neurogenic symptoms, neuropathic pain, refractory pain due to human immunodeficiency virus (HIV), chemotherapy-induced nausea and vomiting, and urinary dysfunction.[7–18] Twenty-five states including Washington, DC, Puerto Rico, and Guam have passed comprehensive medical cannabis and marijuana programs to varying degrees and implementation.[19] Minnesota allows for medical cannabis to those with 10 qualifying conditions, with one specifically being severe and persistent muscle spasms (including those characteristic of multiple sclerosis).[20] Qualifying conditions are determined based on public petitions for specific conditions to a seven-member panel following review of the condition, current treatments, and available research on medical cannabis.

In this study, we observed the effects of medical cannabis therapy, as an adjunctive treatment modality in conjunction with maintenance botulinum toxin therapy, in patients with BEB.

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Methods

We performed a retrospective chart and prospective data gathering review with University of Minnesota Institutional Review Board approval on all patients at the University of Minnesota Department of Ophthalmology and Visual Neurosciences who were certified for medical cannabis use for treatment of BEB from September 2015 through May 2016, and those who were contactable by telephone. The collection and evaluation of protected patient health information was Health Insurance Portability and Accountability Act (HIPAA)-compliant, and in accordance with the Declaration of Helsinki. Inclusion criteria were a clinical diagnosis of BEB, receiving maximally tolerated scheduled standard botulinum toxin treatment, and medical cannabis treatment by one of two registered distributors (Leafline Labs, LLC, and Minnesota Medical Solutions) within the state of Minnesota. Furthermore, patients were only included if they verbally agreed via telephone to discuss their history with the medical cannabis use. Patient demographics (age and gender), prescription type and dose, history of medication use, side effects, patient responses to medication, and responses to the Blepharospasm Disability Index (BSDI) and Jankovic Rating Scale (JRS), if available, were documented (Table 1). The indices were taken during the standardised botulinum toxin treatment received every 3 months, once before and once during cannabis therapy. All patients were contacted by telephone to collect responses and reactions to the medical cannabis therapy.

To receive medical cannabis, each patient was certified for the Minnesota Department of Health medical cannabis program by one of the two senior authors (M.S.L. and A.R.H.) for medical cannabis treatment for severe and persistent muscle spasms. The discussion of medical cannabis therapy was initiated by the senior authors (A.R.H. and M.S.L.) if the patients who had received long-term botulinum toxin therapy were determined to have residual symptoms and could potentially benefit from additional treatment. Following certification, the patient met with a pharmacist at one of the two distribution centres who would determine the type and quantity of medical cannabis to best provide symptom control based on past studies, pharmacist experience, and availability. There was no contact between the certifying doctors and the distribution centres. The patient would then follow up with the distribution centres for alterations to the dosage and type.

Table 1. Blepharospasm Disability Index (BSDI) and Jankovic Rating Scale (JRS).[23]

Jankovic Rating Scale (JRS)
(Originally described by Jankovic and Orman, 1987)
Items
Reading
Driving a vehicle
Watching television
Shopping
Every day activities
Walking (on foot)
Ratings
0 = No impairment
1 = Mild impairment
2 = Moderate impairment
3 = Severe impairment
4 = Not possible due to disease severity
Blepharospasm Disability Index (BSDI)
(Originally described by Goerteimeyer et al., 2002)
Blepharospasm severity
0 = None.
1 = Minimal, increased blinking present only with external stimuli (i.e., bright light or wind).
2 = Mild, spontaneous eyelid fluttering (without active spasm). Symptoms are noticeable, possibly embarrassing, but not functionally disabling.
3 = Moderate, very noticeable spasms of eyelids, only. Mildly incapacitating.
4 = Severe, incapacitating spasms of eyelids and possibly other facial muscles.
Blepharospasm frequency
0 = None.
1 = Slightly increased frequency of blinking.
2 = Eyelid fluttering lasting less than 1 second in duration.
3 = Eyelid spasms lasting for more than 1 second, but eyes open more than 50% of wakeful hours.
4 = Functionally "blind" due to persistent eyelid closure, more than 50% of the waking time.

Results

The senior authors (M.S.L. and A.R.H.) certified 10 patients with BEB with residual symptoms following botulinum therapy for medical cannabis use. Of those 10 patients, 5 began medical cannabis therapy, and all were contacted by telephone. There were three women and two men, and the average age was 61.4 years (range, 54–72 years; standard deviation, 6.54). The average number of botulinum toxin treatments prior to cannabis use was 22.4 (range, 4–64; standard deviation, 24.2), and the average duration of cannabis use was 8.4 weeks (range, 2–12 weeks; standard deviation, 4.10). The conduit

and dose of cannabis is listed in Table 1. Four patients stopped the treatment, two due to no treatment effect noted, one for cost, and one due to concern for related side effects. The most common side effects were disturbed sleep and headache, whereas one patient developed lightheadedness, which led to a thorough cardiac work-up and cessation of the medication (Table 2).

Three of the patients participated in objective measures of two severity indices utilised in the study, the Blepharospasm Severity Index and the Jankovic Rating Scale. The BSDI measures the severity and frequency separately, with 0 being no symptoms and 4 being severe/incapacitating. In addition, the JRS measures the disease severity regarding six different activities, with 0 being no impairment and 4 being too severe to perform (the total score is additive and can measure from no impairment to severe impairment, or 0 to 24). The duration of use of cannabis for these patients were 8, 12, and 12 weeks, respectively. Of note, there was a decrease in both indices when comparing the pre and post averages of the three patients (Table 3).

All the participants receiving medical cannabis therapy were contacted by telephone. Of those contacted, one patient declined to comment about his experience with the medical cannabis, as he only used the medication 2 weeks before stopping. He reported minimal residual symptoms following his standard botulinum toxin injection treatment, and he stopped the cannabis shortly after starting, as he felt there were no improvement in the symptoms after initially starting the treatment. He therefore felt his participation would not provide valid data and declined providing further commentary on history of use. Three of the other patients reported a subjective improvement in clinical symptoms. Lastly, three of the patients had other significant disabling diseases (oromandibular and cervical dystonia, post-herpetic neuralgia, and Meige syndrome). All three described a further reduction in symptoms related to these diseases in addition to the blepharospasm (Table 4).

Table 2. Patient and medication history.

Patient	Age	Sex	Prescription	Number of botulinum therapies prior to cannabis	Prescribed dose	Duration of cannabis use (weeks)	Treatment stopped (Yes/No)	Reason for stop	Side effects
1	60	Female	2.5 mg THC, 47.5 mg CBD capsule	4	1 capsule bid	8	Yes	Cost	None
2	54	Male	5 mg THC 5 mg CBD /1 mL tincture	64	1 mL bid	2	Yes	No treatment effect noted	Disturbed sleep[a]
3	61	Female	1st script: 25 mg THC 25 mg CBD /1 mL tincture 2nd script: 20 mg THC 5 mg CBD /1 mL tincture	9	1/10 mL bid	12	No	NA	Disturbed sleep[a]
4	72	Male	1st script: 2.5 mg THC capsule 2nd script: 4 mg THC 1 mg CBD capsule	13	1 capsule bid	12	Yes	No treatment effect noted	Headache, intermittent
5	60	Female	5 mg THC 5 mg CBD /1 mL tincture	22	Up to 2 mL bid	8	Yes	Side effect[b]	Lightheaded

[a]Noted if medication taken at night.
[b]Admitted two times to emergency department for evaluation of lightheadedness.

Table 3. Pre/post–cannabis therapy blepharospasm scale results.

	Patient 1		Patient 3		Patient 4			
Blepharospasm scale	Pre	Post	Pre	Post	Pre	Post	Pre patient average (SD)	Post patient average (SD)
BSDI Severity (0–4)	3	2	3	2	4	4	3.33 (0.58)	2.67 (1.15)
BSDI Frequency (0–4)	3	1	3	3	4	4	3.33 (0.58)	2.67 (1.53)
JRS (0–24)	10	6	14	12	13	8	12.33 (2.08)	8.67 (3.06)

Note. BSDI = Blepharospasm Disability Index; JRS = Jankovic Rating Scale.

Table 4. Subjective patient responses to cannabis therapy.

Patient	Decrease in symptoms (Yes/No)	Other diseases with noted symptom improvement	Would participate in prospective study (Yes/No)
1	Yes	Oromandibular and cervical dystonia	Yes
2	Declined[a]	None	Yes
3	Yes	Post-herpetic neuralgia	Yes
4	No	None	Yes
5	Yes	Meige syndrome	Yes

[a]Patient stopped after 2 weeks as he did not note response due to complete symptomatic relief by botulinum therapy. He declined and did not feel he could adequately respond to the questions.

Discussion

Use of marijuana, medical or otherwise, remains an offense under federal law, and due to its classification as a schedule I substance by the Food and Drug Administration (FDA), it continues to be a challenge to research its therapeutic properties.[21,22] The principal cause of marijuana's psychoactive effects was found to be attributed to the cannabinoid Δ^9-tetrahydrocannabinol (THC); however, other important cannabinoids have been isolated in cannabis.[22] For example, cannabidiol (CBD) is one of the main non-psychotropic compounds in cannabis. There is continued uncertainty to its actual effect, although it has been postulated to be a potential important inverse agonist; however, its use in Nabiximols (THC:CBD extract) has been well studied for treatment of multiple sclerosis–related muscle spasms.[22] It has been thought that the interplay between these two cannabinoids can be a helpful anti-spastic therapy. Furthermore, reports have found medical cannabis well tolerated, with only mild to moderate adverse effects. However, due to the vast different concentrations of cannabinoids in each product, and the various patient responses to medical cannabis, the adverse effect profiles vary considerably.[22]

Focusing on neurologic conditions, medical cannabis has been found efficacious and safe for specific disorders; however, for others, minimal effect was reported. Cannabis was found effective for reducing patient-centred measures for spasticity, central pain and painful spasm, and urinary dysfunction. It, however, has little effect as a treatment modality for tremor and conditions such as levodopa-induced dyskinesias in Parkinson's disease patients. Further research needs to be performed in regards to cannabis treatment for Huntington's disease, Tourette syndrome, cervical dystonia, and epilepsy, as current efficacy remains unknown.[18]

Our review focused on the outcomes of medical cannabis use in five patients with BEB treated with standard scheduled botulinum toxin therapy who had residual symptoms. Through the collective experiences of these five patients, interesting observations apply. (1) The medical cannabis was tolerated by a majority of the participants, with only one having to stop treatment due to concerns of an adverse event. (2) Objective and subjective measures did not clearly comport. Objectively, the standardised blepharospasm scales showed only 1 of the 3 patients with reduction in all three scales. Subjectively, in those able to respond, a majority of patients reported improvement in symptoms, the belief that medical cannabis could extend the duration of standard botulinum toxin therapy, and symptomatic relief from other co-morbidities. Contrastingly, patient 4 had a notable decrease in the JRS but did not report any symptomatic improvement. Potential reasons behind this disconnect could be the limited sample size collected, the variation of patient treatment plan, approach, and performance when taking the blepharospasm scales, limited patient understanding of disease severity in relation to reported symptoms, or a placebo effect. The potential use of medical cannabis use remains unknown, and further prospective studies are warranted.

There were several important limitations to our observations, with one being the retrospective design. In addition, the follow-up time was too short to determine true potential of adding cannabis to botulinum toxin therapy; there was an inability to control treatment design, as each participant in the medical cannabis program had

unique experiences, treatment plans, and doses. Lastly, the sample size was small. We certified 10 patients, but only 50% proceeded with therapy. Patients in this age group expressed reservations about using "medical marijuana." The cost of medical cannabis, which is several hundred dollars a month, can also be prohibitive.

Medical cannabis has made great strides as a treatment modality for symptom relief for many disease processes, including muscle spasms related to multiple sclerosis. As a muscle spasm disorder, the effect of cannabis on BEB remains uncertain. We believe that this observational case series provides a backdrop to exploring prospective, double-masked studies to determine the therapeutic effect of cannabis for patients suffering from BEB.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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