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CANNABIDIOL IN THE TREATMENT OF REFRACTORY OVERACTIVE BLADDER: CASES REPORT

Rubens Pitliuk
Psychiatric doctor - Hospital Israelita Albert Einstein
São Paulo, SP. Brazil

Carlos Eduardo Czeresnia
Gynecologist and Obstetrician - Hospital Israelita Albert Einstein
São Paulo, SP. Brazil

Christina Morotomi Funatsu Coelho
Neurologist doctor
São Paulo, SP. Brazil

Miriam Dambros Lorenzetti
Urologist doctor – Hospital Israelita Albert Einstein
São Paulo, SP. Brazil

Tatyanny Paula Pinto da Costa Santos Fucci
Nutritionist
São Paulo, SP. Brazil

Abstract: This observational study evaluated the effect of Cannabidiol Oil with 0.3% Tetrahydrocannabinol: *Full Spectrum* that is sublingual, in the symptoms of patients diagnosed with Refractory Overactive Bladder Syndrome. Patients were clinically evaluated and with a validated questionnaire for Portuguese language before and 4 weeks after treatment. The drug dosage was 0.25 mL/day (12.5 mg/day) in the first week, 0.50 mL/day (25 mg/day) in the second, 0.75 mL/day (37.5 mg/day) in the third and 1st week. ml (50 mg/day) in the fourth week (given in the evening, single dose). The study included nine patients who were already in clinical follow-up and received first-line treatment for Overactive Bladder Syndrome with partial or no response (drug and behavioral treatment). The data obtained using the questionnaire showed a significant improvement in all patients (more than 50% reduction in nocturia episodes). Adverse effects were mild and affected only two patients.
Keywords: Overactive Urinary Bladder, Cannabidiol, Urgent Urinary Incontinence, Nocturia.

INTRODUCTION

Overactive Bladder Syndrome (OBH) is defined as urinary urgency, with or without urinary leakage, affecting around 18% of the Brazilian population1, 2.

There are several theories to explain the presence of overactive bladder. Among them, we would mention the decrease in the inhibitory response of the Central Nervous System (CNS), hypersensitivity to acetylcholine, alterations in the urothelium, activation of C3 sensory fibers.

The main objective of treatment is to control the symptoms presented by the patient, providing an improvement in their quality of life. However, the response has been partial in a significant number of patients, generating the need to search for new and promising therapeutic options.

Cannabinoids are the active chemical components of Cannabis sativa. These produce a wide range of central and peripheral effects, some of which may have beneficial clinical applications. Evidence has suggested that components of the endocannabinoid system are involved in the regulation of bladder function, generating great interest in the possible effects on the lower urinary tract and the role of these receptors in normal and abnormal urinary tract function4. Clinical studies of cannabinoid extracts in voiding disorders are scarce and restricted to patients with multiple sclerosis and the results are insufficient to date.

Thus, the authors evaluated, in a group of patients, the effect of a sublingual cannabidiol oil (CBD) with 0.3% of tetrahydrocannabinol (THC) Full Spectrum, on the symptoms of patients who received the clinical diagnosis of Bladder Syndrome. Refractory Hyperactive Disorder (SBHR).

CASES REPORT

Nine patients (7 women - aged between 28 and 80 years and 2 men - aged between 57 and 61 years) with Hyperactive Bladder Syndrome (HBHR) were followed up to drug and behavioral treatment, who were undergoing clinical follow-up. The description of the group (age, time of disease evolution, associated comorbidities, history of pelvic surgeries and medication use) is described in (Table 1).

Patients were followed up for some years (mean between 3 and 4 years) for the treatment of SBHR without significant improvement in urinary symptoms. Clinical treatment consisted of antimuscarinics and beta 3 agonists, in addition to hygienic/dietary measures. No patient had migrated to second-line treatment (intravesical botulinum toxin injection or neurostimulation).

As first-line therapy did not show significant improvement or failed in the long term, we suggest to this group of patients the use of sublingual Cannabidiol oil with 0.3 mg of THC, immediately before bedtime, starting with 0.25 ml (12.5 mg), increasing the dose by 0.25 ml each week, up to a maximum of 1 ml (50 mg).

None of the patients had cognitive deficits, tumors of the genitourinary tract, were being treated with chemotherapy or radiotherapy, had malformations in the genitourinary tract, kidney disease, chronic renal failure, decompensated heart failure, or patients with urolithiasis. There were also no previous reports of THC/CBD allergy or adverse effects from previous use of the compound.

After accepting and signing the Free and Informed Consent Form, patients were submitted to a questionnaire about their health conditions prior to treatment and specific questions about the SBHR (Table 1). To monitor the results, a specific questionnaire for urinary symptoms was applied, translated and validated into Portuguese (OAB-V8 instrument). This consists of 8 questions with a domain from 0 to 5 and is considered a probable diagnosis of BHS when their sum is equal to or greater than 85.

The results observed during the period of use of Cannabidiol oil with 0.3% THC were: decrease of around 50% of the total points referring to the OAB-SF questionnaire, with nocturia being the symptom that presented the most significant improvement. One patient reported mild epigastric pain and another oil flavor intolerance). Both discontinued treatment. There was a significant improvement in sleep quality described by all patients (Table 2).

DISCUSSION

Spasticity, involuntary hyperactivity of muscles, somatic and/or visceral, is related to a variety of etiologies. There are pharmacological and surgical options for treatment mentioned at the time of the introduction. Require high doses and induce side effects [6].

The action of cannabinoids on the control of detrusor muscle contraction is complex [7]. The question remains as to what the mechanisms would be to inhibit the stimulation caused by the detrusor muscle: local, presynaptic or central, but the action of the cannabic elements proves to be dose dependent. The type 1 transient potential vanilloid receptor (TRPV1) appears to be essential for bladder overactivity in animal models in addition to the CB1 and CB2 receptors located in the detrusor muscle and urothelium, with both receptors being expressed higher in the urothelium. [8]. Possibly the cannabinoid components act by inhibiting the muscle contraction chemically induced by the increase in acetylcholine, activating nociceptive stimulus and not by electrical stimulus (distension with sensory activation in the posterior horn)[7,8]. For this reason, there is a suggestion of research with the application of the elements intra-vesically, reducing the side effects by systemic action. [7,8,9].

CONCLUSION

CBD oil with 0.3% THC has been shown to be effective in improving the symptoms of SBHR, particularly nocturia. The number of nocturnal awakenings decreased by more than 50%, improving patients' quality of life. One patient reported mild epigastric pain and another, oil flavor intolerance.

This report suggests new clinical studies to evaluate the use of CBD in the treatment of BHS and especially with doses higher than those used in this study.

Note: Cannabidiol Oil with 0.3% Tetrahydrocannabinol Full Spectrum (Hempflex 3000) was provided free of charge by the company GreenCare, with no

participation in the choice of patients, study design, tabulation of results and elaboration of conclusions.

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