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Short communication

Single center experience with medical cannabis in Gilles de la Tourette syndrome

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ABSTRACT

Introduction: Patients with Gilles de la Tourette syndrome (GTS) experience reduced function and impaired quality of life. The current medical treatments for this syndrome can cause significant side effects and offer partial symptomatic relief. In a few small trials medical cannabis (MC) has been suggested to offer symptomatic relief with a relatively benign side effect profile. We conducted a real-life assessment of clinical benefit and adverse effects of chronic MC treatment among patients with GTS.

Methods: GTS patients treated with MC were interviewed via phone regarding treatment efficacy and side effect profile from chronic MC consumption. Global efficacy was rated on a Likert scale of 1–5 and side effects of treatment were recorded.

Results: Forty-Two GTS patients (33 males, mean age 34.5) were interviewed for this study. The total global impression score of efficacy was 3.85 out of a total 5 possible points. Patients reported during the free discussion part of the interview about reduction in tic severity, better sleep and improved mood as positive effects of MC. Thirty-eight patients reported any kind of benefit from treatment while 10 patients with more than one year of consumption elected to stop treatment with MC for various reasons including severe side effects as psychosis in one patient.

Conclusion: MC seems to hold promise in the treatment of GTS as it demonstrated high subjective satisfaction by most patients however not without side effects and should be further investigated as a treatment option for this syndrome.

1. Introduction

Gilles de la Tourette syndrome (GTS) is diagnosed based on core features of multiple motor and at least one phonic tic lasting more than one year [1]. When tics are severe and debilitating, behavioral therapy is the first-line of treatment but if this fails, different drugs can be used to treat symptoms including dopamine receptor blockers, monoamine depleting agents and α2-adrenergic agonists, however these do not always provide satisfactory symptomatic relief and have disturbing side effects [1]. Generally, GTS attenuates with age in at least half of those who suffer from the condition. However, some individuals have persistently severe symptoms throughout adulthood.

Patients with GTS can experience reduced function and impaired quality of life compared with the general population [2]. These include musculoskeletal pain, social isolation, occupational restrictions and social withdrawal. GTS is associated with significant comorbidities which also affect quality of life such as obsessive-compulsive disorder (OCD), attention-deficit hyperactivity disorder (ADHD), anxiety and depression [1]. Because of this, psychological distress and frustration are common among patients with GTS, with the syndrome having negative effect on employment, income and education status in adults [3].

Cannabis is a natural substance that contains more than 60 different cannabinoids. The two main components, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) differ in concentrations in formulations and exert the different effects. Two distinct cannabinoid receptors have been described; CB-1 receptors are located in areas of the brain that are

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related to reward, appetite and nociception (hippocampus, association cortex, basal ganglia, cerebellum and spinal cord), while CB-2 receptors are located in the striatum, ventral tegmentum, hippocampus and thalamus [4]. Activation of CB-2 receptors has been reported to induce feeling of well-being, impaired memory, slowed locomotor functions and sleep promoting effects [5]. The medical use of cannabis (MC) has been proposed for several conditions and regulated in some western countries.

A 2009 Chochrane review on cannabinoids for GTS detected 2 small trials that assessed THC as either monotherapy or adjuvant therapy with placebo. The first was a double blind single dose crossover trial and the other a six-week parallel group study with a total of 28 participants. Both trials reported a positive effect on the frequency and severity of tics on subjective report, yet objective endpoints were not affected by treatment, thus impairing any definitive conclusion [6].

The Israeli ministry of health approved the use of MC for several indications in 2013, including patients suffering from GTS with significant impairments in daily living who failed to respond favorably to common medications. This treatment is contraindicated in cases of active psychosis. Patients are issued a license and can initially consume 20 g of MC either as oil or for inhalation with increased doses available through a biannual evaluation by a neurologist and psychiatrist who are together required to recommend the continuation of treatment. Upon obtaining a license, patients chose a distributor and acquire the recommended MC formulation with varying concentrations of THC and CBD and the option of monthly change in distributor and MC formulations.

We conducted a real-life efficacy study in order to assess the response, benefits and side effects of use of MC for the treatment of GTS.

2. Methods

A telephoned survey of GTS patients from the Movement Disorders Unit (MDU) of the Tel-Aviv Medical Center (TLVMC) who received MC after individual approval from the Israeli Ministry of Health was performed throughout May–July 2018 after receiving approval from our institutions' IRB. GTS patients that were processed for MC licensing through the MDU since 2013 were contacted at least one year after receiving their MC license. Patients' were approached by either JK or TT, research coordinators in the MDU, indicated consent through the telephone and answered a structured questionnaire which assessed subjective clinical global impression of efficacy of MC on the clinical syndrome on a Likert scale of 1–5. The prevalence of ever suffering from various GTS symptoms was assessed as well. In addition, adverse effects, mode of consumption, current occupation and demographic data were collected, as well a free discussion about the patient's experience (Supplemental Table 1).

3. Results

We identified 63 potential subjects with the diagnosis of GTS who were processed for MC through the MDU of TLVMC since 2013, 5 were excluded from the study as they were subsequently found to suffer from other hyperkinetic movement disorder (tardive dyskinesia and dystonic tics), an additional 10 patients were excluded for consuming MC for less than one year and 6 were lost to follow-up. A total of 42 patients with GTS participated in this study (33 males, mean age 34.45), group characteristics are presented in Table 1. The global impression of efficacy was 3.85 (SD 1.41) out of a total 5 possible points, indicating positive response to MC. In a free text report, patients reported reduction in tic severity, better sleep and improved mood as positive effects of MC.

Seventeen of the participants were taking GTS related medications together with MC, while all participants had previous experience with at least one GTS related therapy. Two patients were taking atypical antipsychotics, typical antipsychotic was used by one patient, SSRI's were used by 8 patients, benzodiazepines by 5, methylphenidate by 3, tricyclic antidepressant by one and tetrabenazine by 2 patients when surveyed for this study. Thus, over half of our cohort was using MC as the only treatment for their disease.

Table 1
Group characteristics.

Age	34.45 (11.84) (20–73)
Gender m/f	33/9
Years of education	13.29 (2.32) (8–18)
Age of diagnosis	15.07 (10.29) (6–41)
Years of cannabis consumption	2.35 (1.25) (1–5)
Mode of consumption (oil/inhalation/both)	4/28/10
Current dosage (grams)	29.37 (9.48) (20–50)
Mean response	3.85 (1.41)
Currently occupied n (%)	31 (73.81)
Stopped treatment n (%)	10 (23.81)
OCD n (%)	27 (64.28)
ADHD n (%)	26 (61.91)
Depression n (%)	15 (35.71)
Anxiety n (%)	20 (47.62)

Results are presented as mean and std with range in relevant categories displayed as well.
m/f – male/female, n-number, OCD-obsessive-compulsive disorder, ADHD – Attention-deficit hyperactivity disorder.

A little less than one quarter of our cohort (10/42) elected to stop treatment with MC after at least a year of treatment, however only 4 patients reported no effect of MC on their symptoms, even though they renewed their license at least once. The other 6 patients stopped consumption for various reasons including side effects. Four patients reported hallucinations, 6 reported irritability and confusion while 7 reported subjective cognitive decline. One patient detailed an acute psychotic episode. Other side effects that were noted but did not affect consumption were increased appetite, dry eyes and fatigue. Aside from the patient with the psychotic episode, all other GTS patients received renewed licenses through the MDU.

4. Discussion

Our cohort of patients seems representative of the GTS population at large in general characteristics which include male predominance [7] and occurrence of comorbidities such as OCD, ADHD and affective disorders [8]. Impressively, the average years of education indicate above basic high school education, with 3/4 of our cohort currently employed, suggesting adequate coping mechanisms.

The mean ranking of MC response was 3.85/5 among our cohort with a slightly over 75% of participants electing to continue use of cannabis to alleviate symptoms. Those who stopped treatment did so for either lack of efficacy or due to side effects. While symptoms of GTS tend to abate with time and are variable across seasons and months [9], the choice of contacting GTC patients with over one years' treatment with MC was in part intended to overcome this.

Less than half of the cohort were taking any form of GTS related medications when assessed for this study even though in order to be eligible for MC, patients were required to have previous use of at least one disease related medication. Recent studies have indicated benefit from use of MC among patients with GTS albeit in small number of participants. Muller-Vahl et al. reported significant clinical improvement among 14/17 GTS patients who were using cannabis in both tic severity, OCD and ADHD with no serious adverse effects [1]. These findings were later replicated in two small randomized double-blind studies [10,11] incorporating a total of 36 participants with 7 dropouts. However, one of these trials was a single dose study while the other being a short six-week follow up study. Interestingly, one of these studies indicated deterioration in OCD symptoms under cannabis treatment. This was not detected in our study as none of the participant described worsening of obsessive or compulsive symptoms, even

though this was not directly questioned.

Common side effects of cannabis include tiredness and dizziness, relaxation, euphoria and reduction in cognitive capabilities. In our cohort, such symptoms caused the termination of use of cannabis in 1/6 of the patients. As we did not control for the type of MC or frequency of treatment, the severity and potential modification of side effects of MC remains to be detailed. Slow titration and habituation might address some of these side effects as attested by the majority of GTC patients that elected to continue treatment. A recent study analyzing side effects of MC that were prescribed for various reasons, detected 6.9% of use cessation due to adverse events within 6 months of initiation, within one year 15% stopped medication [12]. The fact that relatively high percent of our patients chose to stop treatment may indicate that the use of MC among GTS is not based solely on a strong pleasure effect.

5. Limitation

In this retrospective descriptive study, without randomization, some of the effects could be attributed to placebo. In addition, the many formulations and doses of MC make comparative analysis difficult. Even though to the best of our knowledge, this is the largest natural history study addressing GTS treatment with MC, the absolute number of participants remains relatively low. In addition, 6 GTS patients were lost to follow up. However, this was compensated by a relevant long treatment period as we contacted patients at least one year after initiating MC treatment. We did not assess concurrent use of other illicit substances which could affect response to treatment and could shed light on the “gateway drug” theory regarding use of MC. In addition, possible weight gain as a side effect of MC was not addressed. Despite all this, the positive subjective report on the benefit of cannabis on GTS should encourage further studies in this direction.

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Disclosure

Lihi Bar-Lev Schleider is an employee of Tikun Olam Ltd., an Israeli pharmaceutical company which is developing cannabis-based medicinal extracts. Other authors have nothing to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2018.10.004.

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