A Comparison of Sativex® and Aseco® For Treatment of Severe Motor and Vocal Tics; a Single Case Report

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Abstract

Objectives: Severe Tourette Syndrome (TS) can be difficult to treat, and many treatments may be either ineffective or intolerable, due to side effects. There is some evidence for the benefit of cannabinoids in treating TS, and we have previously reported on a case of severe TS, which benefitted from Sativex®. Sativex® is a medication containing Tetrahydrocannabinol (THC): Cannabidiol (CBD) in a 1:1 ratio. In this paper we sought to explore the role of CBD in treating TS, through measuring benefit with Aceso® treatment. Aceso® is a pure CBD preparation.

Method: Our subject was assessed pre-treatment, after one week on Aceso® alone, and after one week on Sativex® alone. We measured subjective response using the Yale Global Tic Severity Scale (YGTSS). We also videoed him at each stage and counted vocal and motor tics, as an objective measure. These videos were rated by two assessors, blind to the stage of the treatment.

Results: The subjective and the objective measures showed little improvement in severity or frequency of motor or vocal tics on treatment with Aceso®. However, there was improvement seen with Sativex®.

Conclusions: Our results suggest that it is primarily THC, rather than CBD, which provides benefit in treatment of TS. Further studies are needed to substantiate our findings.

INTRODUCTION

Tourette's Syndrome (TS)

TS is a condition of childhood that is characterised by multiple motor, and one or more vocal tics, lasting more than a year and arising before 18 years of age. Generally, the condition attenuates with age, but some individuals have persistently severe or worsening symptoms in adulthood, which disrupt function and impair quality of life. Sequelae of ongoing tics include musculoskeletal pain, social isolation, vocational restrictions, peer victimization and interpersonal conflict [1].

The aetiology of TS is partly hereditary, and is often comorbid with other disorders, such as ADHD and OCD. Based on structural and functional neuro imaging studies, an abnormality in basal ganglia and related corticostral-thalamocortical pathways has been suggested. The mainstay of pharmacological treatments has been antipsychotics, such as Haloperidol and Risperidone, which modulate dopamine in these pathways [2-4].

A difficult case to treat

Our subject is well described in our recent paper [5]. He is a 26 year old single man with severe TS, which significantly impacts on his function and relationships. He is in good physical health and has never used illicit substances. Adequate trials of conventional medication had been poorly tolerated and failed to control his symptoms. Our recent case study [5] documents marked subjective and objective improvement with Sativex®, a medicine containing an equal ratio of Tetrahydrocannabinol (THC) to Cannabidiol (CBD).

Using cannabis to treat TS

In 1988 Cannabinoid receptors were identified for the first time in the central and peripheral nervous system of humans. They were found in the basal ganglia, cerebellum, hippocampus and dorsal primary afferent spinal cord regions. There is experimental evidence that cannabinoids affect the activity of many neurotransmitters, including dopamine. THC directly binds to the CB1 receptor. Whilst the exact mechanism by which THC exerts its beneficial effects has not yet been fully elucidated, there is increasing evidence that the stimulation of cannabinoid receptors in the cortico-thalamic pathways leads to a reduction in the hypersensitivity of the neurones. This was originally thought to be via indirect effects, exerted through modulation...
of GABA and glutamate inputs, rather than direct effects in the dopaminergic terminals. However, recent research suggests there may also be a mechanism for direct regulation of dopamine function in the CNS [6]. These direct and indirect mechanisms influence various dopamine related neurobiological processes, such as control of movement.

The first evidence to suggest that cannabis could be a useful treatment for TS came from case reports published in 1988, which discussed the improvement in tics and urges in three patients, aged 15-39, who were smoking cannabis [7]. Retrospective questionnaire data for TS patients, comparing symptoms in cannabis users with non-cannabis users, found the former experienced less tics [8]. The 1990s-2000s had seen publication of case reports using THC, the main psychoactive component of cannabis, in TS treatment [9-12]. Two randomised controlled trials were later carried out, which suggested benefit from THC [13].

CBD, a non-psychotropic constituent, is generally found in relatively high concentrations in Cannabis. CBD has very low affinity for known cannabinoid receptors, but is interacts with non-endocannabinoid signalling systems as a "multitarget" drug [14,15]. It is thought to alter the transport systems around the cannabinoid synapses [14]. Further work is needed to clarify exact mechanism of action, and its relevance to movement disorders. However, interest in this area has grown considerably over the last decade; with promising findings seen in observational studies using CBD to help treat various diseases and symptoms; including type-1 diabetes, cerebral ischemia, paediatric treatment-resistant epilepsy, nausea and anxiety [16,17]. Furthermore, some evidence exists for the use of CBD in other movement disorders [18].

We sought to explore the role of CBD in treating TS using Aceso®, a pure CBD preparation. There are no other published reports of this having been done before.

**Method**

With consent, we assessed our subject on three occasions; initially prior to commencing treatment, then one week after treatment with Aceso® at a maximum dose of 60mg of CBD a day. We had planned to continue Aceso® treatment for a total of four weeks, and measure response at weekly intervals. However, after one week our subject stopped taking Aceso®; owing to an intolerable return of his symptoms. He resumed Sativex®, at a maximum dose of two oro mucosal sprays twice a day (which equated to 10.8mg THC and 10mg CBD). He was assessed one week after recommencing Sativex®.

Assessment involved completing the Yale Global Tic Severity Scale (YGTSS); a subjective scale that rates number, frequency, intensity, complexity, interference and impairment of motor and vocal tics in the preceding week. Assessment also included a 15 minute videotape of the subject, which followed the same format each week. During this assessment he completed maths, then reading tasks, both at a standard suitable for an eleven year old, and each for five minutes. He then spent the remaining five minutes sitting in silence. The videos were independently assessed, by two raters (DT, LE) who were blinded to the phase of treatment. Raters were both psychiatry trainees who had watched videos and read appropriate literature on the subject to prepare to formally rate tics. Any discrepancy in scores resulted in both raters watching the video together to reach consensus. If this was not possible then it was agreed that the video would be rated by the third rater (RB), who has worked extensively with TS patients, and has used formal tools in rating for previous TS research [19].

**RESULTS**

We counted a total of 125 motor tics and 4 vocal tics without treatment, compared to 123 motor tics and 3 vocal tics on Aceso®, and 72 motor tics and 3 vocal tics on Sativex® (Figure 1).

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different cannabinoids, provides the best symptomatic relief. Furthermore, there is uncertainty around whether herbal cannabis, or different natural or synthetic cannabinoids, has the best efficacy to adverse effect profile. We had seen our subject experience dramatic symptomatic relief after using Sativex®. Although well tolerated, our subject returned to a baseline state (with regards to degree of symptoms and impairment ratings, both subjectively and objectively measured) when taking Aceso®, and he remarked that his life had become intolerable again. Rapid and dramatic improvements in motor and vocal tics were seen when he was switched back to Sativex®. This suggests that it is the psychoactive component of cannabis, THC, which is responsible for the benefit seen. There is still a question as to whether the CBD augments THC treatment leading to better outcomes than treatment with THC alone [20]. Furthermore, decreased side effects have also been noted when using a combination THC: CBD when compared to THC alone [21,22]. Further research is needed to substantiate our findings.

This study was recently completed (June 2016) and we have not extended it beyond this single patient. Our subject continues to use Sativex®, with good effect, and he has not experienced any troublesome side effects or developed tolerance. Other TS sufferers have approached us with request a trial of treatment on Sativex®, having seen the benefit our subject derived from the treatment. We are hoping to complete a larger case-control study, with a select group of similar patients, across New Zealand in later 2016-2017. The gold standard research would be a large double-blinded controlled RCT. However, there are only a very small number of patients’ with severe vocal and motor treatment resistant TS, which means it would be a challenge to achieve sufficient power for the research.

LIMITATIONS

Tics are often exacerbated by emotional stress. Our subject had previously responded well to Sativex® and he reported that coming off this, to complete rating scales off medication, was very traumatic and difficult for him. It is likely that our subject was experiencing higher levels of anxiety and stress when on no treatment, and on trialling a new and unknown treatment with Aceso®. His level of anxiety was such that we were unable to complete the initial plan to assess response over one month of treatment with Aceso®. It is possible that there may have been some nocebo effect; with his expectations and apprehensions regarding the medicines skewing the results seen.

This study is on a single patient, and therefore it is important to be cautious about extrapolating the findings to other patient groups.

REFERENCES


Cite this article