Case Report

The Cannabis Extraction Product as an Adjuvant Treatment in Tourette's Syndrome: A Case Report

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Tourette's syndrome (TS) is a pediatric onset of neuropsychiatric disorder characterized by motor and vocal tics. First line medication is dopaminergic blocking agents. Yet, these drugs are not effective in all patients and sometimes the side effects are intolerance. Cannabis and its derivatives are to use as an adjuvant treatment. They are used to improve tics in TS patients who failed from the first line treatment. The aim of the present report was to describe the clinical course after using the Government Pharmaceutical Organization (GPO) medical cannabis extraction product as an adjuvant treatment in TS patient. Here, the researchers reported a case of a 26-year-old female patient who had TS. She had received sublingual medical cannabis product. The clinical course and disease severity were recorded before and during the administration of the medical cannabis extraction product using several standards severity score: The Yale Global Tic Severity Scale (YGTSS), Tourette's Syndrome Severity Scale (TSSS), Tourette's Disorder Scale (TODS), and quality of life using a standardized measure of health-related quality of life developed by the Euro Quality of life group (EQ-5D-5L). The researchers' observation showed that sublingual administration of medical cannabis extraction product [tetrahydrocannabinol (THC):cannabidiol (CBD) 1:1 and THC enriched] improved both motor and vocal tics without significant adverse effect that came out to be improving the patient's quality of life as a whole.

Keywords: Tourette's Syndrome (TS); The Government Pharmaceutical Organization (GPO); Medical cannabis extraction product; Cannabidiol; Tetrahydrocannabinol

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Tourette's syndrome (TS) is a condition of the neurobehavioral disorder. TS causes person to have "tics". Tic defines as a sudden twitching movement, or abnormal sounds that person does. TS composed of multiple motor tics and one or more vocal tics which variable in frequency but have persisted for more than 1 year[1]. Motor tics could range from simple movements such as eye blinking, nose twitching or throat clearing to complex movements. Vocal tics include making meaningless sounds or noises. It could be more complex such as repeated word or phrases. The previous study found that prevalence of TS in children accounted for 0.3% to 0.9%[2]. The pathophysiology of tics is still unclear. Yet, there are some evidences of dopaminergic system involvement[3]. The traditional first line medication of tics disorder is dopaminergic blocking agents. However, these drugs are not effective in all patients and sometimes its side effects are intolerance.

Cannabinoids are well known through many years of its benefit using as an adjuvant treatment in TS[4]. In Thailand, cannabis was still classified as a class-5-narcotic, but according to Thailand National Health Act in 2019 or so-called "Narcotics Act of 2019", it is legal to use the substances for medical purpose under strict and safe practices in medical center.

According to the present study, the researchers reported a case showing an improvement after using sublingual medical cannabis extraction product as an adjuvant treatment after unsatisfied outcomes from the first line treatment.

Case Report

A 26-year-old female had developed several

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Table 1. Clinical data of 26-year-old female experiencing Tourette's syndrome treated with sublingual medical cannabis extraction product in addition to risperidone oral solution 3 mg/day

Time (weeks)	THC (mg/day)	CBD (mg/day)	YGTSS (points)	TODS (points)	TSSS (points)	EQ-5D-5L (points)
Baseline	0	0	71	105	6	8
1	0.25	0	-	-	-	-
2	0.375	0	-	-	-	-
8	0.5	0.5	-	-	-	-
9	1	1	-	-	-	-
15	2	2	-	-	-	-
21	3	3	-	-	-	-
30	4	4	-	-	-	-
39	5	5	48	82	4	4
47	0.78	20	59	93	5	4
49	5	5	-	-	-	-
52	7	6	49	80	4	4
58	8	6	48	82	4	4
60	9	6	48	79	4	4

(-)=no data recorded; THC=tetrahydrocannabinol; CBD=cannabidiol; YGTSS=Yale Global Tic Severity Scale; TODS=Tourette's Disorder Scale; TSSS=Tourette's Syndrome Severity Scale; EQ-5D-5L=quality of life using a standardized measure of health-related quality of life developed by the Euro Quality of life group

small abnormal movements such as eye blinking, nose twitching, chewing and licking the lips since the age of 9 years old. She had been diagnosed with motor tic disorder. Later, by the age of 15 years old, she developed vocal tics such as coughing, throat clearing, sniffing, whistling, and imitating of animal noises. Here, TS was diagnosed based on the Diagnostic and Statistical Manual of Psychiatry, 5th edition[1]. She was prescribed with atypical antipsychotics named risperidone. After administration of risperidone, her tics had slightly improved. Less than a year after the vocal tics developed, her clinical was deteriorated especially her motor aspect despite of the usage of risperidone 3 mg/day. The motor tics increased in both frequency and intensity, including throwing her arms, kicking and stomping hardly. Sometimes it also caused self-injures. She also suffered from many vocal tics, including very loud and irritated voice. Thus, these symptoms caused major difficulties in self-esteem and social acceptance. Moreover, she experienced marked dizziness with higher dosage of risperidone. Due to her intolerance to risperidone dosage adjustment and its ineffectiveness to decrease tics, cannabinoid then became a new choice of the treatment.

She had been participated in The Medical Cannabis Clinic at Buriram Hospital since January 2020. The prescription began with tetrahydrocannabinol (THC) enriched (THC 0.25 mg/day sublingual) from The Government Pharmaceutical Organization (GPO), and later adjusted to a night-time dose of sublingual 0.5 drop of GPO THC:cannabidiol (CBD) 1:1 (equals to 0.5 mg and 0.5 mg of THC and CBD respectively). After the usage of GPO THC:CBD 1:1 with a slowly dose-titration in each monthly visit, her tics had clearly been improved. Her clinicals were then recorded by using the standard rating scales such as Yale Global Tic Severity Scale (YGTSS), Tourette's Syndrome Severity Scale (TSSS), Tourette's Disorder Scale (TODS), and quality of life using a standardized measure of health-related quality of life developed by the Euro Quality of life group (EQ-5D-5L).

Clinical symptoms apparently improved throughout the usage of GPO THC:CBD 1:1. By scoring, the patient's clinical parameters using YGTSS lowering from 71 to 48, accompanied by her improvement in the other 2 severity scales and EQ-5D-5L (Table 1). During the study, the researchers along with the patient and her parents had discussed about using the new prescription of enriched CBD according to many studies supported the used of CBD in other neurological disorders[5-7] with expectation of a better response. Therefore, at the 47th week of treatment, the new prescription to CBD enriched composed of CBD 100.5 mg/mL and THC 3.9 mg/mL made from Khu Muang Hospital was started. The tics were deteriorated after withdrawal from THC. After 2 weeks of THC withdrawal, her motor tics increased in

both frequency and intensity. So, the GPO THC:CBD 1:1 was then given back with an extra dose of GPO THC enriched. The tics then improved again after the resumption of THC, which confirmed the clinically significance of the cannabinoid especially THC, the major psychoactive ingredients of cannabis.

The observation had been continued and revealed that after increasing THC dosage from 5 mg/day to 9 mg/day, there was just a slightly tics reduction. However, the patient did not report any significant adverse effect neither her liver function test nor glomerular filtration rate had been effected, so the prescription remained. To be exact, the patient complained a little drowsiness after using THC. However, the effect occurred in a short period and did not disturb much of her daily activity.

Discussion

To date, in many countries, the cannabinoid is approved for clinical used in treating TS, many studies reported the evidence of its benefit. In 1988[8] and 1993[9], 2 anecdotal reports suggested that using marijuana can reduce both motor and vocal tics along with other behavioral disorder. In 1999[10], a prospective study of uncontrolled case study reported a 25-year-old male with TS treated with oral 10 mg THC. After administered a single dose of 10 mg THC and 2 hours of observation, the patient's tic severity score of the Tourette's Syndrome Global Scale (TSGS) reduced from 41 to 7. In 2003[11], a double-blinded placebo-controlled study reported 6-week randomized trial in 24 patients with TS treated with up to 10 mg/day of THC. Tics severity scores were recorded during and after the treatment in total of 6 visits. As a result, using several tic severity scores suggested a trending of improvement after treatment with THC. These findings show that cannabinoids might be another effective drug and safe enough to be used as an adjuvant treatment in severe TS patient who suffers from refractory disease.

Many more of former medical studies provide evidence of cannabinoid effectiveness especially the THC extraction. Supported by the fact that cannabinoids act throughout specific receptors, cannabinoid receptor (CB) 1 and CB2, and these receptors are densely found in the central nervous system and immune tissue respectively. Especially the CB1 receptor which has the highest density in the basal ganglia, cerebellum, and hippocampus. Moreover, several studies[12-14] stated that CB1 may run a complex relation with dopaminergic pathway, which mainly defined in tics pathophysiological point. Thus, THC may be useful in augmenting the pharmacological response to atypical antipsychotic such as risperidone; corresponded to the present case study. Furthermore, patient with TS may experience anxiety and depressive mood as a co-existing or as a result from clinical burden of the illness. Due to neuropsychiatric effect of cannabinoids, some patient found it beneficial in improving their mood status[15,16].

The major limitation of the present case study is that the documentation of all tic severity scores were not done in real time visit. Some of the clinical points were needed to be recalled. Nevertheless, the trending seems to be very clearly to the patient that after using THC, her tics had distinctly improved.

Conclusion

The researchers' observation suggest that medical cannabinoids might be a successful therapy as an adjuvant medication in patients who failed to improve in traditional treatment alone. However, this is only a single case, further clinical studies and investigations are needed to confirm these data.

What is already known on this topic?

Cannabinoids are well known throughout many years of its benefit using as an adjuvant treatment in TS.

What this study adds?

In this case study, the researchers have shown that only THC, not CBD, has the therapeutic effect for the improvement of tics in TS. The optimal dose should be above 5 mg/day of THC.

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Ethical approval and consent to participate

The present case report was approved by the Ethics Committee of Buriram Hospital (BR0032.102.1/55). The patient and her parents gave informed consents.

Conflict of interest

The authors declare that there is no conflict of interest in this research.

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