Co-medication with Cannabidiol May Slow Down the Progression of Motor Neuron Disease: A Case Report

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Case Description

Amyotrophic lateral sclerosis (ALS, also called Charcot disease, Lou Gehrig disease), is a progressive, neurodegenerative disease caused by the degeneration of motor neurons in the brain and spinal cord. There is no cure. This report describes a case of motor neuron disease with typical weakness in one leg, one hand and the tongue. Despite of treatment with riluzole, symptoms progressed relatively fast. Therefore, the patient decided to take cannabidiol (CBD, 2 × 200 mg/day) as co-medication, which was started 8 weeks after riluzole, and increased to a daily dose of 2 × 300 mg. Within 6 weeks, the impaired function of the right hand and foot reversed almost completely and dysphagia partially. Improvement was maintained for about 10 weeks, when again a slow progression of dysarthria and dysphagia was observed. Eighteen months after onset, speech is almost completely lost, and dysphagia also progressed. However, symptoms of the limbs (weakness, fasciculation, atrophy) worsened much less. It is concluded, that Co-medication with CBD may be able to slow down the progression of some but not all symptoms of motor neuron disease.
sensory abnormalities. Diagnose was made on clinical aspects only; neuroimaging was not done. No risk factor (e.g., positive family history, smoking) was identified.

Riluzole (Rilutek®, Aventis Pharma S.A., Antony, France), 2 × 50 mg/d, was started; an increase to 2 × 100 mg/d was not tolerated due to severe sedation. To this treatment, Sanopan® (a dietary supplement consisting of alpha-ketoglutaric acid, potassium hydroxid, 5-hydroxy-methylfurfural, magnesium chloride, saccharose and water, manufacturer: C.Y.L. Pharmedeutika GmbH, LaQuintazöhne, Austria) was added. However, condition worsened, with fasciculation, muscle cramps, increased weakness, dysarthria as well as dysphagia. Therefore, 8 weeks after starting with riluzole, the patient included 2 × 200 mg cannabidiol (CBD) per day to his treatment regimen. Crystalline CBD of herbal origin (purity>99.5%) is available in Austria as pharmacy preparation in form of capsules, solutions of 10% and 20% or as suppositories (manufacturer: BSPG, Sandwich, UK; import: Trigal Pharma GmbH, Vienna, Austria).

Within two weeks on Co-medication with CBD, the patient noticed improvement of his symptoms, with a further amelioration when the dose was increased to 2 × 300 mg CBD/day. Six weeks after starting CBD, complete reversal of paresthesia in the foot was observed and most of paresthesia in the right hand; only a slight weakness remained in digit 5 and 4. Dysphagia also improved, whereas dysarthria remained almost stable without significant changes. Improvement was maintained for the following 10 weeks after which a slight progression of dysarthria was observed again. A dose increase to 2 × 400 mg CBD had no additional effect. During the following 12 months (now about eighteen months after onset) dysphagia, dysarthria and fatigue progressed; speech is actually almost lost. However, other symptoms worsened much less; the patient can still use his right hand and ride his bicycle, although muscle weakness and atrophy has slightly progressed. Other functions are maintained with no significant changes.

Discussion and Conclusion

Despite of growing evidence for an implication of the endocannabinoid system in the pathophysiology of motor neuron disease including ALS, as well as of potential benefits from cannabinoids, this is, to the best of our knowledge, the first report with pure CBD for treating a motor neuron disease.

Preclinical studies suggest neuroprotective and antiapoptotic activities of cannabinoids in neurodegenerative processes whereby animal experiments using a transgenic ALS mouse model demonstrated a prolongation of survival with Delta-9-tetrahydrocannabinol [8]. Later, a combination of phytochemicals, THC and CBD in a ratio of about 1:1 (nabiximols/Sativex®), was tested in SOD1-G93A mice with moderately positive results [9]. In two anonymous surveys, each including over 100 ALS patients, 10% to 21% judged medical marijuana very effective, particularly in stimulating appetite (75%), aiding sleep (65%), relieving anxiety (80%), relieving depression (70%), and providing muscle relaxation (60%) [10,11]. Annecodal community reports exist as well. Further on, a four weeks, randomized, double-blind, cross-over pilot study of 19 ALS patients, 2.5-10 mg of dronabinol (synthetic THC) per day was associated with improvements in sleep and appetite; however cramps or fasciculation did not improve. A dose of 10 mg THC is considered dose-limiting [12]. These few clinical studies with medical marijuana, extracts or dronabinol demonstrate alleviation of some ALS-related symptoms; however, control of disease progression or even reversal was not reported. As up to one half of the motor neurons innervating a muscle may be lost in ALS before clinical signs of weakness or atrophy are found [13], rapid diagnosis and early onset of treatment seems to be crucial to delay symptom development.

CBD, a non-psychotropic cannabinoid, is well known for its multi-target effects, with potent anti-inflammatory and neuro-protective properties in neurological preclinical models [14], although the anti-inflammatory mechanism is still incompletely understood. Experiments have demonstrated that low doses of CBD act as adenosine A2A receptor-and Peroxisome Proliferator Activated Receptor gamma (PPARg) agonist, and as G-protein coupled receptor 55 (GPR55) antagonist, decreasing the levels of inflammatory mediators such as TNF-alpha, IL-6 and IL-12, without acting directly on cyclooxygenase 1 or 2 (COX-1, COX-2 [15]. In addition, CBD is a very potent anti-oxidant, more protective than α-tocopherol or vitamin C [16]. On CB1 receptors, CBD acts as negative allosterical modulator, decreasing partially the activity of ligands [17]. On CB2 receptors, CBD can act as receptor-inverse agonist. This may explain, at least in part, its anti-inflammatory effects and its inhibition of the migration of macrophages, microglial cells and neutrophils [18]. CBD shares with Riluzole effects on ion channels that are responsible for repetitive firing and transmitter release [19]. As some cases seem to be associated with mutations in the gene for copper-zinc superoxide dismutase 1 (Cu-Zn SOD1), a powerful natural antioxidant, it is noteworthy that CBD alters the expression of a wide range of genes involved in zinc homeostasis, oxidative stress, mitochondrial dysfunction, excitotoxicity, glutathione deprivation and anti-inflammatory signalling pathways [20,21].

These mechanisms of CBD are interesting as they fit many of the current hypothetical requirements for a successful drug for motor neuron diseases. Further on, CBD seems to be well tolerated and safe in humans, even at high doses and with chronic use [22], and can easily be combined with existing treatment regimens. However, more observations and thorough investigations are needed for assessing the potential role of CBD in this deadly disease.

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