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Experience with cannabidiol (CBD) in the multimodal management of children and young adults with Cerebral palsy (CP) and complex comorbidities.

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Introduction and background

The **«Center of Developmental and Pediatric Neurorehabilitation» (C.D.N)** in Switzerland is a neuropediatric competence center for children and adolescents diagnosed with acquired and innate brain pathologies. In our everyday practice we have to deal with patients suffering from severe spastic CP and/ or refractory epilepsy as well as with different comorbid conditions that can significantly decrease the quality of life such as chronic pain, sleep disorders, irritability and nausea.

Cannabidiol (CBD) products can be valid alleys against these disorders. CBD oils are legal in Switzerland since 2016 if they contain less than 1% THC. Palliative medicine physicians are challenged by lack of guidance regarding effectiveness and dosing of cannabis products in the setting of their emerging popularity.

Cannabidiol (CBD) is one of the prominent phytocannabinoids found in Cannabis sativa. It is differentiating from Δ9-tetrahydrocannabinol (THC) for its **non-psychotomimetic** profile and its therapeutic effects in different range of neurological and psychiatric disorders including, **refractory epilepsy, spasticity, neuropathic pain, nausea, mood disorders, schizophrenia, Parkinson disease and multiple sclerosis.** There is a growing body of preclinical and clinical evidence to support use of CBD oils for the above-mentioned conditions. In June 2018, the first CBD-based drug, Epidiolex, was approved by the US Food and Drug Administration for treatment of rare, severe epilepsy.

The mechanism of action of CBD in epilepsy is not yet fully understood. Some studies show that CBD is a multi-target drug whose anti-convulsant properties are supposed to be independent of endocannabinoid receptor CB1 and might be related to several underlying mechanisms, such as antagonism on the orphan GPR55 receptor, regulation of adenosine tone, activation of 5HT1A receptors and modulation of calcium intracellular levels. CBD is a lipophilic compound with low oral bioavailability (6%) due to poor intestinal absorption and high first-pass metabolism. Its exposure parameters are greatly influenced by feeding status (ie, high fat-containing meals). It is mainly metabolized by cytochrome P 450 (CYP) 3A4 and 2C19, which it strongly inhibits. Important interactions with antiepileptic drugs include an increased risk of hepatotoxicity with valproic acid and an increased level of active metabolites with benzodiazepines, contributing to somnolence and potentially to efficacy. However CBD has shown an adequate safety profile and an acceptable tolerability in children and young adults.

Objectives

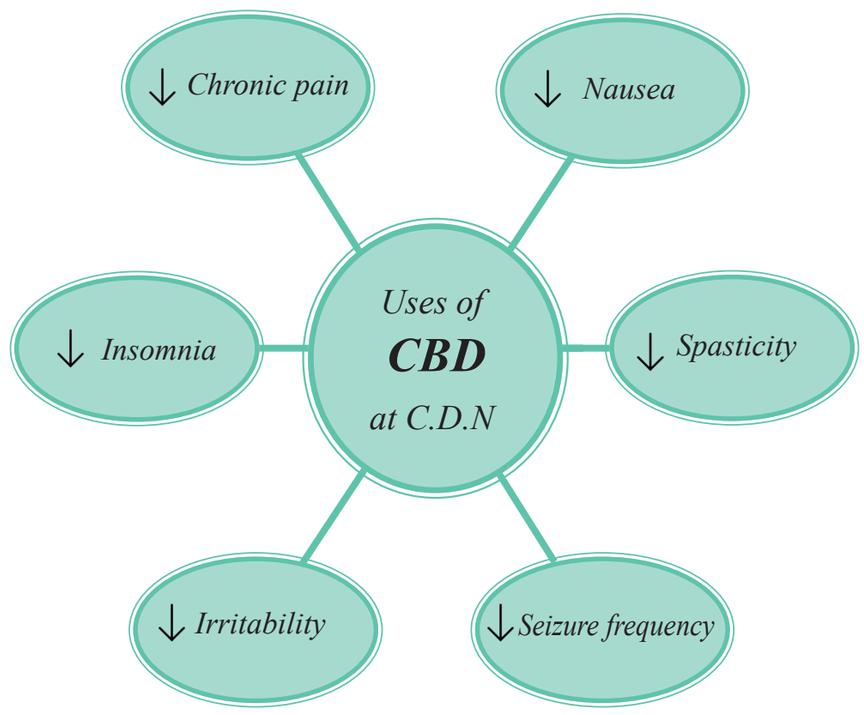
The aim of our experience-based study is to describe the experience in our centre with a regimen of medical cannabidiol oil on individuals with severe and complex disabilities and in a general palliative care.

Patients and Methods

The included patients were diagnosed severe spastic CP (5) , dystonic CP (2), refractory epilepsy (4) and suffered from different comorbid conditions such as chronic pain, sleep disorders, irritability and nausea.
The selected formula contained CBD in different concentrations and < 1% tetrahydrocannabinol (THC) in sunflower oil for a sublingual application. 1 drop of CBD oil 5 % contains 2 mg CBD. The CBD dose ranged from 2 to 20 mg/kg for at least 12 weeks. Seizure frequency, gradient of irritability,change in the muscle tone, intensity of pain, nausea frequency, and secondary effects were assessed daily by nurses redacting calendars and and semi-quantitative questionnaires.

Results

Promising results were reported in management of the refractory epilepsy, with two patients who became seizure-free since the beginning of therapy with CBD in a dose range of 5 to 10 mg/kg, 3x/day.
Unsatisfactory results were observed concerning decreasing of severe spasticity. In 1 child with severe spasticity, the therapy was changed for THC (with better results in decreasing of spasticity) because of absence of effective benefits after 12 weeks of treatment with CBD at maximal doses of 10 mg/kg/day. Better results are observed however in the muscle tone's control in patients with dystonia at max doses of 10 mg/kg/day.
Very good results were shown regarding reduction of irritability and increase in attention and awareness levels, especially in children with autismus, intellectual disability and attention deficit disorder. As well as goo results in the control of chronic pain, nausea and amelioration of sleep quality.
As side effects diarrhea was the most prominent, in 1 patient stopped the therapy because of permanent diarrhea under of treatment at a CBD dose of 1.1 mg/kg/d.



Conclusion

Literature shows strong evidence for clinical benefits of CBD in different medical conditions. Our experience with CBD treatment in the multimodal management of a population of children and young adults with CP and complex comorbidities is varied and depends on the symptoms/disease treated. Generally CBD oil was well tolerated and nonsevere or mild adverse effects (mainly diarrhea) were reported. In the long term therapy ineffective results were shown in decreasing of severe spasticity as opposed to very good results in controlling the number of seizure in patients with refractory epilepsy. CBD appears as well as a good ally in clinical management of additional symptoms (irritability, pain, sickness and sleep disorders) in multiple comorbidity patients, improving quality of life.

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