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Short communication

Optimization of the CBD:THC ratio with a progressive titration of daily CBD intake in parallel with slight increase of THC in patients with various neurological conditions

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Introduction

Cannabis-based medicinal products containing Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) as principal bioactive compounds in mutual synergism with a multitude of other naturally occurring phytochemicals - concept known as "entourage effect" in full-spectrum extracts, have become increasingly famous in the supplementary treatment of neurological disorders (Russo, 2011).

According to this concept, the therapeutic activity of cannabis-based preparations does not depend solely on any single cannabinoid, but rather on the balanced interaction between all present cannabinoids and other multiple bioactive compounds that modulates the therapeutic action of cannabinoids. That proves that full-spectrum extracts compared to purified cannabinoid isolates, provides superior benefits, primarily important in treatment-resistant neurological diseases (Pamplona et al., 2018).

Neurological patients are often highly sensitive to the psychoactive side effects associated with THC such as anxiety, sedation, cognitive impairment, and other dose-related adverse reactions (Russo, 2011), requiring dose optimization during long-term cannabis-based therapy. Modern therapeutic approaches increasingly favor cannabis treatment containing low daily doses of THC combined with higher daily doses of CBD. High-dose CBD administration has demonstrated anticonvulsant, anxiolytic, anti-inflammatory, and neuroprotective properties, while simultaneously contributing to improved tolerability of THC (Blessing et al., 2015; Ibeas Bih et al., 2015, Whiting et al., 2015). Such an approach may be particularly beneficial in chronic neurological diseases requiring individualized treatment strategies in gradual dose adjustment.

Increasing evidence suggests that therapeutic efficacy significantly depends on CBD:THC ratio, presence of additional phytocannabinoids and terpenes and the gradual titration strategy used during treatment initiation, rather than solely doses of THC and CBD (Pamplona et al., 2018).

Therefore, individualized titration protocols based on low-dose increasing THC titration combined with variable progressive CBD up-titration, using full-spectrum cannabis extracts may represent a rational adjuvant treatment to standard conventional therapy of neurological patients. Such strategies could potentially maximize clinical benefits while minimizing dose-dependent adverse reactions, ultimately contributing to safer and more effective cannabinoid therapy.

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Materials and methods

The following preparations were used to support this evaluation:

1. OM Eliksir Magistral medicinal cannabis extract containing (10 mg THC + 10 mg CBD)/mL, as mixture of two standardized HAPA Pharm supercritical CO_2 extracts - THC and CBD, suitably diluted, providing CBD:THC ratio of 1:1;

2. OM Eliksir Magistral medicinal cannabis extract containing 100 mg CBD/mL, obtained by standardized HAPA Pharm supercritical CO_2 CBD dominant extract, suitably diluted to CBD 10% (w/v).

A simultaneous titration method of the daily intake of the two primary cannabinoids, THC and CBD, was employed across six dosing intervals ranging from 1 to 6 mg of THC, with a gradual increment of only 1 mg THC per interval. Since the first preparation presents a mixture of two individually standardized extracts, providing a CBD:THC ratio of 1:1, each THC dose interval (mg) was accompanied by the simultaneous administration of an equivalent dose of CBD (mg).

Targeted dose upgrade of CBD within each interval was provided by use of the second preparation, following the fundamental principles governing the dosing of cannabis-based medicinal products.

Within each titration interval THC dose (mg), several targeted escalations of the CBD dose (mg) were performed, resulting in a gradual increase of the CBD:THC ratio from approximately 20:1 up to 30:1. This approach was implemented to evaluate differences in treatment response associated with varying CBD:THC balance ratios.

Results and discussion

The purpose of the slight increase of THC in daily intake in each of 6 intervals in range of 1mg THC to 6mg THC, with slow increase of 1mg THC per interval, is predicted to obtain a clear representation of the impact of THC regarding the patient's overall condition.

On the other hand, the parallel sequential addition of significantly increasing daily doses of CBD, per each of the THC level intervals in range of 1mg THC to 6mg THC is performed. By monitoring the patient's condition at each THC dose interval separately, accompanied by CBD increase in daily administration providing CBD:THC ratio of 20:1 up to 30:1, per interval, presents opportunity to observe differences in the patient's condition regarding balance of benefits and side effects, at each level of evaluation.

Conclusion

By this approach, each patient gets the opportunity of safe introduction in cannabis-based treatment, leading to individual maintenance dose regarding separately daily intake of the both primarily cannabinoids with highlight on achieving CBD:THC optimal ratio, in order to provide positive balance of benefits vs side effects, which is the primary goal of this paper. In this way, the patient can achieve the desired therapeutic effects with low daily doses of the psychotropic THC administered alongside significantly higher daily doses of the non-psychotropic CBD. This combination may provide positive effects that would otherwise require substantially higher doses of THC if used alone, while simultaneously reducing the likelihood of psychotropic side effects of THC during treatment.

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