

Basic Recommendations for Creation of Dosage Schedule of Cannabis-based Products based on Benefit / Side Effects Ratio in Supplementary Treatment of Malignant Diseases

Gordana Trendovska Serafimovska^{*1}

¹HAPA PHARM, Blvd. "8^{mi} Septemvri"2-2, 1000, Skopje, N.Macedonia

Introduction

Cannabis-based formulations, containing declared content of cannabinoids provided by Cannabis natural extracts are recommended as supplementary treatment in addition to conventional anticancer therapy. They do not present alternatives to such therapy, nor are intended to exclude evidence-based conventional therapy prescribed by doctors, specialists of Oncology.

Approach to Cannabis treatment is shown to be quite individual, as well as adaptability, effectiveness and possible side-effects. Still, there are several basic recommendations that help in avoiding unwanted side-effects of such additional treatment:

- Starting with low doses, slowly increasing the doses in certain, adaptable time intervals.

The approach in introduction in Cannabis treatment and titration of the daily doses of cannabinoids (primarily THC and CBD) from low to higher quantities as well as the duration of each time interval of titration must be individual, in correspondence with the needs of any patient and their general health condition.

The aim of this study was to give basic recommendations for creation of individual dosing schedule of products containing cannabinoids in treatment of malignant diseases, based on benefit/side effects ratio and available literature data (Fischer et al., 2017; Gourlay, 2005; Kicman & Toczek, 2020; Pisanti et al., 2017; Romero-Sandoval et al., 2017; Sachs et al., 2015; VanDolah et al., 2019).

Materials and methods

The following formulations, supplied by a local manufacturer of products containing cannabinoids, were used during this research:

- Medicinal Cannabis extract (10 mg THC + 10 mg CBD)/ml;
- Medicinal Cannabis extract (20 mg THC + 20 mg CBD)/ml;
- Medicinal Cannabis extract (40 mg THC + 40 mg CBD)/ml;
- 10% CBD Oil solution.

Medicinal Cannabis extracts containing declared content of THC and CBD, in ratio 1:1, were administered to patients with malignant diseases by method of continuous slow titration of dose, in predefined time intervals. CBD 10% Oil solution was additionally included to increase TDI of CBD, to reach optimal balance of THC and CBD, with maximum benefit and minimum side-effects.

The presented approach in creation and concepts of dosage schedules is based on my large and abundant more than 6 year's experience with patients who wish to remain anonymous, gained and confirmed on many international symposia, seminars and presentations, as well as communication with highly appreciate foreign experts and Cannabis therapy consultants and consumers.

Results and discussion

Total daily dosage and time required for adaptation of

a patient to each dose is individual, and should last sufficiently long to make evaluation available for both benefits and side-effects of Cannabis treatment on the global health condition of a patient. Total daily dose must be strictly controlled, gradually increasing with a suitable delay on each interval of increase of the dosage, lasting for around 2-3 days in lower doses and intervals of 3-5-7 days or even longer, if necessary, for higher doses of cannabinoids. Nevertheless, every assessment of a dose as "low" or "high" is very relative, that is the main reason for the need of individual approach in dosage for each patient. The introduction in the treatment must always start with a low dose, for example about 2 mg THC. If there is objective need for rapid increase of the dosage, especially if it regards to THC dose, the duration of each dosing interval may last even shorter than the usually accepted 2-3 days, only if the patient tolerates the titration of dose relatively well without occurring significant side-effects. Eventually occurring side-effects may be successfully corrected by prolonging the interval of continuous titration for a few more days, so the patient can adjust to a lower dose interval and tolerate it well, before going to higher, subsequent dose interval.

- Individual doses of THC should be carefully distributed within total daily dose (TDI), so that the main quantity of THC has to be administered about 1 hour before going to bed, since then the psychotropic effect does not present unwanted adverse effect.

Total daily doses of cannabinoids (TDI) are conveniently divided and distributed in several lower single doses, usually administered at least 2-3 times during daytime. Correspondingly, about less than 50% of TDI dose of THC should be distributed in several smaller doses in daytime and the rest, usually about 50-70, even 80% of TDI of THC is preferably to be administered before going to sleep.

- One must be patient regarding the duration of the treatment and acquiring its health benefits.

This in practice can be a frustrating factor for patients with acute symptoms, such as chronically pain, nausea, vomiting, spasms, etc. It is well known that Cannabis treatment has a different effect on any individual patient, but, its effects do not appear immediately, since it takes enough time that is difficult to be predicted for each individual patient. By controlled dosage increase, followed by continuous monitoring and dose adjustments, if necessary, the most appropriate dose for each patient is assessed, in relation to the recognition of benefits and gaining tolerance or even elimination of occurring unwanted adverse effects.

- To overcome the psychotropic effects of THC, when using medical formulation with a declared content of THC or medical formulation with a declared THC and

CBD content, it is necessary to enrich the treatment with an additional primarily CBD containing product.

Parallel administration of additional, primarily CBD containing product (limited to max. 0.2% - 0.3% THC), is recommended to be included in the treatment, especially concentrated at first part of day.

CBD is recognized for its many health benefits, but, if taken in parallel with THC, CBD is beneficial in increasing the positive effects of THC, while in the same time reducing THC's psychotropic side-effects.

Accordingly, most unwanted adverse effects of THC during Cannabis-based products treatment may be successfully reduced or completely avoided if in the duration of careful gradual increase of THC dose, a significant increase of CBD dosage (3-5 times that of THC) is administered alongside.

Conclusion

According the presented way of individual approach in dosage creation, each individual patient should reach optimal dosage and balance of THC and CBD. The patients, their family and doctor, by gradual titration of doses of both primarily cannabinoids and monitoring of their general health condition, should achieve an optimal benefit / side effects ratio which represent their individual Maintenance Dose as continuous supplementary treatment of malignant diseases.

References

- Fischer, B., Russell, C., Sabioni, P., van den Brink, W., Le Foll, B., Hall, W., Rehm, J. 2017. Lower-Risk Cannabis Use Guidelines: A Comprehensive Update of Evidence and Recommendations. *AJPH*, 107(8), pp. e1-e12. <https://doi.org/10.2105/AJPH.2017.303818>.
- Gourlay, D., 2005. *Addiction and Pain Medicine*. *Pain Res. Manag.*, 10 Suppl A:38A-43A. <https://doi.org/10.1155/2005/512653>.
- Kicman, A., Toczek, M., 2020. The Effects of Cannabidiol, a Non-Intoxicating Compound of Cannabis, on the Cardiovascular System in Health and Disease. *Int. J. Mol. Sci.*, 21(18), 6740. <https://doi.org/10.3390/ijms21186740>.
- Pisanti, S., Malfitano, A.M., Ciaglia, E., Lamberti, A., Ranieri, R., Cuomo, G., Abate, M., Faggiana, G., Proto, M.C., Fiore, F., Laezza, C., Bifulco, M. 2017. Cannabidiol: State of the Art and New Challenges for Therapeutic Applications. *Pharmacol. Ther.*, 175, 133-150. <https://doi.org/10.1016/j.pharmthera.2017.02.041>.
- Romero-Sandoval, E.A., Kolano, A.L., Alvarado-Vázquez, P.A., 2017. Cannabis and Cannabinoids for Chronic Pain. *Curr. Rheumatol. Rep.*, 19(11) 67. DOI:10.1007/s11926-017-0693-1.
- Sachs, J., McGlade, E., Yurgelun-Todd, D., 2015. Safety and Toxicology of Cannabinoids. *Neurotherapeutics*, 12(4), 735-46. <https://doi.org/10.1007/s13311-015-0380-8>.
- VanDolah, H.J., Bauer, B.A., Mauck, K.F. 2019. Clinicians' Guide to Cannabidiol and Hemp Oils. *Mayo Clin. Proc.*, 94(9), 1840-1851. <https://doi.org/10.1016/j.mayocp.2019.01.003>.