



Doses of cannabis and cannabinoid products in clinical trials - A rapid review

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BACKGROUND

- Cannabis and cannabinoid (CaC) products are increasingly used for various medical conditions.
- Identifying evidence that supports safe and effective dosing is important to guide policy and clinical practice.
- The objective of this rapid review was to summarize doses of CaC in randomized clinical trials (RCT) investigating the effectiveness and safety of CaC products.

METHODS

- To retrieve RCTs that assessed the effectiveness and safety of CaC in clinical settings we identified relevant studies from previously published reviews and updated this information with a new literature search in PubMed, Embase, and Web of Science, to retrieve recently published RCTs between November 2019 and October 2021.
- We excluded articles that were inaccessible or not written in English. Two reviewers (NES, SJ) extracted information about indication, route of administration (RoA), products used (e.g., tablet), agents used (e.g., cannabidiol (CBD)), doses, and publication year.
- We conducted a qualitative synthesis of included studies.

Table 1. Doses of cannabis and cannabinoid products investigated in randomized clinical trials

Investigated agent	Included Trials	Minimum daily dose in mg (protocol)	Maximum daily dose in mg (protocol)	Highest consumed daily mean dose in mg
THC	18	1.2	216	82.8
CBD	8	20	800	74.8
THC / CBD	28	2.7/2.5	142/145.8	30.8/31.6
Dronabinol	12	2.5	40	NA
Nabilone	12	0.5	9	1.95
Levonandradol	2	2	4	NA
CT3	1	10	80	NA

-NA= not available

Table 2. Number of randomized clinical trials in different indications that investigated cannabis and cannabinoids products

Indication	Included Trials	Investigated THC	Investigated CBD	Investigated THC /CBD	Investigated Dronabinol	Investigated Nabilone
ALS	2	0	0	0	2	0
Cancer	18	1	0	7	4	6
Chronic non-malignant pain	24	8	0	11	2	3
Glaucoma	2	1	1	0	0	0
HIV	3	1	0	0	2	0
Multiple sclerosis	10	2	0	8	0	0
PTSD	4	1	1	1	0	1
Seizures / epilepsy	3	0	3	0	0	0
Other	12	4	3	1	2	2

-ALS= Amyotrophic lateral sclerosis; HIV=Human immunodeficiency virus; PTSD= Posttraumatic stress disorder;
 -other: Anxiety, Parkinson's disease, psychosis, anorexia, inflammatory bowel disease, fibromyalgia, dystonia, paraplegia, dementia, Tourette's syndrome, sickle cell disease

RESULTS

- We identified 81 RCTs. Doses were either defined by content of delta-9-Tetrahydrocannabinol (THC) (18), CBD (8), THC and CBD (28), Dronabinol (12), Nabilone (12), Levonandradol (2), or CT3 (1) (table 1).
- Minimum and maximum daily doses as defined per protocols were 1.2–216, 20–800, 2.7/2.5–142/145.8 mg, for THC, CBD, and THC/CBD defined products, respectively.
- The consumed daily mean dose was reported in only 10 publications, and out of those the highest was 82.8, 74.8, and 30.8 /31.6 mg for THC, CBD, and THC /CBD defined products, respectively.
- The majority of identified trials were in patients with chronic pain (24), cancer (18), and multiple sclerosis (10) (table 2).
- Investigated agents differed across indications, and products defined by THC / CBD content were the most frequent investigated products.
- Investigated doses differed widely across products, RoA and indication:
 - For, THC and THC/CBD defined products, the maximum daily dose (216 mg , 142 /145.8 mg) was found in a trial that evaluated inhalation in patients with posttraumatic stress disorder.
 - For CBD defined products the maximum allowed daily dose was in patients with psychosis.

CONCLUSIONS

- CaC RCT protocols included a wide range of doses, which differed by indication, product, and RoA. However, the consumed dose was often uncertain.
- Investigated doses appeared generally lower than those certified for medical marijuana patients in Florida.
- In selected conditions, for specific RoAs and products, evidence exists to guide safe and effective dosing, but more evidence is needed for the majority of CaC products across medical conditions.

DISCLOSURES

All authors have no relevant disclosures.

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