Oral THC: CBD cannabis extract for refractory chemotherapy-induced nausea and vomiting: a randomised, placebo-controlled, phase II crossover trial

Grimison, P. et al. Annals of Oncology. 2020; 31:11, 1553-60.

Introduction

Chemotherapy-induced nausea and vomiting (CINV) are distressing and commonly encountered adverse effects of cancer treatment that impact patients' quality of life and treatment compliance.

Some patients undergoing emetogenic chemotherapy have refractory CINV, defined as the failure to control nausea and vomiting even with optimal antiemetic therapy. **As many as 1 in 2 experience significant nausea and 1 in 3 continue to experience vomiting.**

While evidence for the efficacy of inhaled medical cannabis and THC-only medications in refractory CINV are limited, pilot studies indicate that 1:1 delta-9-tetrahydrocannabinol **(THC) and cannabidiol (CBD) as an oral formulation has greater treatment potential.**

Aim of the study

To evaluate an oral THC:CBD cannabis extract in preventing refractory CINV over multiple chemotherapy cycles compared to placebo.

Methods and materials

This study was a randomised, double-blind, placebo-controlled, phase II crossover trial of **81 adult patients with refractory CINV**, comparing oral THC:CBD with placebo, alongside prophylactic antiemetics.

Patients were receiving **curative and palliative intravenous chemotherapy** for cancer of any stage and any intervention line (1st- 3rd or more). Enrolled patients had a mean age of 55, were typically female, and had a good ECOG performance status (0-1).

The **crossover design** randomised patients to either receive THC:CBD or placebo for 6 days, starting one day before their first chemotherapy cycle. For the following cycle, patients received the alternative intervention.

The oral cannabis extract capsules contained **THC and CBD in a 1:1 ratio.** The starting dose was 12.5mg THC:CBD daily, split over three doses. Based on the patient's CINV and side effects, the dose was adjusted accordingly up to a maximum total of 30mg THC:CBD daily.

Primary outcomes

The primary outcome was the **difference in the proportion of patients achieving complete response** (no vomiting and no use of rescue medications) during the overall phase of treatment (0-120 hours post-chemotherapy) when treated with THC:CBD vs. placebo.

The secondary outcomes include:

- Differences for self-reported 'complete response', 'no vomiting', 'no clinically significant nausea' (defined as nausea <2 on a 10-point scale) and 'no use of rescue medications' during the overall phase (0-120 hours) of chemotherapy
- Quality of life assessed by the Functional Living Index-Emesis (FLIE) questionnaire and Assessment of Quality of Life-8 Dimensions (AQOL-8D)
- Adverse events

Results

The primary outcome was met, with a higher proportion of patients achieving complete response in the THC:CBD group compared to the placebo group (25% vs 14%, p=0.04).

Improvements were observed in THC:CBD patient group vs placebo for the following outcomes:

- Proportion of patients experiencing:
  - no vomiting (p=0.05)
  - no use of rescue medications (p=0.04)
  - no significant nausea (p=0.03)
- Mean and maximum number of vomiting events per day (p=0.003, 0.001)
- Mean and maximum nausea scores (p<0.001)

There was no significant carryover or period effect observed between cycles, suggesting that the order of THC:CBD to placebo and the period that THC:CBD was taken in did not significantly affect its efficacy.

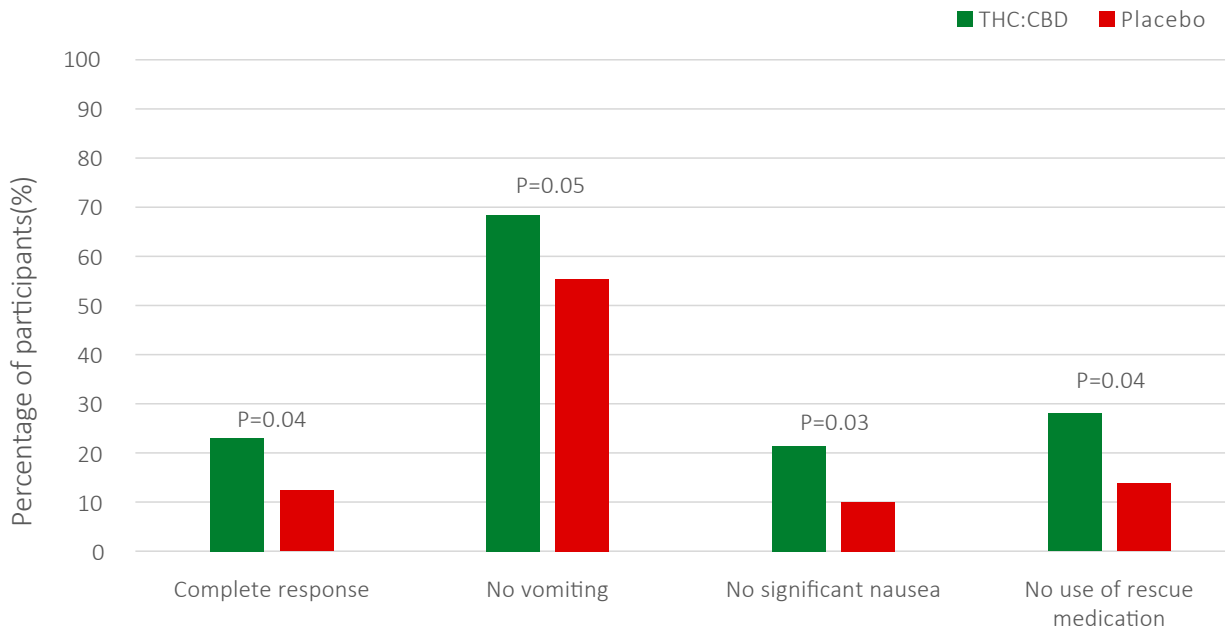

Figure 1: Efficacy of THC:CBD versus placebo during 0-120 h, within-patient comparisons between cycles A and B

There was an improvement in AQOL-8D quality of life (0.04, 95% CI; 0.01- 0.07, p=0.019), with significant improvements reached in the mental health and pain subdimensions.

Of the serious adverse events reported, none were attributed to study treatments and the incidence of adverse events were similar between the two groups.

Discussion

This study met its primary outcome, demonstrating the **activity and tolerability** of oral THC:CBD cannabis extract for the prevention of refractory CINV in cancer patients. The intervention was well-tolerated with no treatment-associated serious adverse events.

These findings support further investigation of oral THC:CBD cannabis extract as a potential treatment option for patients with refractory CINV and the study will progress to phase III.

Further studies are needed to determine the optimal dosing and administration of THC:CBD cannabis extract and its efficacy in different patient populations.

References

Grimison, P., Mersiades, A., Kirby, A., Lintzeris, N., Morton, R., Haber, P., Olver, I., Walsh, A., McGregor, I., Cheung, Y. and Tognela, A. 2020. Oral THC:CBD cannabis extract for refractory chemotherapy-induced nausea and vomiting: a randomised, placebo-controlled, phase II crossover trial". Annals of Oncology, 31:11, 2020, pp 1553-1560

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