Therapeutic use of Cannabis sativa on chemotherapy-induced nausea and vomiting among cancer patients: systematic review and meta-analysis

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CRD summary
The review concluded that dronabinol was statistically and clinically more effective as an anti-emetic than neuroleptics. Nabilone and levonantradol were not statistically more effective than neuroleptics, but were clinically more effective. There were some methodological problems with the review and the authors’ statement that caution was warranted when interpreting the results appears justified.

Authors' objectives
To evaluate the use of cannabis as a therapeutic agent for treating chemotherapy-induced nausea and vomiting in cancer patients.

Searching
PubMed, EMBASE, PsycINFO, LILACS and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to December 2006 without language restrictions. Search terms were reported. Reference lists of selected articles were searched. Authors of the articles were contacted.

Study selection
Randomised controlled trials (RCTs) in patients who received chemotherapy for any type of cancer and were treated with a substance derived from cannabis and/or smoked cannabis compared with any control were eligible for inclusion. Chemotherapy regimens included agents with low, moderate and high emetic potential. There were no limitations on the setting, age and gender of participants, timing of intervention and cointerventions for nausea and vomiting.

The included trials evaluated nabilone, dronabinol or levonantradol versus placebo or neuroleptics in patients with various types of cancer. The reported outcomes included nausea, vomiting, appetite, preference and adverse events. Many of the trials allowed anti-emetic dose adjustment and/or other anti-emetic drugs to be administered.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
Two reviewers independently assessed trial quality using Jadad criteria (results not presented) and Mulrow and Oxman criteria. Trials were categorised into three groups according to the randomisation procedure of allocation concealment: A (low risk of bias), B (moderate risk of bias) and C (high risk of bias).

Data extraction
Data was extracted on anti-emetic efficacy and preference for anti-emetic and used to calculate relative risks (RRs) and 95% confidence intervals (CIs).

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
A random-effects meta-analysis was used to pool relative risks for anti-emetic efficacy and preference. Separate analyses were performed for each outcome according to cannabinoid drug and comparison. Statistical heterogeneity was assessed using $X^2$ and $I^2$ statistics. The number needed to treat (NNT) was calculated for anti-emetic efficacy. Publication bias was assessed using funnel plot analysis.

Results of the review
Thirty RCTs (n=1,719 participants) were included in the review. Most trials were cross-over design. Half of the trials...
had a sample size of less than 50 patients. Six trials were rated A (low risk of bias) and 24 trials were rated B (moderate risk of bias).

**Anti-emetic efficacy:** Compared with neuroleptics, dronabinol had a statistically significantly lower risk of nausea and vomiting (RR 0.67, 95% CI 0.47 to 0.96, I²=79%; five trials). The number needed to treat with dronabinol to prevent one episode of vomiting was 3.4 patients. Compared with placebo, there was no statistically significant difference in risk of nausea and vomiting with dronabinol (RR 0.47, 95% CI 0.19 to 1.16, I²=91%; two trials). Compared with neuroleptics, there was no statistically significant difference in risk of nausea and vomiting with nabilone (RR 0.88, 95% CI 0.72 to 1.08, I²=64%; five trials) and levonantradol (RR 0.94, 95% CI 0.75 to 1.18, I²=37%; four trials).

**Preference for anti-emetic therapy:** Pooling 18 trials of anti-emetics demonstrated a statistically significant preference for cannabis-based treatment compared with control (RR 0.33, 95% CI 0.24 to 0.44, I²=65%).

Funnel plot assessment showed symmetry, which indicated a low risk of publication bias.

**Authors' conclusions**
In terms of anti-emetic efficacy, dronabinol was statistically and clinically more effective than neuroleptics. Nabilone and levonantradol were not statistically more effective than neuroleptics, but were clinically more effective. Caution is warranted due to the small sample size and number of studies.

**CRD commentary**
Inclusion criteria for the review were clearly defined and several relevant databases were searched. No specific attempts to locate unpublished studies were made. Publication bias was assessed and was not detected. Suitable methods were used to minimise the risk of reviewer bias during the quality assessment; the authors did not report on whether such methods were used for study selection and data extraction. Quality assessment was undertaken using Jadad criteria and Mulrow and Oxman criteria; results of the Jadad assessment were not presented. Many of the trials had small sample sizes (acknowledged by the authors). The trial outcomes were assessed using random-effects meta-analysis; however, many eligible trials were excluded due to lack of data and it was unclear whether attempts were made to contact the trial authors. It was unclear how crossover trials were treated within the meta-analysis, which was crucial as they were pooled with the parallel group trials. Statistical heterogeneity was calculated, but this was not explored further even though many analyses showed high statistical heterogeneity.

Overall, there were some methodological problems with the review and the authors’ statement that caution is warranted when interpreting the results appears justified.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that recent findings could help with developing new synthetic cannabinoid antagonists for therapeutic use.

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