

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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Do cannabinoids constitute a therapeutic alternative for anorexia nervosa?

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Abstract

INTRODUCTION

Cannabinoids have been postulated as an alternative for anorexia nervosa. However, their actual clinical efficacy and safety are still discussed.

METHODS

To answer this question we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies and generated a summary of findings table using the GRADE approach.

RESULTS AND CONCLUSIONS

We identified four systematic reviews including two primary studies, both corresponding to randomized trials. We concluded cannabinoids might not increase weight or improve symptoms in anorexia nervosa, and are probably associated to frequent adverse effects.

Problem

Anorexia nervosa is an eating disorder characterized by distortion in body image perception leading to weight loss and malnutrition. It causes important work, social and family dysfunction, and in severe cases it can be fatal.

Cannabinoids, by their effects as appetite stimulants would promote weight gain and so constitute a therapeutic alternative in anorexia nervosa. However, its clinical

effects and safety still generate controversy among patients and clinicians.

Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and

reanalyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a

summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- Cannabinoids might not increase weight or improve symptoms in anorexia nervosa.
- Cannabinoids are probably associated to frequent adverse effects in patients with anorexia nervosa, so the risk / benefit balance is not favorable.

About the body of evidence for this question

| | |
|--|---|
| What is the evidence. See evidence matrix in Epistemonikos later | We found four systematic reviews [1],[2],[3],[4] which included two primary studies that answered the question of interest, reported in three references [5],[6],[7]. Both studies correspond to randomized trials. |
| What types of patients were included* | One trial [5] included 11 women with a primary diagnosis of anorexia nervosa in a hospital setting. The average age was 23.6 years. The diagnosis of anorexia nervosa was made based on the Feighner criteria. All patients had amenorrhea and had lost at least 25% of their weight but were not below 15% of ideal weight **. The other trial [6] included 25 women aged over 18 years, diagnosed with DSM-IV anorexia nervosa for at least 5 years. Patients were considered in ambulatory and hospitalized setting. |
| What types of interventions were included* | In one trial [5] THC (delta-9-tetrahydrocannabinol) was used orally in doses between 2.5 and 10 mg three times daily. The control group received an active placebo (oral diazepam between 3 and 15 mg three times daily). In addition to the pharmacological treatment under study, patients received individual psychotherapy twice a week, group therapy once a week, and nasogastric tube feeding occasionally **. In another trial [6] dronabinol 2.5 mg twice daily was compared orally versus placebo. In both groups, the regular baseline treatment was maintained. |
| What types of outcomes were measured | The main outcome used by systematic reviews was weight gain measured in kilograms [5],[6]. In addition, the following psychiatric scales were used [5]. HSCL-90: Hopkins Symptom Checklist-90 GAAQ: Goldberg Anorectic Attitude Questionnaire SDS: Goldberg Situational Discomfort Scale PRS: Psychiatric Rating Scale Other outcomes evaluated were the presence of adverse effects, such as sleep disturbance, paranoia and dysphoria. Follow-up was performed in one trial for 4 weeks [5] and for 8 weeks in the other trial [6]. |

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

** Information obtained directly from the primary study, because information provided by systematic reviews was incomplete.

Summary of findings

The information on the effects of cannabinoids for anorexia nervosa is based on two trials that included a total of 36 patients [5],[6],[7].

The trials measured weight and symptoms based on clinical efficacy scales: HSCL-90, GAAQ, SDS, and PRS. The summary of findings is the following:

- Cannabinoids might not increase weight in anorexia nervosa. The certainty of the evidence is low.
- Cannabinoids might not improve symptoms in anorexia nervosa. The certainty of the evidence is low.
- Cannabinoids are probably associated to frequent adverse effects in patients with anorexia nervosa. The certainty of the evidence is moderate.

| Cannabinoids for anorexia nervosa | | |
|---|--|-----------------------------------|
| Patients | Anorexia nervosa | |
| Intervention | Cannabinoids | |
| Comparison | Diazepam | |
| Outcomes | Effects | Certainty of the evidence (GRADE) |
| Weight | No effect was found on this outcome for THC [1] or dronabinol use [4]. | ⊕⊕○○ Low ^{1,2} |
| Clinical effectiveness scales (HSCL-90, GAAQ, SDS y PRS)* | No effect was found on any scale [3]. | ⊕⊕○○ Low ^{1,2} |
| Adverse effects | There was an increase in sleep disturbance [2], and presence of paranoia and dysphoria [1]. In addition, adverse effects in other populations are common [8] | ⊕⊕⊕○ Moderate ³ |
| GRADE: evidence grades of the GRADE Working Group (see later in this article) | | |
| * HSCL-90: Hopkins Symptom Checklist-90, GAAQ: Goldberg Anorectic Attitude Questionnaire, SDS: Goldberg Situational Discomfort Scale, PRS: Psychiatric Rating Scale. | | |
| ¹ We decided not to downgrade the certainty of the evidence due to risk of bias, because the presence of bias would reinforce the conclusion of no effect. | | |
| ² We downgraded the certainty of the evidence in two levels for imprecision due to the small sample of population studied. | | |
| ³ We downgraded the certainty of the evidence in one level for indirectness since it comes from patients with other conditions. | | |

Follow the link to access the interactive version of this table ([Interactive Summary of Findings – iSoF](#))

| About the certainty of the evidence (GRADE)* |
|--|
| <p>⊕⊕⊕⊕</p> <p>High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.</p> |
| <p>⊕⊕⊕○</p> <p>Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate</p> |
| <p>⊕⊕○○</p> <p>Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.</p> |
| <p>⊕○○○</p> <p>Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.</p> |
| <p>*This concept is also called ‘quality of the evidence’ or ‘confidence in effect estimates’.</p> <p>† Substantially different = a large enough difference that it might affect a decision.</p> |

Other considerations for decision-making

To whom this evidence does and does not apply

- The evidence presented in this summary applies to women diagnosed with anorexia nervosa.
 - The population studied includes inpatients and outpatients, so it is applicable to any setting.
 - In one trial the diagnosis of anorexia nervosa was based on Feighner criteria, which are part of the DSM-III and in the other it was based on DSM-IV.
-

About the outcomes included in this summary

- The outcomes presented in the summary of findings table are those considered critical for health decision-making by the authors of this article.
 - We searched for a core outcome set for anorexia nervosa in the COMET initiative database (Core Outcome Measures in Effectiveness Trials) but it is not yet available.
-

Balance between benefits and risks, and certainty of the evidence

- It is an intervention that might have no benefit and that entails adverse effects, so the risk-benefit balance is not favorable.
-

Resource considerations

- Commercial cannabinoid formulations are generally expensive.
 - The cost-benefit balance is not favorable, since it is a costly intervention with no clear benefit and entails adverse effects.
 - In addition, the use and marketing of these drugs is not authorized in many countries, so the cost associated with legalization, production and marketing is probably substantive.
-

What would patients and their doctors think about this intervention

- Faced with the evidence presented in this summary, most patients and clinicians should lean against the use of cannabinoids in anorexia nervosa.
 - There is currently a positive perception of the therapeutic effects of cannabinoids, both in the public and health professionals, which puts additional difficulties for informed decision-making in this context.
-

Differences between this summary and other sources

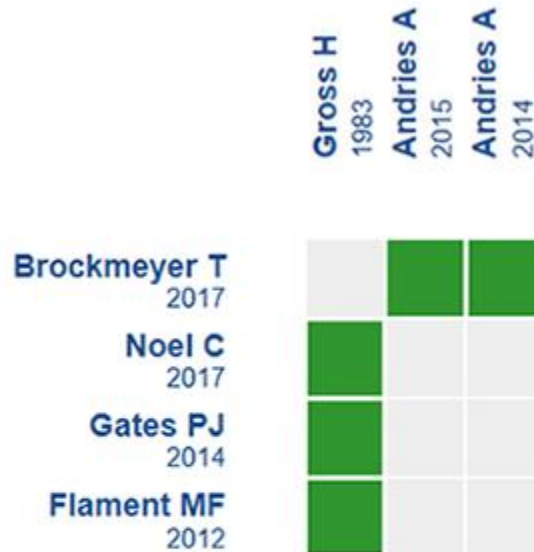
- The conclusions of this summary coincide with the different systematic reviews identified, both in terms of the absence of effect and the presence of adverse effects.
 - The conclusions of this summary agree with the main guidelines, such as The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research, which state there is insufficient evidence to support or refute the use of cannabinoids in anorexia nervosa [\[9\]](#).
-

Could this evidence change in the future?

- The likelihood of future evidence changing the conclusions of this summary regarding the benefits of cannabinoids in anorexia nervosa is high, due to the existing uncertainty.
 - There are no ongoing trials addressing this question according to the International Clinical Trials Registry Platform of the World Health Organization.
 - New systematic reviews could provide clearer conclusions, since the ones identified for this summary may not contain the totality of the evidence available for this topic, and have important limitations. We did not identify ongoing systematic reviews in PROSPERO database.
-

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question. Rows represent systematic reviews, and columns show primary studies. The boxes in green correspond to studies included in the respective revisions. The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version**: [Cannabinoids for anorexia nervosa](#)

Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the

body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (<http://dx.doi.org/10.5867/medwave.2014.06.5997>)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

Potential conflicts of interest

The authors do not have relevant interests to declare.

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