INPLASY

Effects of cannabinoids use in temporomandibular disorders: a scoping review

INPLASY2024120087

doi: 10.37766/inplasy2024.12.0087

Received: 20 December 2024

Published: 20 December 2024

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2024120087

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 December 2024 and was last updated on 20 December 2024.

INTRODUCTION

Review question / Objective Is the use of cannabinoids effective in controlling TMD-related pain?

Background Temporomandibular disorders (TMD) refer to a group of conditions affecting the temporomandibular joints (TMJ), masticatory muscles, and related structures, characterized by symptoms such as jaw pain, limited movement, joint noises during function, and generalized myofascial discomfort. These disorders are recognized as the second most common musculoskeletal condition associated with pain and disability, with a prevalence of about 31% among adults/elderly and 11% in children/adolescents. According to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), TMD can be categorized into pain-related disorders and joint-related disorders. Myofascial pain, primarily affecting the masticatory muscles, is the most common pain-related disorder. Myofascial pain often manifests as chronic pain in the masticatory muscles, radiating to areas like the ears, neck, and head. It can also result in muscle strain, spasms, and functional limitations. Diagnosis typically relies on a detailed patient history and physical examination, supplemented by radiographic studies when necessary. Treatment for myofascial pain aims to reduce pain and restore function, often beginning with noninvasive approaches. Pharmacological therapies, such as nonsteroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, corticosteroids, analgesics, benzodiazepines, and tricyclic antidepressants, are commonly used adjunctively to manage pain and inflammation. However, the use of these medications is often limited by their associated adverse effects, which may restrict their suitability

for some patients. In recent years, cannabis has emerged as a potential therapeutic option for managing pain and inflammation, particularly in cases where traditional treatments have proven inadequate. Cannabis sativa, a plant commonly known as cannabis, contains over 565 chemical compounds, including more than 100 cannabinoids. The primary cannabinoids of interest are delta-9-tetrahydrocannabinol (THC), cannabidiol (CBD), and cannabinol (CBN). THC is the primary psychoactive component of cannabis and is known for its analgesic properties, while CBD also demonstrates significant effects on pain control and possesses anti-inflammatory characteristics. The human body's endocannabinoid system is integral to the action of cannabinoids, operating through two main receptors: CB1 and CB2. CB1 receptors are predominantly located in the central nervous system but are also found in peripheral tissues, including the trigeminal ganglion neurons. CB2 receptors are primarily associated with the immune system. These receptors have become attractive targets for therapeutic pain management, as their activation has been shown to induce pain relief in various models of nociceptive, inflammatory, and neuropathic pain. Given the promise of cannabinoids, both clinical and preclinical studies have explored their effectiveness in managing pain associated with TMD. The potential benefits of cannabinoids for TMD patients lie in their dual action: reducing pain and addressing inflammation, offering an alternative approach for those who experience limited success with conventional treatments.

Rationale In the human body, cannabinoids act on the endocannabinoid system through two cannabinoid receptors: CB1, primarily found in the central nervous system, but has also been found in many peripheral tissues, including trigeminal ganglion neurons, and CB2, which occurs mainly in the immune system. Both receptors have been considered attractive therapeutic targets for pain management, as they induce pain relief in various models of nociceptive, inflammatory, and neuropathic pain. In light of this, clinical and pre-clinical studies have investigated the effectiveness of cannabinoids in managing pain associated with temporomandibular disorders (TMD).

METHODS

Strategy of data synthesis A logical and descriptive summary of the results was made based on the review objective and question. A table was developed describing the characteristics of the included studies and the key information relevant to the review question.

Eligibility criteria The following inclusion criteria were adopted based on the following PPC criteria: (P) Population: patients/animals with TMD; (C) Concept: cannabinoids use; (C) Context: not applied. Clinical studies [including randomized clinical trials (RCTs), controlled clinical studies, cohort studies (prospective or retrospective), case series, case reports) and animal studies reporting data about the use of cannabinoids for TMD-related pain control were included. Original research articles that did not follow all the criteria defined above were excluded from this scoping review. Moreover, letters to the editor, conference proceedings, protocol articles, historical reviews, in vitro studies (cellular models), and unpublished articles were also excluded.

Source of evidence screening and selection Electronic searches of PubMed, EMBASE, Web of Science, Scopus, and Cochrane Library databases were conducted for publications up to August 2024. The search strategies were created using the Medical Subject Headings (MeSH) and Embase Subject Headings (Emtree). Boolean operators (AND and OR) combined the descriptors and improved the search strategy through different combinations, respecting each database syntax rule No filters were utilized in the search strategy. The publications found in all electronic databases were transferred to the EndNote Program™ X9 version (Thomson Reuters, New York, NY, USA) to remove duplicate references. Then, the results were exported to Rayyan QCRI software (Qatar Computing Research Institute, Doha, Qatar) for selection by titles and abstracts. The reference lists of the identified articles were also hand-searched for additional studies.

Two investigators (L.C.S and C.F.B) made the initial search for the evaluation of titles and abstracts independently using the previous eligibility criteria. Irrelevant studies were excluded, and the full text of the articles included based on title and abstract were independently read and evaluated according to selection criteria (L.C.S and C.F.B). Disagreements between reviewers were resolved by discussion, including a third investigator (D.A.F.A) for the final decision. The articles excluded in the full-text analysis were listed separately, and the reasons for exclusion were specified.

Data management Two investigators (L.C.S and C.F.B) independently read all studies and extracted the following data for animal studies: (a) animal type, (b) TMD model, (c) experimental groups, (d)

methods of pain evaluation, and (e) main outcomes. For clinical studies, the data extracted were: (a) study type; (b) patients' number, gender, and mean age in each group; (c) medical history; (d) TMD treatment protocol; (e) methods of pain evaluation; (f) follow-up and (g) main outcomes. After completing the data extraction, disagreements were discussed and resolved through consensus with the third reviewer (XXX).

Language restriction No language restriction.

Country(ies) involved Brazil.

Keywords Temporomandibular Joint Disorders; Cannabinoids; Masseter Muscle.

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