CANNABIDIOL AS AN ADJUVANT THERAPY IN THE MANAGEMENT OF POST-CHIKUNGUNYA INFLAMMATORY PAIN

USO DO CANABIDIOL COMO ADJUVANTE NO TRATAMENTO DA DOR INFLAMATÓRIA PÓS-CHIKUNGUNYA

USO DE CANNABIDIOL COMO ADYUVANTE EN EL TRATAMIENTO DEL DOLOR INFLAMATORIO TRAS CHIKUNGUNYA

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ABSTRACT

Chikungunya virus infection is associated, in a significant proportion of affected individuals, with the development of persistent inflammatory musculoskeletal pain, resulting in negative impacts on functionality and quality of life. Conventional therapeutic approaches used to manage this condition show limited long-term effectiveness, which has encouraged the investigation of adjuvant therapies capable of modulating the underlying inflammatory response. In this context, cannabidiol has attracted scientific interest due to its analgesic and

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anti-inflammatory properties described in different models of inflammatory and arthritic pain. This study aimed to critically analyze the available scientific evidence on the use of cannabidiol as an adjuvant therapy in the treatment of persistent inflammatory pain associated with Chikungunya virus infection. This qualitative study was conducted as a narrative and analytical literature review, based on searches in the PubMed, SciELO, and ScienceDirect databases, covering publications from the last ten years. The findings indicate that, although there are no clinical studies specifically evaluating the use of cannabidiol in post-Chikungunya inflammatory pain, evidence from other chronic inflammatory conditions demonstrates consistent analgesic and anti-inflammatory effects, supporting its biological plausibility as an adjuvant therapy. It is concluded that cannabidiol presents therapeutic potential in the management of persistent inflammatory pain; however, its clinical application in this specific context should be interpreted with caution, and well-designed clinical trials are required to confirm its efficacy and safety.

Keywords: Chikungunya. Inflammatory Pain. Cannabidiol. Adjuvant Therapy. Narrative Review.

RESUMO

A infecção pelo vírus Chikungunya está associada, em uma parcela significativa dos indivíduos acometidos, ao desenvolvimento de dor musculoesquelética persistente de caráter inflamatório, com impacto negativo na funcionalidade e na qualidade de vida. As abordagens terapêuticas convencionais utilizadas no manejo dessa condição apresentam eficácia limitada a longo prazo, o que tem motivado a investigação de terapias adjuvantes capazes de modular a resposta inflamatória subjacente. Nesse contexto, o canabidiol tem despertado interesse científico devido às suas propriedades analgésicas e anti-inflamatórias descritas em diferentes modelos de dor inflamatória e artrítica. O presente estudo teve como objetivo analisar criticamente as evidências científicas disponíveis sobre o uso do canabidiol como terapia adjuvante no tratamento da dor inflamatória persistente associada à infecção pelo vírus Chikungunya. Trata-se de um estudo de natureza qualitativa, caracterizado como um levantamento bibliográfico de caráter narrativo e analítico, realizado a partir de buscas nas bases de dados PubMed, SciELO e ScienceDirect, contemplando publicações dos últimos dez anos. Os resultados indicam que, embora não existam estudos clínicos específicos avaliando o uso do canabidiol na dor inflamatória pós-Chikungunya, evidências provenientes de outras condições inflamatórias crônicas demonstram efeitos analgésicos e anti-inflamatórios consistentes, sustentando sua plausibilidade biológica como terapia adjuvante. Conclui-se que o canabidiol apresenta potencial terapêutico no manejo da dor inflamatória persistente, entretanto sua aplicação clínica nesse contexto específico deve ser interpretada com cautela, sendo necessária a realização de ensaios clínicos bem delineados para confirmar sua eficácia e segurança.

Palavras-chave: Chikungunya. Dor Inflamatória. Canabidiol. Terapia Adjuvante. Revisão Narrativa.

RESUMEN

La infección por el virus Chikungunya se asocia, en una proporción significativa de las personas afectadas, con el desarrollo de dolor musculoesquelético persistente de naturaleza inflamatoria, lo que afecta negativamente la funcionalidad y la calidad de vida. Los enfoques terapéuticos convencionales utilizados en el manejo de esta afección tienen una eficacia limitada a largo plazo, lo que ha motivado la investigación de terapias adyuvantes capaces de modular la respuesta inflamatoria subyacente. En este contexto, el cannabidiol ha

despertado interés científico debido a sus propiedades analgésicas y antiinflamatorias descritas en diferentes modelos de dolor inflamatorio y artrítico. Este estudio tuvo como objetivo analizar críticamente la evidencia científica disponible sobre el uso del cannabidiol como terapia adyuvante en el tratamiento del dolor inflamatorio persistente asociado con la infección por el virus Chikungunya. Se trata de un estudio cualitativo, caracterizado como una revisión bibliográfica narrativa y analítica, realizada a partir de búsquedas en las bases de datos PubMed, SciELO y ScienceDirect, que abarcan publicaciones de los últimos diez años. Los resultados indican que, si bien no existen estudios clínicos específicos que evalúen el uso del cannabidiol en el dolor inflamatorio post-Chikungunya, la evidencia de otras afecciones inflamatorias crónicas demuestra efectos analgésicos y antiinflamatorios consistentes, lo que respalda su viabilidad biológica como terapia adyuvante. Se concluye que el cannabidiol presenta potencial terapéutico en el manejo del dolor inflamatorio persistente; sin embargo, su aplicación clínica en este contexto específico debe interpretarse con cautela, y se requieren ensayos clínicos bien diseñados para confirmar su eficacia y seguridad.

Palabras clave: Chikungunya. Dolor Inflamatorio. Cannabidiol. Terapia Adyuvante. Revisión Narrativa.

1 INTRODUCTION

Chikungunya virus (CHIKV) infection is an important public health problem in tropical and subtropical regions, mainly due to its persistent musculoskeletal manifestations. Although the acute phase of infection is generally self-limiting, a significant portion of individuals evolve with chronic inflammatory joint pain, morning stiffness, fatigue, and functional limitation, symptoms that may persist for months or years after the initial infection, negatively impacting quality of life (CHOPRA et al., 2011; CHOPRA; VENUGOPALAN, 2011; RODRÍGUEZ-MORALES et al., 2016; GUILLOT et al., 2020).

The persistence of pain after CHIKV infection is associated with the maintenance of a chronic inflammatory state, characterized by the sustained elevation of proinflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), as well as by the activation of immunological mechanisms similar to those observed in inflammatory rheumatological diseases. This pathophysiological profile contributes to the chronicity of symptoms and to the complexity of the clinical management of these patients (CHOPRA et al., 2011; PATHAK; MOHAN; RAVINDRAN, 2019).

Conventional therapeutic approaches used in the management of CHIKV-associated pain are predominantly based on the use of analgesics and non-steroidal anti-inflammatory drugs. However, scientific evidence indicates that these strategies have limited efficacy in long-term pain control, in addition to being associated with potential adverse effects resulting from prolonged use, reinforcing the need for complementary therapeutic alternatives (RODRIGO et al., 2022).

In this context, cannabidiol (CBD), a non-psychoactive phytocannabinoid derived from *Cannabis sativa*, has been widely investigated for its analgesic and anti-inflammatory properties. Experimental studies and scientific reviews demonstrate that CBD acts through different mechanisms, including modulating the endocannabinoid system, reducing the production of pro-inflammatory cytokines, and attenuating oxidative stress, mechanisms directly involved in the pathophysiology of chronic inflammatory pain (BOOZ, 2011; MLOST; BRYK; STAROWICZ, 2020; SKLENÁROVÁ; ŠÍMA; SLANAŘ, 2023).

Despite the promising results observed in models of inflammatory pain and other rheumatological conditions, there are still no specific clinical studies evaluating the application of cannabidiol in the management of persistent inflammatory pain after Chikungunya virus infection, setting up a relevant gap in the scientific literature. In view of this, the present study aims to critically analyze the available scientific evidence on the use of cannabidiol in the treatment of inflammatory pain, with emphasis on its possible application

in the post-CHIKV infection context (ARGUETA et al., 2020; LEFEBVRE; TAWIL; YAHIA, 2024).

2 METHODOLOGY

This is a qualitative study, characterized as a bibliographic survey of narrative and analytical character, whose objective was to critically analyze the available scientific evidence on the use of cannabidiol as an adjuvant therapy in the treatment of persistent inflammatory pain associated with Chikungunya virus infection.

The option for a narrative review is justified by the need to integrate and discuss results from different methodological designs, considering the scarcity of specific clinical studies that evaluate the use of cannabidiol in the context of persistent pain after infection by the Chikungunya virus, which makes it impossible to conduct systematic reviews or meta-analyses on the subject.

The bibliographic search was carried out in the **PubMed**, **Scientific Electronic Library Online (SciELO)** and **ScienceDirect** databases, selected for their relevance in the health area and for bringing together indexed and peer-reviewed scientific journals. The searches took place from January to March 2025 and included publications published between 2014 and 2024.

Controlled and uncontrolled descriptors were used, in Portuguese and English, combined using Boolean operators, including the terms: *"Chikungunya virus", "post-chikungunya arthritis", "chronic inflammatory pain*", *"cannabidiol", "CBD", "inflammatory pain"* and *"arthritis"*. The search strategies were adjusted according to the particularities of each database, aiming to maximize sensitivity and specificity in the retrieval of relevant studies.

The inclusion criteria included: (i) original scientific articles and narrative or systematic reviews; (ii) studies published in the delimited period; (iii) publications available in full; (iv) articles written in Portuguese, English or Spanish; and (v) studies addressing inflammatory pain associated with Chikungunya virus infection and/or the analgesic and anti-inflammatory effects of cannabidiol in contexts of inflammatory or arthritic pain. Editorials, letters to the editor, conference abstracts, opinion reports, duplicate studies, and publications that were not directly related to the research objective were excluded.

The study selection process took place in sequential stages. Initially, the titles and abstracts were read to identify the thematic relevance. Then, potentially eligible articles were submitted for reading in full. The final selection considered criteria such as methodological consistency, clarity of objectives, adequacy of the methods used, and relevance of the findings to the theme investigated.

Data extraction was carried out in a systematic way, including information regarding the authors, year of publication, type of study, population investigated, clinical context, mechanisms of action of cannabidiol related to inflammatory pain, main results and conclusions. The data obtained were organized into previously defined analytical categories, allowing the comparison and integration of the findings.

Data analysis was conducted through critical narrative synthesis, with an interpretative focus, enabling the identification of convergences, divergences and gaps in scientific knowledge about the use of cannabidiol in the management of inflammatory pain. This approach allowed us to discuss the biological plausibility and therapeutic potential of cannabidiol in the context of persistent inflammatory pain after Chikungunya virus infection.

As this is a study based exclusively on secondary data, available in public databases of scientific access, there was no need to submit it to a Research Ethics Committee, in accordance with the current ethical guidelines.

3 RESULTS AND DISCUSSION

The literature review showed that Chikungunya virus infection is often associated with the development of persistent musculoskeletal pain, of an inflammatory nature, which can extend for months or years after the acute phase of infection. Observational and long-term follow-up studies show that a significant portion of affected individuals evolve with chronic arthralgia, morning stiffness, fatigue, and functional limitation, resulting in a negative impact on quality of life (CHOPRA et al., 2011; CHOPRA; VENUGOPALAN, 2011; GUILLOT et al., 2020; RODRÍGUEZ-MORALES et al., 2016).

The findings indicate that the persistence of pain after CHIKV infection is related to the maintenance of a chronic inflammatory state, characterized by a sustained elevation of proinflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), even after resolution of the viral infection. This inflammatory profile has been described both in population studies and in narrative reviews of CHIKV-associated arthritis, reinforcing the hypothesis of an underlying immune-mediated inflammatory process (CHOPRA et al., 2011; PATHAK; MOHAN; RAVINDRAN, 2019).

With regard to conventional therapeutic approaches, the studies analyzed indicate that the use of analgesics and non-steroidal anti-inflammatory drugs has limited efficacy in controlling chronic pain after Chikungunya, especially in the long term. Systematic reviews indicate a lack of robust evidence supporting lasting benefits of these interventions, in addition to the risk of adverse effects associated with continued use (RODRIGO et al., 2022).

Regarding cannabidiol, evidence from scientific reviews demonstrates that this phytocannabinoid has consistent analgesic and anti-inflammatory effects in different models of inflammatory and arthritic pain. The studies report a reduction in hyperalgesia, modulation of the inflammatory response, and decreased release of pro-inflammatory cytokines, especially in inflammatory rheumatological conditions (MLOST; BRYK; STAROWICZ, 2020; SKLENÁROVÁ; ŠÍMA; SLANAŘ, 2023).

Although no specific clinical studies evaluating the use of cannabidiol in persistent inflammatory pain after Chikungunya virus infection have been identified, the results observed in other chronic inflammatory conditions and in alternative administration strategies suggest that its use as an adjunctive therapy may contribute to the control of pain and residual inflammation (ARGUETA et al., 2020; LEFEBVRE; TAWIL; YAHIA, 2024).

The results of the present study reinforce the clinical relevance of persistent inflammatory pain after Chikungunya virus infection, corroborating evidence that points to the chronicity of musculoskeletal symptoms in a significant portion of affected individuals. Pain persistence is associated with the maintenance of a chronic inflammatory state, supported by immunological mechanisms similar to those observed in other inflammatory rheumatological diseases, which contributes to the complexity and difficulty in the therapeutic management of these patients (CHOPRA et al., 2011; RODRÍGUEZ-MORALES et al., 2016).

The limitation of conventional therapies in the control of post-CHIKV pain, widely described in the literature, highlights the need for complementary therapeutic strategies that are not restricted to immediate symptomatic relief, but that act to modulate the underlying inflammatory response. Systematic reviews demonstrate that available pharmacological treatments have modest and inconsistent long-term benefits (RODRIGO et al., 2022).

In this scenario, cannabidiol has been investigated as an adjuvant therapeutic alternative due to its anti-inflammatory and analgesic properties. The proposed mechanisms include modulation of the endocannabinoid system, reduction of pro-inflammatory cytokine production, and attenuation of oxidative stress, factors directly involved in the pathophysiology of chronic inflammatory pain (BOOZ, 2011; MLOST; BRYK; STAROWICZ, 2020).

In addition, recent reviews indicate that different routes of administration of cannabidiol, including topical and transdermal formulations, may represent promising strategies in the management of inflammatory pain, with potential reduction of systemic adverse effects (LEFEBVRE; TAWIL; YAHIA, 2024). These findings broaden the discussion about the therapeutic possibilities of CBD in chronic inflammatory contexts.

Despite the promising results observed in experimental models and in other inflammatory conditions, the absence of specific clinical trials evaluating the use of cannabidiol in inflammatory pain after CHIKV infection remains an important limitation of current knowledge. This gap reinforces the need for well-designed clinical studies that evaluate the efficacy, safety, and most appropriate therapeutic regimens, as pointed out by recent reviews (SKLENÁROVÁ; ŠÍMA; SLANAŘ, 2023).

4 CONCLUSION

The persistence of painful inflammatory manifestations after infection with the Chikungunya virus is a relevant clinical problem, with significant repercussions on the functionality and quality of life of affected individuals. The evidence analyzed in this study indicates that the chronicity of this condition is related to the maintenance of a prolonged inflammatory process, supported by immunological mechanisms similar to those observed in other inflammatory rheumatological conditions, which contributes to the limited efficacy of conventional therapeutic approaches.

The literature review demonstrated that, although analgesics and non-steroidal anti-inflammatory drugs are widely used in the management of symptoms, their long-term benefits are restricted and often accompanied by adverse effects. This scenario reinforces the need for complementary therapeutic strategies capable of acting not only in the relief of symptoms, but also in the modulation of the underlying inflammatory mechanisms.

In this context, cannabidiol has aroused scientific interest due to its analgesic and anti-inflammatory properties, widely described in different models of inflammatory and arthritic pain. The findings of this literature review indicate that this phytocannabinoid has biological plausibility to be considered as an adjuvant therapy, especially due to its ability to interfere with inflammatory and nociceptive pathways involved in the pathophysiology of chronic pain.

However, the absence of specific clinical studies evaluating its use in individuals with persistent pain after Chikungunya virus infection limits the direct application of this evidence to clinical practice. Thus, although the available results are promising, their use should be interpreted with caution. It is essential to carry out well-designed clinical trials that investigate the efficacy, safety, doses, and forms of administration of this substance, in order to support its incorporation in a safe and evidence-based manner.

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