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UPDATES IN THE TREATMENT OF DEPRESSION WITH THE USE OF CANNABIS

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Abstract: The objective of the present study was to look at current developments in the treatment of depression with the use of cannabis, which aims at its benefits and therapeutic action and to report its mechanism of action in the treatment of Depression. The study was developed based on an integrative review of the literature in which books, dissertations, articles and theses that were published between the years 2017 and 2023 were researched. Documents published in Portuguese and English that were available in the databases were selected. Scielo, CAPES periodicals, PUBMED and LILACS. In addition to the databases, official documents from PAHO (Pan American Health Organization) and the Ministry of Health were used in the construction of this review. Depression is a disabling disease that affects around 350 million people worldwide. Considering that currently available antidepressants take 2 to 4 weeks to produce an effect, being ineffective in around 40% of cases, new medications with rapid antidepressant action, such as that observed by CBD, are of great clinical relevance. It highlighted the efficiency of medicines based on Cannabis sativa, which is a medicinal plant with pharmacological properties that present effects as close to or similar to neuroleptic medicines, whose active ingredient used to manufacture psychoactive medicines is Cannabidiol (CBD) which helps the central nervous system and the body, reducing and alleviating the effects of depression.
Keywords: Cannabis; Depression; Treatment.

INTRODUCTION

The use of medicinal plants has been used for several centuries, treating illnesses and improving the individual's quality of life with their use in a homemade way, and their knowledge passed through oratory from generation to generation (Duarte 2006). Recently studies that explore ways to optimize the extraction of active compounds from herbs, as well as the search for the identification and application of new bioactivities of metabolites found in medicinal plants have become a trend in the current scientific community (Santos, et al. 2018; Cruz, et al. 2021).

In Brazil, there is a wide diversity in terms of different beliefs, ideas, customs and methods in relation to medicinal plants and their therapeutic effects, which must be considered in everyday life (Arnous, Santos, & Beinner, 2005). People commonly use medicinal plants to treat their illnesses, as they are easily accessible and low cost, in addition to being much less aggressive to the patient compared to any other medicine that is not of plant origin.

Some people have genetic predispositions to acquire depression, however this is not the determining factor but one of these factors, the set of traumatic events, health problems, and psychological or physical stress can contribute to the emergence of this disease (Varella, 2013).

Due to Cannabis sativa having pharmacological properties, Porcionato et al., (2021) says that medicines based on cannabinoid compounds have been considered as an alternative in the treatment of some diseases related to the central nervous system. It is worth highlighting that even with existing evidence on the application of active compounds from C. sativa, the industrial production of herbal medicines derived from marijuana is still little explored in Brazil. The main fact identified is the recreational use of marijuana, previously considered illicit (Lima, Alexandre, & Santos, 2021).

The main effects expressed that medical cannabis patients showed less severe signs than patients who do not use the cannabidiol-based medicine, those who do use it showed an improvement in quality of life, sleep and

reduced pain (Vieira, 2021).

The use of cannabinoid-based medicines is still new in Brazil, and even though there is already scientific evidence that proves their pharmacological effect, there are still barriers that make the use of these medicines difficult for the patient (Porcionato, et al, 2021).

There is some reluctance against the use of medicines made from Cannabis sativa. which precedes the lack of knowledge regarding its pharmacological action, and this lack of information ends up invalidating the use of substances that are extracted from this medicinal plant, where the medicine from this plant still undergoes judgment due to its psychoactive effects

Knowledge regarding the use of medicines based on Cannabidiol, a substance with pharmacological action, which is extracted from the medicinal plant Cannabis sativa L, to treat people with psychological illnesses such as Depression, in a safe and effective way (Medeiros, 2017).

Cannabis sativa is a very controversial plant, so much so that its studies are still largely unexplored due to its complexity and the debate that this would imply. Marijuana or hemp is used several times for recreational use, however some studies are clarifying that there are more pharmacological benefits of this plant. Matos, et al. (2017) explains that, while delta-9-THC works to generate a state of euphoria, CBD works to block and inhibit the sense of humor. The same authors also warn that; however, the therapeutic use of delta-9-THC has become limited due to the existence of severe adverse effects. Therefore, the objective of the present study was to highlight the use of medicines based on Cannabis Sativa, which aims at its benefits and therapeutic action and to report its mechanism of action in the treatment of Depression.

METHOD

This is a literature review, of a narrative type, which aims to describe the treatment of depression with the use of cannabis, its indications and when to indicate, from a theoretical point of view, through materials that have already been published on the topic in question, through analysis and interpretation of the literature. The inclusion criteria were: articles in Portuguese and English; published between 2017 and 2023 and which addressed the themes proposed for this research, review-type studies made available in full. The exclusion criteria were: duplicate articles, available in abstract form, which did not directly address the proposal studied and which did not meet the other inclusion criteria.

The review was carried out from August to December 2023, through searches in the databases Virtual Health Library (VHL), Latin American and Caribbean Literature in Health Sciences (LILACS), National Institutes of Health's Library of Medicine (PubMed) and Scientific Electronic Library Online (SciELO). The following descriptors were used: "Cannabis", "depression", "treatment", in order to find articles relevant to the subject covered. After the selection criteria, 6 articles remained that were subjected to thorough reading for data collection. The results were presented in a descriptive way, divided into thematic categories addressing: describing the subtitles or points that were mentioned in the discussion.

RESULT AND DISCUSSION

THE DEPRESSION

Depression is a disabling disease that affects around 350 million people worldwide. The conditions vary in intensity and duration and can be classified into three different degrees: mild, moderate and severe. Some people have

genetic predispositions to acquire depression, however this is not the determining factor but rather one of these factors, the set of traumatic events, health problems, and psychological or physical stress can corroborate the emergence of this disease (Varella, 2013).

A person with depressive disorder may present several symptoms that can be emotional: lack of motivation, difficulty concentrating, deep pessimism, irritability, slow thinking, anguish, insomnia and the desire to commit suicide. And physical symptoms that can be: headaches, pain in the chest area, decreased immunity, body aches, hair loss. When the depressive disorder is in its initial stage, it does not require the use of medication, so symptoms can be alleviated with therapy and physical exercise (Deus, 2021).

Depression has mild, moderate and severe levels, the mild level can be controlled without the use of medication, therapy and physical exercise can be used, and the moderate and severe levels require the use of medication that will control the symptoms. of depression (Deus, 2021). PAHO (2017) reports that the new global report also shows that depression affects 5.8% of the Brazilian population (11,548,577). After treatment with medicines extracted from Cannabis in young people with autism spectrum disorder, these young people had an improvement in their communication and anxiety of 39% and 47%, respectively (Lima, et al. 2020).

CANNABIS USE AND DEPRESSION

EPIDEMIOLOGICAL AND CLINICAL ASPECTS

For decades, there have been case reports of the development of depressive symptoms related to cannabis use. However, as previously mentioned, cases have also been described in which manic symptoms developed after use and also of cannabis being used as an antidepressant or mood stabilizer (Gruber AJ, Pope HG Jr, Brown ME. 1996).

Studies on the relationship between cannabis use and depression in populations undergoing psychiatric treatment suggest that the presence of abuse/dependence is related to a greater number of depressive episodes throughout life and that the treatment of dependence comorbid with major depression is associated with a worse result in males (Compton WM. Et al 2003).

Prevalence studies carried out with samples not representative of the general population (among adolescents, young adults, university students and patients in primary care services) found conflicting results, difficult to interpret together due to the different methodologies and definitions used (e.g. regarding what is considered a heavy or occasional user), in addition to involving small samples that were often not representative of the specific population studied (Degenhardt L. et al 2004)).

Since the publication of the Epidemiologic Catchment Area (ECA) results (Regier DA et al. 1990), studies involving representative samples of the general population have been described, some of which have assessed cross-sectional associations between cannabis use and depression.

Some of these studies have described the incidence of major depression or affective disorders in cannabis users compared with the incidence in adults in general or in adolescents and young adults. Two North American studies addressed the issue: one of them found, in the adult population, a 6.4 times higher risk of experiencing depression among those who suffered from cannabis abuse or dependence65 and the other study found a 3.4 times higher risk. In Australia, cannabis users were found to be at greater risk than the general population of experiencing

affective disorders, with the prevalence of these disorders reaching 14% among cannabis dependents compared to non-users (Degenhardt L, Hall W, Lynskey M., 2001).

Other studies in representative samples of adolescents and young adults have also found similar results. An Australian study found that teenagers who had already used cannabis were three times more likely to develop depression compared to those who had never used it68; a New Zealand study found a progressively increased risk of depression as frequency of cannabis use increased (Fergusson DM, Horwood LJ, Swain-Campbell N, 2002).

Regarding the incidence of frequent use of cannabis or A/DC among depressed individuals, one of the North American studies already mentioned found that the chance of an adult being dependent on cannabis was 2.4 times greater among those who had major depression compared to to the general population66. A European study found a 2.3-fold increased risk of weekly marijuana use among young adults with depression compared to those not depressed (Angst J. 1996).

ETIOLOGICAL MODELS FOR THE ASSOCIATION BETWEEN CANNABIS USE AND DEPRESSION

The association between cannabis use and depression, as in the case of the association with bipolar disorder, can also be explained by basically four models: 1) there are common factors that cause both depression and cannabis use; 2) depression is a cause of cannabis use; 3) cannabis use is a cause of depression; and 4) bidirectional models. Probably the best way to evaluate these possibilities is through longitudinal studies (Degenhardt L. et al 2004).

Thus, longitudinal studies that assessed whether the presence of depression in adolescence was related to an increased risk of later cannabis use did not find significant associations (Kandel D, Chen K. 2000).

A systematic review (Moore TH. Et al 2007) published in 2007 evaluated 10 studies that examined the relationship between cannabis use in adolescence and/or early adulthood and later diagnosis of depression (done through structured interviews or with the use of validated questionnaires). Five of these studies found significant associations even after statistical adjustment considering other variables. The other studies found non-significant associations or no association at all. In the set of studies (five in total) that evaluated exposure to cannabis through frequency measures - which was considered suitable for meta-analysis by the authors - four described a dose-response association between frequency of cannabis use and risk of develop depression; a relative risk of 1.4976 was found. The authors chose not to perform a meta-analysis of the 10 studies due to the heterogeneity of cannabis exposure measures (which included any use, frequency of use, and abuse and dependence (Moore TH et al 2007).

In three other studies - published after the creation of this meta-analysis - both results indicating no association between cannabis use and depression and a significant association were described. (van Laar M. et al 2007).

Therefore, we can consider that - both due to the set of results and the unsatisfactory methodological quality of several studies - it is not clearly defined whether the use of cannabis implies an increased risk of depression.

If this increased risk does occur, the reasons for this may be related to several factors. It does not appear that cannabis' actions on neurotransmitter systems are related to facilitating the onset of depressive conditions. Probably, the effects of cannabis use related to increased risk of depression are socially

mediated, as there is evidence that regular and/or early use of this substance can facilitate situations such as unemployment, difficulty accessing education and involvement in crimes. Finally, it is not yet possible to completely rule out that common factors related to the family and/or social environment may be the cause of the association (Degenhardt L et al 2004).

To clarify these issues, more longitudinal population and twin studies discordant for cannabis use and/or abuse and/or dependence and depression are needed (Kandel D, Chen K 2000).

TREATING DEPRESSION WITH CANNABIS USE

As it was already mentioned regarding BAD, there are few studies specifically addressing the treatment of comorbid depression and use/abuse/dependence on psychoactive substances.

Therapies based on motivational interviewing, cognitive-behavioral and contingency management are also useful to treat this comorbidity. Motivational interviewing in particular has demonstrated good results in the treatment of cannabis dependence in a multicenter study (Carroll KM 2004). Regarding drug treatment, only one randomized double-blind study investigating the response to selective serotonin reuptake inhibitors included adolescents with cannabis abuse and dependence, finding that these medications are effective for treating depression in this population. An interesting finding from the same study was the high response rate to the treatment of depression with cognitive-behavioral therapy associated with placebo, again showing the importance of non-pharmacological therapies (Riggs PD. et al 2007).

THE PHARMACOLOGICAL ACTION OF CANNABIDIOL IN THE TREATMENT OF DEPRESSION

According to Mattos et al. (2018) cannabidiol is mainly metabolized by the liver and, due to its lipophilic properties, is quickly distributed to the brain. Considering that currently available antidepressants take 2 to 4 weeks to produce an effect, being ineffective in around 40% of cases, new medications with rapid antidepressant action, such as that observed by CBD, are of great clinical relevance (Sampaio, et al, 2020).

Sampaio, et al. (2020) reports that with the development of research on its use to treat the symptoms of various diseases, ANVISA (National Health Surveillance Agency) recognized the potential of cannabidiol for treatment and placed it on the list of controlled substances, releasing its import, and its use by laboratories, aiming to deepen studies on the subject, and authorizing its therapeutic use in January 2015.

The main effects expressed that medical cannabis patients showed less severe signs than patients who do not use cannabidiol-based medication, those who use it showed an improvement in quality of life, sleep and reduced pain (Vieira, 2021).

The use of cannabinoid-based medicines is still new in Brazil, and even though there is already scientific evidence that proves their pharmacological effect, there are still barriers that make the use of these medicines difficult for the patient (Porcionato, et al, 2021).

CONCLUSION

It was evidenced about the efficiency of medicines based on Cannabis sativa, which is a medicinal plant with pharmacological properties that present effects as close to or similar to neuroleptic medicines, whose active ingredient used to manufacture psychoactive medicines is Cannabidiol (CBD) which helps the central nervous system and the body by reducing and alleviating the effects of depression.

The suggestion that provides improvements regarding the use of these medicines and the reduction of prejudice regarding their use is information from reliable sources found and scientifically proven, considering that Cannabis sativa is not limited to its recreational use as many believe., which ends up invalidating its properties pharmacological.

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