

Use of alternative therapy with Psilocybin in oncologic patients with depression and/or anxiety disorders - integrative review

Uso de terapia alternativa com psilocibina em pacientes oncológicos com depressão e/ou distúrbios de ansiedade - revisão integrativa

Uso de terapia alternativa con psilocibina en pacientes oncológicos con depresión y/o trastornos de ansiedad - revisión integradora

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Abstract

Cancer is not limited to the physical dimension, but it also affects the entire biopsychosocial context in which the patient is inserted, making him more susceptible to psychiatric disorders such as depression and anxiety. These often require pharmacological intervention, and the use of psilocybin, a substance found in mushroom species, is one of the alternatives considered today. The present study aims to carry out an integrative review regarding the use of alternative therapies, in this case Psilocybin, in cancer patients suffering from anxiety and / or depression disorders. The type of study carried out was an integrative literature review, which was based on a bibliographic survey of texts published between 2010 and 2021 on the PubMed platform. This survey took place between December 2020 and February 2021, with a review of three articles in total. Studies show a potential new line of alternative treatment for anxiety and depression in cancer patients, the use of psilocybin. The treatment is done quickly, sustained and lasting, in conjunction with psychotherapy there is improvement in a single dose. All the studies analyzed so far have been shown to be effective for the treatment of anxiety and depression in cancer patients. With this, psilocybin can be an alternative therapy for those patients in psychological distress due to cancer, especially for those who did not obtain a

satisfactory response with the use of conventional treatment, allowing that in the future the substance may become a definitive therapeutic modality for patients in psychological distress due to cancer.

Keywords: Anxiety; Depression; Psilocybin; Oncology.

Resumo

O câncer não se limita à dimensão física, mas afeta também todo o contexto biopsicossocial em que o paciente está inserido, o tornando mais suscetíveis a transtornos psiquiátricos como a depressão e ansiedade. Essas frequentemente requerem intervenção farmacológica, sendo o uso da psilocibina, uma substância encontrada em espécies de cogumelo, uma das alternativas consideradas hoje. O presente trabalho tem como objetivo realizar uma revisão integrativa a respeito da utilização de terapias alternativas, no caso a Psilocibina, em pacientes oncológicos que sofrem dos transtornos de ansiedade e/ou depressão. O tipo de estudo realizado foi uma revisão de literatura, a qual se baseou em um levantamento bibliográfico de textos publicados entre 2010 e 2021 na plataforma PubMed. Este levantamento ocorreu entre dezembro de 2020 a fevereiro de 2021, sendo feita revisão de três artigos no total. Os estudos mostram uma potencial nova linha de tratamento alternativo para ansiedade e depressão em pacientes oncológicos, o uso da psilocibina. O tratamento é feito de forma rápida, sustentada e duradoura, em ação conjunta à psicoterapia há melhora em uma única dose. Todos os estudos analisados até o presente momento se mostraram eficazes para o tratamento de ansiedade e depressão em pacientes oncológicos. Com isso, a psilocibina pode ser uma terapêutica alternativa para aqueles pacientes em sofrimento psicológico devido ao câncer, principalmente para aqueles que não obtiveram resposta satisfatória com a utilização do tratamento convencional, permitindo que no futuro a substância possa se tornar uma modalidade terapêutica definitiva para pacientes em sofrimento psicológico devido ao câncer.

Palavras-chave: Ansiedade; Depressão; Psilocibina; Oncologia.

Resumen

El cáncer no se limita a la dimensión física, sino que también afecta a todo el contexto biopsicosocial en el que se inserta el paciente, haciéndolo más susceptible de sufrir trastornos psiquiátricos como la depresión y la ansiedad. A menudo requieren una intervención farmacológica, y el uso de la psilocibina, una sustancia que se encuentra en las especies de hongos, es una de las alternativas que se consideran hoy en día. El presente trabajo pretende realizar una revisión integradora sobre el uso de terapias alternativas, en este caso la Psilocibina, en pacientes con cáncer que sufren trastornos de ansiedad y/o depresión. El tipo de estudio realizado fue una revisión de la literatura, que se basó en un estudio bibliográfico de los textos publicados entre 2010 y 2021 en la plataforma PubMed. Esta encuesta se realizó entre diciembre de 2020 y febrero de 2021, revisando tres artículos en total. Los estudios muestran una nueva línea potencial de tratamiento alternativo para la ansiedad y la depresión en pacientes con cáncer, el uso de psilocibina. El tratamiento es rápido, sostenido y duradero, en acción conjunta con la psicoterapia se produce una mejora en una sola dosis. Todos los estudios analizados hasta ahora han demostrado su eficacia para el tratamiento de la ansiedad y la depresión en pacientes con cáncer. Por lo tanto, la psilocibina puede ser una terapia alternativa para los pacientes con angustia psicológica por cáncer, especialmente para aquellos que no obtuvieron una respuesta satisfactoria con el tratamiento convencional, permitiendo que en el futuro la sustancia pueda convertirse en una modalidad terapéutica definitiva para los pacientes con angustia psicológica por cáncer.

Palabras clave: Ansiedad; Depresión; Psilocibina; Oncología.

1. Introduction

Depression and anxiety are two of the most prevalent psychiatric disorders in the world (Muttoni et al, 2019). In the first analysis, depression is a disease characterized as a multifactorial disorder of the affective area or mood, presenting as main symptoms depressed mood and loss of pleasure or interest in almost all activities. It also has a great functional impact involving several aspects of a psychological, biological and social nature (Carreira et al., 2011). As a symptom, depression can appear in several clinical conditions and has the possibility of appearing as responses to conflicting, stressful situations and in adverse social and economic circumstances. As a syndrome, there can be not only changes in mood (nervousness, fear, sadness, lack of ability to feel pleasure), but also a possibility of cognitive and vegetative changes (appetite and sleep) (Del Porto et al, 2009).

In the second analysis, anxiety is characterized by an anxious psychic state, in which the individual is constantly worried about the future or afraid (American Psychiatric Association, 2014). People with anxiety have difficulty controlling their concerns, which can cause symptoms such as: agitation, nervousness, tension, easy tiredness, difficulty concentrating, irritability, sleep disorders, constant worries, constant fear, tremors, tachycardia, sweating, in addition to other symptoms

(Haller et al., 2014). In light of this, the diagnosis for a possible anxiety disorder depends on the frequency and severity of the symptoms, as well as being linked to traumatic episodes, phobias or stressful situations (Stubbs et al., 2017).

These psychiatric illnesses, mentioned above, are extremely common in cancer patients, but are often neglected, influencing quality of life, adherence to treatment and cancer survival. In patients undergoing cancer treatment, the prevalence of major depression is 15%, minor depression 20% and anxiety 10%. However, although it has a significant prevalence, 73% of patients who have these neurological symptoms do not receive effective psychiatric treatment and only 5% see a mental health professional (Pitman et al, 2018).

In this sense, these disorders can affect the evolution, prognosis and treatment of the disease. First, anxiety is directly associated with several somatic expressions, in which the individual expresses concern, tension and nervousness; being externalized at various times, such as: at diagnosis, during treatment, in periods of relapse, in advanced or terminal states and throughout the chemotherapy process. Depression, in turn, is capable of affecting self-care skills during chemotherapy, due to the depressed state and recurrent sadness characteristic of this disease. (Alcedo et al, 2015).

Therefore, it can be inferred that cancer exceeds the physical dimension, also impacting the psychological, social and spiritual dimensions of the patient. (Acosta et al, 2015). Thus, it is necessary to pay attention to the processes involved in the biopsychosocial sphere and the specific neuropsychiatric effects that certain types of cancer and their treatments can cause. (Pitman et al, 2018).

Regarding the pharmacotherapy of anxiety disorders, Levitan et al. (2011), states that the first line of treatment is based on the use of selective serotonin reuptake inhibitors (SSRIs) - such as escitalopram, fluvoxamine, sertraline and paroxetine, in addition to serotonin and norepinephrine reuptake inhibitors (SNIRs), being these determined by the effective results in RCTs (Randomized Clinical Trials) with placebo and the greater safety of their side effects.

In turn, the second line of treatment, according to Murrough et al. (2015), is characterized by the use of tricyclics, which in chronic use have shown an anxiolytic effect (Andreatini et al, 2001), nevertheless, they are considered as a second line of treatment due to issues of safety and tolerance. Benzodiazepines (BZD) such as clonazepam, bromazepam and alprazolam also fall into this classification. These have an important effect on somatic symptoms of anxiety (Andreatini et al, 2001), however they have problems related to tolerance and abuse. Despite being considered as a second line of treatment, these drugs have a faster action in relation to SNIRs and SSRIs when administered together (Murrough et al, 2015).

Concerning to the treatment of depressive disorders, the market has a large availability of drugs with efficacy, which act by several mechanisms of action and, despite structural differences, have the same ability to sharply increase the synaptic availability of one or more neurotransmitters, through action on several specific receptors and enzymes (Vismari et al, 2008),

Many of those who suffer from anxiety and depression disorders benefit from conventional therapeutic methods, yet, there is a large proportion that do not respond to treatment and remain symptomatic or have adverse side effects. Thus, new treatment approaches emerge. Recently, researchers are looking for alternative ways, such as the use of psilocybin, for the treatment of these disorders, this has proven to be an effective therapy for those who do not respond to traditional methods (Goldberg et al, 2019)

Psilocybin, found in more than 100 species of mushrooms belonging to the genus *Psilocybe* (Johnson & Griffiths, 2017), is a molecule with structural similarities to serotonin, an endogenous neurotransmitter. This substance is responsible for inducing a profound change in consciousness, with an increase in affective responses, and with positive effects on cognition, behavior and spirituality (Vargas et al, 2020).

In this context, the present study aimed to carry out an integrative review regarding the use of alternative therapies, in this case Psilocybin, in cancer patients suffering from depression and/or anxiety disorders.

2. Methodology

In the present study, an integrative review was conducted, which consists of a research that allows the assessment, synthesis and knowledge about a phenomenon from evidence, aiming to produce an overview of complex concepts, theories or relevant health problems from studies pre-existing, enabling the intervention proposal (Galvão et al., 2004; Whittemore & Knafl, 2005).

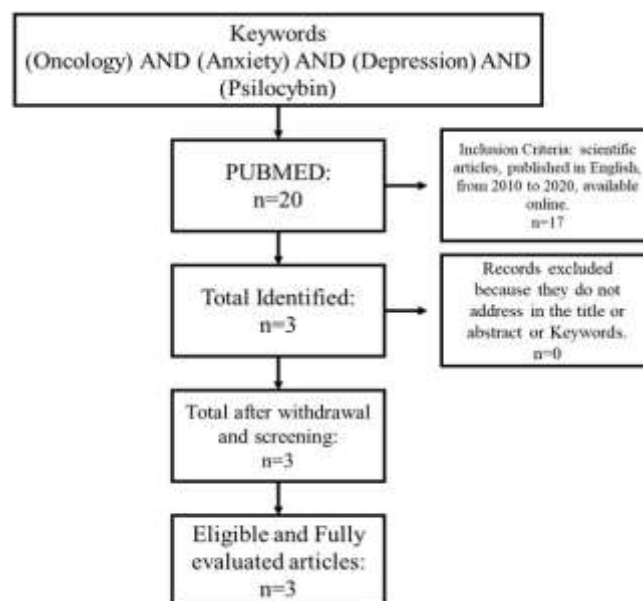
For the selection of articles, 6 methodological steps were carried out, namely: 1. elaboration of the guiding question or hypothesis of the research, that is, the problem was identified, the search engine and the keywords or keywords were presented; 2. establishment of the inclusion and exclusion criteria of the articles to be selected to compose the sample; 3. exploratory reading of the titles and abstracts of the articles for pre-selection; 4. analytical reading of the articles in order to compile, analyze and categorize the information; 5. interpretation of results. 6. synthesis followed by the presentation of the identified results, which permeate the guiding question (De Sousa et al., 2011).

Therefore, in this study it was decided to search for the concepts: psilocybin, mushroom, oncology, cancer, depression, anxiety. From these concepts, the guiding question was defined: How effective is the use of psilocybin in the treatment of anxiety and depression in cancer patients?

After formulating the question to be researched, a bibliographic survey was carried out on the PubMed platform. The survey of the study took place between December 2020 and February 2021. And the selection of texts proceeded with searches on the platform, using the filters available for texts published between 2010 and 2020. For the selection of publications, the following criteria were adopted: inclusion: scientific articles, published in the English language, between 2010 and 2020, available online and free of charge in full. Articles without an abstract in the database or incomplete, editorials, letters to the editor, reflective studies, systematic or integrative literature reviews were excluded.

After defining the guiding question, location and selection of articles, 20 potentially eligible publications were identified to be included in this review. After applying the inclusion and exclusion criteria, “Clinical Trial” and “Randomized Controlled Trial”, the sample consisted of 3 publications, of which the abstracts were analyzed, to check if they met the eligibility criteria and if they answered the question that guides this review, thus, they were analyzed in full to confirm the eligibility for the quantitative synthesis and analysis data according to the selection flowchart (Figure 1).

Figure 1: Publication Selection Flowchart,



Source: Authors (2021).

3. Results and Discussion

Within the period established for this study (2010-2020), and respecting the inclusion criteria, 3 publications were found and analyzed. In 2010, 1 article was published (33.3%) and in 2016 there were 2 publications (66.7%).

According to the methodology of the selected articles, the types of study were randomized searches using a double-blind test and a controlled trial or randomized clinical trial.

The publications resulted from the following magazines: Arch Gen Psychiatry, Journal of Psychopharmacology and American Medical Association. Analyzing the study sites, 2 articles were carried out in the United States (33.3%) and the other article developed in China (16.7%).

The first article analyzed was the pilot study of the treatment of psilocybin for anxiety in patients with advanced cancer, conducted by Grob et al. (2010), sought to analyze the efficacy and safety of using low doses of the substance (0.2-mg / kg) in cancer patients diagnosed with anxiety. Twelve participants aged 26 to 58 years of both sexes were evaluated and vital signs (heart rate, blood pressure and temperature) were analyzed, as well as the psychological state based on the Beck Depression Scale (BDS), Profile of Mood States (POMS), profile 5-Dimension Altered States of Consciousness (5D-ASC), Brief Psychiatric Assessment Scale and State-Trait Anxiety Inventory (STAI).

At the end of the study, although the dose of psilocybin was low, positive results were obtained indicating a therapeutic benefit that could be enhanced in larger doses. A reduction in anxiety by STAI was observed in the first and third months of treatment. BDI showed improvement in mood in the sixth month as well as POMS, however in the last one its result was not significant. There were no significant adverse effects, as well as no improvement in somatic symptoms such as pain, as this is seen when higher doses are administered (Grob et al., 2010).

The main results about the use of psilocybin in cancer patients are listed in Table 1. The randomized, double-blind, crossover study by Griffiths et al. (2016), investigated the effects of a very low dose of psilocybin (similar to placebo) (1 or 3 mg / 70 kg) versus a moderately high dose (22 or 30 mg / 70 kg) of psilocybin in 51 cancer patients diagnosed with a risk of life and symptoms of depression and / or anxiety, assessing a range of clinically relevant measures. Thus, participants were randomly assigned to two groups: The "1st low dose" group received the low dose of psilocybin in the first session and the high dose in the second session, while the "1st high dose" group received the high dose in the first session. Session and the low dose in the second session. This method was administered in a counterbalanced sequence with 5 weeks between sessions and 6 months of follow-up, in order to find out if there were improvements in the symptoms of depression and / or anxiety in these patients.

In view of the above, the present study demonstrated the efficacy of psilocybin administered under conditions of psychological support, whose data show that psilocybin produced substantial, long-lasting and significant reductions in measures of depression, anxiety or mood disorder and increases in measures of quality of life, meaning of life, acceptance of death and optimism in cancer patients (Griffiths et al., 2016).

The third study to be analyzed, entitled "Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial", was a double-blind, placebo-controlled trial conducted by Stephen Ross and his collaborators (2016), in which they evaluated 29 patients with anxiety and depression diagnosed with cancer. These were randomized and received treatment with single dose psilocybin (0.3mg / kg) 14 volunteers or niacin (placebo) 15 volunteers, both in conjunction with psychotherapy.

The results were decreased anxiety and depression in the group after 7 weeks. Psilocybin produced immediate, sustained and significant improvements in anxiety and depression, in addition to decreasing demotivation and hopelessness related to cancer, improving spiritual well-being and quality of life. After 5 to 6 months of treatment, psilocybin was associated with permanent anxiolytic and antidepressant effects (approximately 60-80% of participants continued to significantly reduce

depression or anxiety), in addition to improving symptoms related to existential anxieties and improving in quality of life, in addition to an improvement in the individual relationship of each participant with death. The mystical experience with psilocybin allowed a therapeutic treatment for anxiety and depression.

Table 1: The selected articles are summarized and the main results about the use of psilocybin in cancer patients are listed.

Reference	Type of Study	Intervention	Studied Variables	Key Results	Conclusions
Grob et al (2010)	Double-blind, placebo-controlled study	Use of 0.2 mg / kg dose of psilocybin and placebo in advanced stage cancer and diagnosis of acute stress disorder, generalized anxiety disorder, cancer anxiety disorder or anxiety adjustment disorder	12 individuals with advanced cancer diagnosed with stress and anxiety disorder	The results of STAIT, BDI and POMS showed an initial improvement in the patients' mood and state of anxiety, indicating benefits.	The study presents a potential new line of alternative treatment for anxiety in cancer patients at an advanced stage from the controlled use of psilocybin.
Griffiths et al (2016)	Randomized double-blind clinical trial	Use of a very low dose of psilocybin (placebo) and a moderately high dose in cancer patients with anxiety and depression	51 cancer patients with diagnoses and life-threatening symptoms of depression and / or anxiety	Effectiveness of a high dose of psilocybin. Significant decreases in measures of depression and anxiety	A single dose of psilocybin produced substantial and long-lasting reductions in depressed mood and anxiety, along with increases in quality of life and decreases in death anxiety in patients diagnosed with life-threatening cancer.
Ross et al (2016)	Randomized double-blind clinical trial	Use of psilocybin (0.3mg / kg) and placebo in cancer patients with anxiety and depression, distributed at random, both in conjunction with psychotherapy	29 cancer patients with anxiety and depression	Immediate reduction in symptoms of anxiety and depression after 7 weeks of treatment, and after 6.5 months, has been linked to long-lasting anxiolytic and antidepressant effects	In conjunction with psychotherapy, psilocybin in a single, moderate dose produced anxiolytic and antidepressant effects in a fast, sustained and long-lasting manner in cancer patients.

Source: Authors (2021).

4. Final Considerations

Symptoms of anxiety and/or depression are frequent in cancer patients and many conventional pharmacological therapeutic methods are ineffective for certain patients, due to the permanence of symptoms or side effects. Therefore, studies related to the use of psilocybin, as an alternative therapy, proved to be safe and effective, when administered in low and moderately high doses, producing an increase in quality of life and generating insignificant side effects in cancer patients.

With this, psilocybin can become a treatment option for anxiety and depression in cancer patients. For this to be possible, there is still a need for further studies regarding the use of the substance, considering that all studies analyzed so far have been satisfactory and with positive effects in relation to the improvement of symptoms of psychological distress related to the cancer.

Taken together, we suggest that more studies using psilocybin be conducted, comparing it with gold standard therapies and in more types of tumors, so that it is possible to verify the actions with more evidence of its benefit and safety.

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