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Nutritional supplements in Anxiety Disorder

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In recent years, a direct relation between the occurrence of anxiety disorders, sleep disturbances, and mood disorders has been observed as a consequence of poor or inadequate diet. Eating habits in Western societies have greatly changed in recent decades, with an increase in the consumption of foods low in vitamin and mineral content, high in caloric value, and rapidly prepared and easily consumed. It may be that the new lifestyles that directly affect family organization and planning interfere with following a proper diet. However, with increasing frequency, especially among young adults, there is interest in healthy and balanced nutrition, as well as learning culinary techniques.

We reviewed the literature for this study, and describe the concept of anxiety and its existence in relation to dietary disorders, as well as alternatives for the treatment of these symptoms. The characteristics of these disorders and their impact on patients are analyzed.

The information used in this work was obtained mainly from PubMed, PsycARTICLES, PsycCRITIQUES, and PsycINFO. It was retrieved using the keywords "mental health", "nutrition", "diet", "phytotherapy", "natural alternatives", "anxiety", "mood", and "sleep disturbance".

Key words: Eating, Anxiety, Diet, Phytotherapy, Nutrition, Mental health

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Suplementos nutricionales en el trastorno de ansiedad

En los últimos años se ha observado la existencia de una relación directa entre la aparición de trastornos de ansiedad, así como alteraciones del sueño, y del estado de ánimo, como consecuencia de una alimentación deficiente, o inadecuada. Los hábitos alimenticios en las sociedades occidentales han cambiado mucho en las últimas décadas aumentando la ingesta de alimentos de bajo contenido en vitaminas y minerales, elevado nivel calórico y consumo fácil por su rápida preparación. Quizá es debido a los nuevos estilos de vida que afectan directamente a la organización y planificación familiar impidiendo que cumplamos una dieta adecuada. Sin embargo, cada vez más y sobre todo en adultos jóvenes hay más interés por aspectos relacionados con la nutrición sana y equilibrada, así como por el aprendizaje de técnicas culinarias.

En este trabajo se ha realizado una revisión bibliográfica y descriptiva del concepto ansiedad y su existencia vinculada a las alteraciones en la dieta y alternativas para el tratamiento de dicha sintomatología. Se analizan sus características y la repercusión en el paciente.

La información utilizada para el trabajo se ha obtenido sobre todo de PubMed, PsycARTICLES, PsycCRITIQUES y PsicINFO introduciendo las palabras clave "salud mental", "nutrición", "diet", "fitoterapia", "alternativas naturales", "anxiety", "estado de ánimo", "alteración del sueño".

Palabras clave: Alimentación, Ansiedad, Dieta, Fitoterapia, Nutrición, Salud mental

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INTRODUCTION

Anxiety is a response of the body to situations that involve an emotional demand in order to adjust to the threats or hazards of the environment. This response can be differentiated between adaptive or detrimental, depending on the individual's capabilities.

Normal anxiety can be understood to be those reactions or necessary responses that prepare us for a fight or flight response to life events in order to overcome them. On the other hand, pathological anxiety can be considered to be anxiety that is excessive and inappropriate, or that has no purpose and limits and hinders the performance of the person. Pathological anxiety deteriorates the overall functioning of the person as well as the quality of life. Its appearance will depend on the intensity of the stressful event and the genetic adaptive skills and those learned through early experiences and personality development.

Anxiety is experienced at the cognitive, physiological, and psychic level. At the cognitive level, anxiety involves collecting all the thoughts and beliefs that are generated when we are nervous, through which we assess whether the situation involves danger or not. In the same way, we assess whether cognitive abilities such as attention, concentration, and memory can be altered. At the physiological level the most frequent symptoms are palpitations, subjective feelings of suffocation, insomnia, sweating, tremor, tingling, restlessness, dizziness, headache, and chest oppression, as well as digestive discomfort or diarrhea, among others, and any other associated symptoms may occur. Finally, on the psychic level, irritability, fear, and frustration should be highlighted.

The presence of anxiety symptoms is very common in the general population as a response to stressful situations of daily life, as part of a mental disorder, or accompanying multiple organic pathologies of other medical specialties. When the mere presence of anxiety in a subject is considered by the physician as the main symptom, and is of severe intensity and causes significant discomfort and important deterioration in the general functioning of the individual, affecting the person's quality of life, it could be included within the diagnosis of anxiety disorders. These anxiety disorders are among the most frequent mental disorders, affecting 25% of the population with an annual prevalence between 15% and 18% between 18 and 65 years of the population.[1] Anxiety disorders include agoraphobia, panic disorders, specific phobias, social anxiety, generalized anxiety disorder, post-traumatic stress disorder, or obsessive-compulsive disorder.

Among the symptoms associated with anxiety, sleep disturbances may be present, these symptoms being the most frequent in the general population and having a major impact on the person who has them. As a result, secondary symptoms such as irritability, deficits in attention and concentration, fatigue, tremors, and even delusions, or visual or tactile hallucinations may occur.[2] Insomnia can affect both quality and quantity of sleep, and it can be associated or not with other mental or physical pathology.

On the other hand, it is necessary to emphasize that anxiety can trigger alterations in a person's mood, which can take the form of a sad mood, emptiness, or irritability accompanied by somatic and cognitive changes, that affect the functional capacity of the individual. There are differences in the age at onset and form of onset of these disturbances, their clinical manifestations, the duration of symptoms, and the causes,[3] the latter being biological, psychosocial, or environmental factors.

Nutritional Abnormalities in Anxiety Disorder

The deficit of certain minerals and vitamins in our body, such as iron, folic acid, selenium, calcium, essential fatty acids, or vitamin B12, among others, may be involved in diseases such as mood disorders, cognitive deficits, anxiety disorders, and sleep disturbances, among others. In addition, these deficits may be the cause of other symptoms, such as weakness, fatigue, concentration difficulties, or generally affecting other cognitive and behavioral disorders. In many cases these nutrient deficits make the psychopharmacological treatment itself refractory.[4]

Studies demonstrate a relation between essential fatty acids and folic acid with the mood state, and the appearance of symptoms like depression, so essential fatty acids could be very useful in the adjuvant treatment of these disorders.[5]

The same occurs with the ingestion of polyunsaturated fatty acids, which are involved in the prevention of mood disorders.[6] These fatty acids are found in foods such as fish, vegetable oils, or other seafood. Ingestion of these fatty acids has been associated with a decreased risk of depression, and an adequate level of polyunsaturated fatty acids has been observed to improve certain cognitive disorders.[5]

A relation has been demonstrated between a balanced diet rich in omega-3 fatty acids, cognitive deterioration, and functional disorders characteristic of diseases such as Alzheimer disease.

It is known that omega 3 fatty acids are necessary for proper functioning of the nervous system, as well as for the control of cholesterol levels and even for cancer prevention.

Those following a weight-loss diet should not neglect the need for the body to have adequate omega 3 levels.[7]

It is known that folic acid and vitamin B12 are involved in the synthesis of serotonin and other neurotransmitters, so it has been assigned a relevant role in mood regulation, based on the fact that a vitamin B12 deficiency has been found in many patients with depression, and it has been observed that many patients with folic acid deficiency may present a lower response to psychopharmacological treatment than those with normal levels,[5] which incorporates new strategies for the treatment of these diseases.

Vitamin B12 deficiency is not only involved in mood, it is also often associated with deficits in attention, concentration, and memory, and generally with mental dysfunction. The same occurs with low folic acid levels, which in addition to being associated with the presence of depressive symptoms, are often related to symptoms such as confusion, apathy, abulia, fatigue, and irritability.

The other disease with which vitamin B12 deficiency has been most associated is with dementias. In both folic acid deficiency and vitamin B12 deficiency, the intensity of the deficiency has been associated with the severity of the symptoms of depression and with the cognitive deficit associated with dementias.

Vitamin B6 has special importance as a precursor of serotonin and tryptophan, and is involved in the initiation or maintenance of symptoms, or diseases that do not course with symptoms of anxiety. Vitamin B6 is not stored by the body, so it is necessary that it be regenerated, if possible by consuming vitamin complexes, although it is more beneficial for the organism to obtain vitamin B6 through certain food sources. Foods such as fish, tuna, or salmon, dairy products, spinach, carrots or sunflower seeds, for example, are rich in vitamin B6.[8]

The use of antioxidants (vitamin C and E) has been linked to the prevention of mood disorders, although there is little evidence about it, and what evidence exists is empirical. Vitamin C (ascorbic acid) has been related with a decreased severity of mood disorders, and vitamin E (α-tocopherol) has been linked to a decrease in the frequency of depressive symptoms.

Iron deficiency, in addition to causing anemia, can produce symptoms such as irritability, lack of concentration, fatigue, and apathy, which may occur alone or integrated in one of the disorders treated here, such as mood or sleep disorders, dementia, or anxiety. Further evidence has been found in women using oral contraceptives with an associated iron deficiency but without anemia, who are more likely to experience depression.[5]

The deficiency in the essential mineral zinc is known to produce immunosuppression, and may be associated with the onset of depressive and anxious symptoms, as well as in their maintenance. Evidence of this hypothesis lies in the fact that treatment with immunosuppressive drugs increases the risk of depression and anxiety.

People with healthy habits may suffer from depression or even sleep disorders due to the lack of tryptophan mainly, because of an unbalanced diet. Tryptophan is essential for the synthesis of serotonin and melatonin, which are necessary for improving mood and fundamental in the regulation of sleep-wake cycles. It is well known that women with an adequate diet may be more vulnerable to obtaining the benefit of improved mood thanks to tryptophan than men. It has also been concluded that tryptophan is effective in patients with a family history of mood disorders. At the cognitive level it has been shown that the lack of tryptophan directly influences the processes of visual discrimination, episodic memory, and cognitive flexibility, among others. Among people with sleep disorders, the use of tryptophan has been recommended since it has therapeutic effects through melatonin-related mechanisms. At the behavioral level, impulsivity and aggressiveness may, in part, depend on changes in serotonin synthesis involved in the inhibitory control of aggression.[9]

Treatment for Anxiety Disorders

For the treatment of anxiety disorders, a multidisciplinary approach consisting of psychopharmacology and psychotherapy is indicated.

Guidelines for good clinical practice recommend treating anxiety disorders with a selective serotonin reuptake inhibitor (SSRI), as well as cognitive behavioral therapy. Despite these recommendations for routine clinical practice, benzodiazepines were, and still are, the treatment of first choice by most clinicians, usually prescribed long-term despite the risks and complications associated with their use.[10]

Other effective treatments for controlling anxiety symptoms are selective inhibitors of serotonin reuptake and norepinephrine, antiepileptic drugs like pregabalin and gabapentin, and some atypical antipsychotics like quetiapine or olanzapine.[1]

However, traditionally the most commonly used treatment for the symptoms of anxiety are the benzodiazepine drugs, which are also used to treat insomnia, which is closely associated with anxiety disorders, and are considered one of the most consumed drugs in the world. Prescription of the benzodiazepines is increasing,[11] especially in primary care, where 58% is prescribed, compared to 18% prescribed in psychiatry.[12,13] According to the prescribing information, the use of benzodiazepines should be limited, with a maximum duration of 4 weeks for insomnia and 12 weeks for

anxiety, with gradual withdrawal recommended for both conditions. It is indisputable that the short-term use of benzodiazepines is effective, but prolonged use of these drugs is a risk. Long-term use has been directly related to a risk of dependence, as well as tolerance, resulting in a withdrawal syndrome with abrupt discontinuation. Patients treated with benzodiazepines for a prolonged period have a higher probability of experiencing typical side effects, such as problems with attention, memory, aggressive behavior, depression symptoms, and symptoms of dependence and tolerance fundamentally.[14] In addition, benzodiazepines are related to an increase in the possibility of having traffic accidents, falls and fractures, the risk being greater in people over the age of 65 years.[15] Another very frequent effect is cognitive deterioration, which can fundamentally affect memory, most frequently producing anterograde amnesia, although it may also affect other cognitive domains, such as attention, learning, and visual-spatial capacity.[16]

As part of the fundamental multidisciplinary treatment in anxiety disorders, psychotherapy using a cognitive-behavioral approach is conducted. It is centered on increasing the patient's ability to identify his or her concerns, control the symptoms associated with these concerns, facilitate adaptive coping, and modify dysfunctional beliefs.

Similarly, techniques of imaginary exposure or in vivo exposure, as well as systematic desensitization, can be used. Systematic desensitization is a technique primarily aimed at reducing anxiety responses and eliminating motor avoidance behaviors. The starting point is the fact that the appearance of certain situations, stimuli, or people automatically generates anxiety responses in the subject. A suitable procedure should enable the appearance of responses incompatible with anxiety when the subject is exposed to such situations, stimuli, or people. This prevents the development of anxiety as well as the avoidance behaviors set in motion.

Alternative Anxiety Treatment

Different pharmacological and dietary supplement alternatives are proposed for the treatment of anxiety disorders, as well as the above mentioned associated symptomatology.

Phytotherapy is understood as the use of products of plant origin for therapeutic purposes for the prevention, relief, or cure of pathologies. A medicinal plant is a plant species that possesses substances that can be used for therapeutic purposes or whose active ingredients may be precursors for the synthesis of new drugs.

According to WHO, 80% of the general population in developed countries use these treatments as alternative therapies, or as an adjunct to medical needs, or for the treatment of certain symptoms, such as sleep disorders, mood disorders, and anxiety. This percentage continues to grow.[17]

There are many plants that are used for a therapeutic purpose and they have indications in multiple pathologies, whether individually or in combinations. In the field that concerns us here we, we can highlight, among others, passion flower, valerian, lemon balm, chamomile, mint, limeflower, lemon verbena, lavender, poppy, and hops.

Passion flower (Passiflora incarnata), which has a sedative action, is attributed central nervous system relaxant effects, hypotensive action, analgesic, antispasmodic, and sedative. Its main indications are in the treatment of anxiety, insomnia, hyperactivity in children, and even tremors in Parkinson disease. Numerous studies show that it is as effective as allopathic therapeutic modalities, without being associated with any adverse effects.[18]

A drug containing 200 mg of the dry extract of the aerial parts of passion flower, equivalent to 700-1000 mg of passion flower, is available on the market. Its fundamental indication is for moderate symptoms of mental stress, sporadic depression, anxiety, irritability, restlessness, and more frequently as a sleep inducer.[19] On the other hand, it should be noted that the use of dried passion flower extract in comparison with benzodiazepine use avoids the typical side effects, especially the feeling of sedation and memory problems, the latter being one of the fundamental complaints of patients due to the limitations it may impose on the activities of daily living and work or professional life.[14]

Another combination that is currently marketed is composed of melatonin and certain plant extracts, such as poppy, valerian, and passion flower. Its fundamental indication is for sleep disorders, both sleep onset and sleep maintenance insomnia, since these substances favor physiological sleep and the maintenance of normal circadian rhythms.[20]

Finally, it is worth mentioning a product marketed consisting of dried extract of Valerian root together with dry extract of lemon balm leaves, which is indicated for mild and occasional symptoms of anxiety and insomnia consisting of difficulty falling asleep.[21]

There are other alternatives for the treatment of these conditions, such as melatonin, which, as mentioned, is involved in the regulation of circadian rhythms and in sleep induction, as well as in other physiological processes such as blood pressure regulation, immune function, antioxidant action, and free radical uptake. Its main therapeutic indication is sleep disorders, and it is indicated mainly for

insomnia with difficulties falling asleep, since it reduces sleep latency and improves sleep quality, even compared with drugs of the benzodiazepine group.[22]

Melatonin, in addition, reduces the subjective symptoms of jet lag. An important point to take into account in the indication of melatonin is the low incidence of side effects, especially compared with those described with benzodiazepine treatment; another benefit of using melatonin rather than benzodiazepines is that melatonin does not produce rebound insomnia or withdrawal effects after stopping melatonin treatment. In other studies, melatonin has also been found to improve sleep quality compared to placebo.[23]

Among these alternatives is ramelteon, an agonist of the melatonin receptors (MT1 and MT2) that is very useful in treating sleep-onset and sleep-maintenance insomnia, as it decreases wakefulness and improves the total amount of sleep. It may thus be useful for treating early awakening, and it has scant adverse effects. Finally, we have a hypnotic agent called suvorexant, which was approved in 2014 by the FDA. It has a mechanism of action of dual antagonism of the orexin receptors (OX1R and OX2R), which results in sleep induction, and its indication is for sleep-onset and sleep-maintenance insomnia.[24]

Equally important for the treatment of these disorders are food supplements, the most frequent being valerian (*Valeriana officinalis L*). Valerian is considered to have a similar action to the benzodiazepines in the treatment of the symptoms of anxiety and in the treatment of sleep-onset insomnia, improving sleep quality, although the mechanism of action and the components involved in this therapeutic effect are unknown.[25]

This group also includes lemon balm (*Melissa officinalis L.*), which has anxiolytic therapeutic properties, functioning as a GABA-T inhibitor and having affinity for the GABA-A receptor. Lemon balm is also attributed neuroprotective properties, which produces an improvement at the cognitive level, especially in the mnemonic deficits associated with dementia processes.[17]

Chamomile (*Matricaria chamomilla L.*), which also has a GABAergic activity, is also considered a good minor anxiolytic.[26]

Peppermint (*Menta x piperita L.*) has a therapeutic effect for anxiety, especially somatic-type anxiety, fundamentally with gastrointestinal symptoms. Studies show that peppermint has coadjuvant efficacy in irritable bowel syndrome.[27]

This group includes limeflower (*Tilia platyphyllos*), which is also attributed anxiolytic and sedative effects, together with antispasmodic, minor analgesic, diaphoretic, and anti-inflammatory properties, as well as an antimicrobial action because its leaves contain vitamin C.[28] In the case of lemon verbena (*Aloysia citriodora Kunth*), the most common indication is in insomnia and the treatment of anxiety.[29]

Hops is another medicinal plant that is used for hypnotic purposes because of its effect of prolonging the duration of sleep. The California poppy (*Eschscholzia californica*) is in the same therapeutic category, standing out for its ability to promote physiological sleep and reduce the number of nocturnal awakenings, thus improving the structure of sleep, and it has been widely used for its analgesic properties.[30]

Crocus sativus L, as saffron threads, is used for its antidepressant, antioxidant, and digestive properties. This medicinal extract acts on numerous neurotransmitters, improving mood and relieving anxiety and stress. *Crocus sativus L* has been studied in comparison with fluoxetine for the treatment of mild-to-moderate depression. The results indicate that saffron is an effective alternative for reducing depressive symptomatology in mild-to-moderate episodes. Another study of saffron for the treatment of anxiety and depressive disorders confirms its efficacy in individuals with symptoms of mild-to-moderate intensity, although it is not conclusive and further investigation is proposed.[31]

Finally, lavender oil merits mention. The formula for lavender oil includes extract from the plant *Lavender angustifolia*, linalol, and linalyl acetate, among other ingredients. Lavender oil is recommended for the treatment of generalized anxiety and mood disorders due to its antidepressant effect, and it improves general mental health. It is especially indicated in patients with restlessness, agitation, and sleep problems, and in the treatment of anxious moods.[32]

As mentioned, it may be used alone or in combination, as in the case of passion flower, valerian, and hops, which reinforce its anxiolytic and hypnotic effects. It may also be useful in the treatment of benzodiazepine withdrawal.[33] Studies of this combination show that it can also improve sleep quality.[34]

Deficits in vitamin intake in poorly balanced diets can be compensated with supplements of vitamins and omega 3 fatty acids.

The ingestion of EPA and DHA, which are two compounds based on omega 3, is associated with a reduction in the likelihood of experiencing anxiety and cognitive impairment, independently of other risk factors, including toxic habits, age, sex, or an individual's sociocultural level.

Physical Exercise

Physical activity is associated with the perception of a good or very good health status, as well as obtaining an adequate score on the subjective mental health scale, General Health Questionnaire (GHC). Moreover, there is a lower probability of taking antidepressant and anxiolytic drugs among people with healthy habits who exercise regularly than among people with a sedentary lifestyle.[35]

It is demonstrated the practice of aerobic activity as a therapy reduces the symptoms of anxiety and stress and promotes positive emotional states. Similarly, physical activity can be understood as a social experience favoring interpersonal relationships and satisfying social needs, which improves self-confidence, self-esteem, the sense of well-being, and intellectual functioning.[36]

Healthy habits include eating properly and the Mediterranean diet is considered to be one of the healthiest diets because it helps to prevent disease and favor life expectancy. This diet is made up of fruits, vegetables, cereals, olive oil, legumes, and nuts, which replace saturated fat intake and provides the necessary minerals, vitamins, and fiber, assuming that the necessary quantities are consumed.[37]

CONCLUSIONS

It is important to bear in mind that a clear determinant of patients' mental health is their nutritional status. It would be interesting and beneficial when prescribing psychopharmacological treatment for mental disorders to take a holistic approach and consider the nutritional status of the patient and, if necessary, prescribe nutritional supplements as primary treatment or as adjuvants to medical treatment.[5]

The use of dietary supplements, phytotherapy, and alternative drugs, as well as the implementation of healthy nutrition, could be useful for treating many psychiatric conditions, including depression, psychosis, and dementias, and may even reduce the prevalence of these conditions.

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