Alternative therapies and management of dementia in Alzheimer's disease

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ABSTRACT

Neurocognitive disorders are defined by an "significant cognitive impairment in one or more areas: complex attention, executive function, learning and memory, language, perceptual motor ability and social cognition. These dysfunctions represent a decline from a previous level of functioning, so dementia. does not refer to low or reduced intellectual functioning, or mental retardation, which are developmental and static disorders. "(1)

Dementia of the Alzheimer's type is the most common nosological form of dementia, characterized by memory loss and other cognitive skills severe enough to interfere with daily life. Dementia of the Alzheimer's type has a prevalence of 60-80% of dementia cases. (2)

The factors that differentiate the dementia subtypes are: "evolution over time, the specific areas affected and the associated symptoms" (5)

The therapeutic strategies are based on the increase of the cholinergic transmission and on the modeling of the glutamatergic transmission, validated etiopathogenic hypotheses in dementia Alzheimer's focus on acetylcholine transmission deficiency and NMDA receptor hyperactivity. (19) Patients diagnosed with a neurocognitive disorder such as dementia of the Alzheimer's type, represent a special group, with special needs, in which the concept of quality of life differs from that used for patients diagnosed with conditions that are certainly less disabling.

A series of prospective cohort studies have suggested that in addition to anti - dementia psychotropic therapy, regular physical activity associated with standardized herbal oily

maceration such as garlic (*Allium sativum*), hawthorn (*Crataegus oxyacantha* - linne) and white mistletoe (*Viscum album*) may have a real effect on risk factors (diabetes, HTA, cerebrovascular disorders, X-metabolic syndrome).

This paper proposes an analysis of both current psychotropic therapy, risk factors and the impact of non-pharmacological treatment on the quality of life of people affected by this pathology.

KEY WORDS:

Dementia of the Alzheimer's type, anti-dementia, alternative therapies, quality of life

INTRODUCTION

Neurocognitive disorders are defined by an "significant cognitive impairment in one or more areas: complex attention, executive function, learning and memory, language, perceptual motor ability and social cognition. These dysfunctions represent a decline from a previous level of functioning, so dementia. does not refer to low or reduced intellectual functioning, or mental retardation, which are developmental and static disorders. "(5)

Neurocognitive dysfunction mentioned above are commonly associated with behavioral symptoms. They reflect disruptions in one or more of these areas and are often complicated with behavioral symptoms. "(17)

Neurocognitive disorders have a wide range of subtypes, being classified based on etiological or pathological entities, which would have had an implication in the onset of cognitive decline.

The factors that differentiate the dementia subtypes are: "evolution over time, the specific areas affected and the associated symptoms" (1)

A classification based on the etiology of dementias will highlight the following groups: degenerative dementia (where dementia of Alzheimer's type is reported,), vascular dementia; dementia secondary to space occupying processes; secondary to infectious diseases; those produced by disturbances of

internal homeostasis; secondary to endocrine and metabolic diseases; secondary to repeated cerebral microtrauma (boxer dementia); dementia secondary to hydrocephalus with normal pressure and dementia secondary to the consumption of psychoactive substances. Dementias can also be classified into cortical or subcortical subtypes, the Alzheimer's type is a dementia of the cortical category.

Both within ICD-10 Classification of mental and behavioral disorders, we find described within the organic mental disorders including symptomatic, dementia subtypes of Alzheimer's disease (with early onset, late onset, atypical or mixed type and unspecified form), as well as within DSM V Manual of diagnosis and statistical classification of mental disorders, in the subchapter dedicated to neurocognitive disorders.

Alzheimer's disease is defined as a degenerative cognitive disorder with progressive evolution leading to loss of self-management capacity, associating both non-cognitive psychiatric complications (behavioral disorders, depression, anxiety, delusion etc.) and somatic / neurological disorders that cause poor outcome. (3)

ETIOLOGY

Dementia of the Alzheimer's type is the most common nosological form of dementia, characterized by memory loss and other cognitive skills severe enough to interfere

with daily life. Dementia of the Alzheimer's type has a prevalence of 60-80% of dementia cases. (2)

With the aging of the population, the prevalence of dementia is rising rapidly. Age is the main risk factor for dementia and prevalence doubles every 5 years, from about 1.9 percent at age 65 to 70 percent to 6.3 percent at age 75 to 80, 21.7 percent at age 85 to 90, and 47.5 percent over 90. (6)

The aging of the population associated with the increase of the prevalence of cognitive disorders, including dementia, automatically implies an increase of the expenses in the medical field, the elderly population being the main consumer of medical services.

Both direct costs are involved. resulting from the use of social assistance services, drug therapy and continuous care and indirect, caused by a decrease in productivity, resulting in the decreased ability to work and the loss of employment for the patient initially and subsequently for some family members.

The literature reinforces the involvement of genetic factors in the case of early-onset Alzheimer's disease, apparently discoveries have been made about the correlations between genetic changes and neurodegenerative mechanisms.(3)

This condition involves at least three etiopathogenic levels, as follows:

- Neurodegenerative elements (beta-amyloid, neurofibrils) correlated with genetic vulnerability (chromosome abnormalities 21, 14, 9, 4);(3)

The efficiency of neurotransmitters, particularly acetylcholine (main neurotransmitter involved in cognition) is low, this being associated with the amplification of glutamate activity, especially

in the moderate and severe stages of the disease, having as a consequence increased cerebral lesionality; (3)

Vascular-cerebral disorders, hypoxia, metabolic dysfunction (drug-induced hypercortisolemia, secondary to depressive disorder), disturb the balance of the neurofunctional unit, the neuronal binomial / glial cell. This imbalance increases the involvement of the glial cell, at which level glutamate is synthesized. Glutamate hyperactivity is thus a risk factor in the evolution of cerebral or neurodegenerative vascular lesions. (3)

Research on Alzheimer's dementia has undergone a paradigm shift, from the fact that it was regarded as a disease of the elderly, from a life-long perspective, today the evolution of the disease also involves lifestyle changes.

Genetic, psychological, lifestyle factors are involved in the etiopathogenesis of Alzheimer's type dementia; factors that, during the latent period of disease evolution, can act both independently and through mutual enhancement. Consequently, these risk factors are used to obtain risk scores in assessing the likelihood of dementia. Despite population differences, age, low education, and vascular risk factors were identified as key factors in all scoring systems. Risk scores can help identify high-risk individuals who may benefit from different interventions. The European Dementia Prevention Initiative (EDPI), an international collaboration, encourages the exchange of data between various randomized controlled trials. (4)

Although research has been conducted on the protective factors to prevent the onset of dementia, including vitamin E, folic acid, vitamin B6 and vitamin B12, the results of

clinical trials have been negative. Evidence from epidemiological studies on statins that may reduce the risk of dementia has not been confirmed; however, a 2009 Cochrane review did not reveal any effect of the use of older statins in the prevention of Alzheimer's or other types of dementia. (6)

Differential diagnoses with somatic diseases represent a crucial point in addressing this pathology, they must be made as early as possible. "These include treatable entities such as thyroid diseases, vitamin deficiencies, brain tumors, intoxication with medicinal products or drugs, chronic infections and severe depression (pseudodementia). (18)

Neuroimaging tests (CT scan-CT and nuclear magnetic resonance-MRI) are not specific for BA and may be normal in the early stages. However, CT and MRI help to exclude other conditions: primary and secondary neoplasms, multi-infarct dementia, diffuse white matter disease and normotensive hydrocephalus. As Alzheimer's disease progresses, diffuse cortical atrophy becomes visible, and detailed MRI examination reveals atrophy of the hippocampus (Figure 1). (18)

The electroencephalogram (EEG) may be normal or show nonspecific slowness. Routine examination of cerebrospinal fluid (CSF) is normal; More careful studies have shown a decrease in acetylcholine and amyloid A β with an increase in your protein. The considerable increase of these levels is related to the normal elderly population and the usefulness of these determinations in diagnosis remains unclear. "(18)

CURRENT THERAPEUTIC APPROACHES

The therapeutic strategies are based on the increase of the cholinergic transmission and on the modeling of the glutamatergic

transmission, hypotheses validated in the etiopathogenesis dementia of Alzheimer's type, the psychopharmacology focusing on the acetylcholine transmission deficit and the hyperactivity of NMDA receptors. (19)

Currently approved medication for dementia patients is limited to antidementials such as glutamatergic modulator (Memantine), acetylcholinesterase inhibitors (Donepezil, Galantamina), acetylcholinesterase inhibitor and butyrylcholinesterase (Rivastigmine) and adjuvant nootropic medication.

Pharmacokinetics and pharmacodynamics are significantly altered in the elderly. The treatment given to these persons must be "effective and with minimal side effects". (26) Neurocognitive disorder patients diagnosed with dementia of Alzheimer's type, are a special group with special needs, the concept of quality of life differs from that used for patients diagnosed with conditions that are clearly less debilitating.

COMPONENTS OF ALTERNATIVE THERAPY

Nonpharmacological therapies are considered therapeutic interventions that can be performed safely, quite cheaply compared to the costs associated with drug therapies, and whose effects can be monitored through evaluation scales. This type of therapy aims to facilitate, as much as possible, the maintenance of an effective cognition in the case of persons affected by dementia of Alzheimer's type or from the mild cognitive disorder.

A series of prospective cohort studies have suggested that in addition to anti - dementia psychotropic therapy, regular physical activity associated with standardized maceration herbal oily such as garlic (*Allium sativum*), hawthorn (*Crataegus oxyacantha* - linne) and

white mistletoe (*Viscum album*) can have a real effect on the risk factors involved in the etiopathogenesis of Alzheimer's dementia: diabetes, HTA, cerebrovascular disorders, X-metabolic syndrome.

In the absence of effective drug options for dementia, complementary medication (MC) have been thoroughly explored. Randomized controlled trials (RCTs) were conducted on a series of MC for dementia, cognitive decline and mild cognitive impairment (MCI), with many ongoing studies. (6)

Garlic (*Allium sativum*)

Allium sativum has been used for thousands of years for medical purposes; Sanskrit records indicate its medical use about 5000 years ago and has been used for at least 3000 years in Chinese medicine. It has been extensively studied in vitro in animal and human clinical trials and in epidemiological evaluations for its multiple medicinal properties. The quality of clinical trials is heterogeneous, making it difficult to compare them.

The antimicrobial, hypolipidemic, antioxidant and antithrombotic effects that have been attributed to garlic are supposed to be primarily linked to allicin, and the antineoplastic effects may be related to sulfur compounds or other unknown components.

Many randomized clinical studies have studied the effects of garlic on lipid levels, this role was underlined by two meta-analyses conducted in 1993 and 1994, regarding the effect of garlic on total cholesterol, which revealed a significant reduction in total cholesterol level (9 up to 12%) compared to placebo.

A more recent meta-analysis of 10 placebo-controlled studies using standard dry garlic powder showed significant decreases in total

cholesterol levels (19.2 mg per dL [0.50 mmol per L]), low levels of lipoprotein cholesterol (6.7 mg per dL (0.20 mmol per L)) and triglyceride levels (21.1 mg per dL [0.24 mmol per L]) at eight to twelve weeks.

Researchers at the Curtin's Life Science Facility have found that a certain garlic extract could help or even prevent the destruction the blood-brain barrier. This would be a real help in treating dementia of Alzheimer's type.

Hawthorn. (*Crataegus oxyacantha*)

Another study by 2017 researchers at Banasthali University, Jaipur, India and the Pinnacle Biomedical Research Institute, Bhopal, India, demonstrates the promising effect of *Crataegus oxyacantha* (hawthorn) in improving learning and memory due to the presence of certain phytochemicals.

Regarding cardiovascular effects, the primary activity of the hawthorn is to increase coronary blood flow, probably due to relaxation of the coronary arteries, resulting in direct increase in blood flow. Positive inotropic action of hawthorn may be due to Na⁺ / K⁺ inhibition, myocardial ATPase. It also lowers blood pressure, which results in increased effort tolerance during the early stage of congestive heart failure (CHF).

Surprisingly, hawthorn has the ability to adjust blood pressure (HTA / HTA). Since bioflavonoids dilate both peripheral and coronary blood vessels, it is recommended to use in angina pectoris.

The hawthorn increases the intracellular efficacy of vitamin C, thus having a protective effect on oxidative processes.

Anti-inflammatory effects have been discovered by preventing the synthesis and release of pro-inflammatory markers such as histamines, prostaglandins, leukotrienes, etc.

White mistletoe (*Viscum album*)

White mistletoe, known for immunomodulatory activity, is a real benefit in the prevention and therapeutic action of risk factors for dementia of Alzheimer's type by: homeostasis effect, stimulating effects on metabolism and beneficial action on the pancreas by regulating blood glucose.

Alternative and complementary therapies are used for dementia of Alzheimer's type in the prodromal phase, with the goal of reducing risk factors and at the same time improving quality of life, together with regular physical activity, a balanced diet containing fruits and vegetables rich in vitamin C, unsaturated fatty acids, smoking cessation and intellectual activity.

The mechanisms by which exercise can improve the cognition of patients with MCI or dementia are: increased blood flow and oxygen supply to the brain, decreased blood pressure, reduced inflammatory markers, improved endothelial function. It may also increase the volume of the hippocampus. It has been shown in animal studies that exercise stimulates the proliferation of neurons in hippocampal areas. (20)

METHODOLOGY

In this study, PUBMED, the Central Register of Cochrane Controlled Studies, the site of the Alzheimer's association, NCBI, was used for a preliminary search of the specialized literature.

Input data were taken after they have been identified randomized controlled trials (RCTs) which have the relevant data for the work. Terms were used in the search algorithm such as, "Alzheimer's type dementia", "Alzheimer's disease", "anti-dementia therapies", "alternative dementia therapies", "cognitive methods", "risk

factors", "dementia assisted protocols", "nutritional support "or" homeopathic therapy".

It was further examined the bibliography of studies identified in published meta-analyzes. The articles which proved to be duplicates or which did not meet the eligibility criteria imposed were not taken into account.

The process of searching and conducting the study took into account the PRISMA criteria. (23)

At the same time, we have analyzed extensively the specialized literature on the subject of Alzheimer's type dementia.

DISCUSSIONS

So far there are no known means of preventing Alzheimer's type dementia.

Due to the limited effectiveness of the drug therapy used and the involvement of a large number of professionals (eg doctors, psychologists, occupational therapists, assistants, carers, etc.) research based on non / pharmacological treatment (NPT) becomes important in the complex and individualized management of Alzheimer's type dementia.

NPT can improve the quality of life (QoL) of patients diagnosed with MCI and / or Alzheimer's type dementia, being noninvasive and having reduced side effects. (8)

NPT interventions are numerous, they play a role in reducing patient symptoms, caregiver stress and can be both simple (eg environmental interventions) to more complex approaches (eg, virtual reality, home automation). (7)

Non-pharmacological therapies do not act on the etiopathogenic mechanisms of Alzheimer dementia. but to improve the quality of life of the patient and of the caregiver while

maintaining its functionality and factors as well as the impact of non-pharmacological treatment on the quality of life of patients diagnosed with dementia of Alzheimer's type. independence as long as possible, however, a direct effect of NPT on neuronal plasticity / adaptation cannot be ruled out, especially in the latent, early stages of the disease.

This research analyzes both the effects of current anti-dementia therapy and the risk

ACKNOWLEDGEMENTS AND DISCLOSURES

The authors declare that they have no potential conflicts of interest to disclose.

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Submission: 10 aug 2019

Acceptance: 29 oct 2019