ASSOCIATION OF ORAL HEALTH WITH ALZHEIMER'S DISEASE: A REVIEW

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Abstract:
The relationship between oral infections, inflammation and some chronic non-communicable diseases highlights the importance of the mouth to the body and shows how oral health affects systemic health. Specific relationships have been identified with oral infection/inflammation and certain systemic diseases and conditions like cerebrovascular disease, diabetes mellitus, cardiovascular diseases, pregnancy outcomes and respiratory diseases. Another very interesting link is the relationship between oral infections and cognitive impairment, particularly the type of dementia known as Alzheimer's disease.

Key words: Alzheimer's disease, brain disorder, oral health

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DOI: 10.53555/ecb/2023.12.Si13.220

Introduction:

Alzheimer's disease is a disorder of the brain which slowly starts destroying the ability to do the simple work, thinking skills and memory.[1] In mid-60s of age, patients with Alzheimer's disease, late symptoms first appears. Occasionally, juvenile alzheimer's disease begins at 30-60 years of age.

Dementia in the elderly people is caused by Alzheimer's disease.[1] Dr. Alois Alzheimer named Alzheimer's disease. In 1906, a woman died of mental illness, Dr. Alzheimer observed changes in her tissue of the brain. Patient's symptoms were her behavior which was unpredictable, slurred speech and forgetfulness. Following her death, doctor investigated her brain and discovered many amyloid plaques (previously called abnormal clumps) and tau tangles or neurofibrillary tangles (previously called tangled bundles of fibers). Main symptoms of Alzheimer's disease are knots and plaques in the brain. Detached connections between neurons in the brain is also a sign. Neurons pass chemical and electrical signals between brain's different parts and from their to body's muscles and organs. In Alzheimer's disease, complicated changes in the brain changes can also be involved.

This impairment first occurs in the brain section which is memory based, like hippocampus and entorhinal cortex.[1] It then involves the cerebral cortex which is responsible for reasoning, language and social behavior. With time, many other brain areas are involved.

Alzheimer's disease cause is not well known.[2] Genetic and environmental risk factors may cause this disease. APOE (Apolipoprotein E) alleles is the main genetic factors.[2] Hypertension, head injury history and clinical depression are also the risk factors.[3]

Alzheimer's disease is primarily linked with detachment of connections of brain neurons, neurofibrillary tangles and amyloid plaques.[4] Provisional diagnosis is established by blood tests, medical history and analytical testing with medical imaging. Early symptoms are mostly misdiagnosed as aging process. Definitive diagnosis requires examination of brain tissue, which is performed only after the patient's death. Social, physical activity and proper nutrition are generally favorable for aging and be beneficial to reduce the risk of Alzheimer's disease. Clinical trials were done to investigate Alzheimer's in 2019. No supplements or drugs were helpful to reduce the risk.[5]

Two main components of the association between Alzheimer's disease and oral diseases are potential mechanisms to determine how oral infections affect the onset and Alzheimer's disease progression and how Alzheimer's disease affects oral health and the challenges of providing dental care to Alzheimer's patients.

Meta analysis and systematic review disclosed that there is a two way association between periodontal disease and dementia. Out of 12 articles, four articles reported on the effect of periodontal disease on dementia 08 articles on effect of dementia on periodontal disease. A meta-analysis concluded that there was 17% increased chances of dementia in the presence of periodontal disease (CI = 1.02–1.34, odds ratio = 1.17).[8] Moreover, he presence of dementia was associated with a 69% greater likelihood of periodontal disease (CI = 1.23–2.30, odds ratio = 1.69;). Longitudinal study of older age group (range 60–96 years) over 6 years showed that cognitive decline was associated with a number of risk factors like underweight (BMI <25), illiterate or little education, living solitary and cardiac disease history. Regarding the dental variables, the risk factors are presence of 4 mm of bone loss in more than 30% of the recorded sites, reduced teeth in number (1-19) and loss of teeth.[9]

Many review articles have speculated about a mechanistic relationship between Alzheimer's disease and periodontal disease. Teixeira et al.[11] showed that logical binding is caused by inflammation. Alzheimer's disease pathogenesis is linked to inflammation, which affects inflammation of the brain and affects microglial cells. It is an inflammatory condition that can exist for years and contributes to the systemic inflammatory burden.

Periodontitis can lead to an increased tumor necrosis factor-α, interleukin-1 and interleukin-6 (mediators of inflammation) in the serum. Circulation due to periodontitis and periodontal pathogens which enters the systemic circulation may both be precipitating factors. The prevalence increases with age in both the disorders.

A review which examines the possible infections importance which includes oral infections, in the etiology of Alzheimer's disease reported fungi (Candida), viruses (herpes simplex type 1) and bacteria (anaerobic bacteria Porphyromonas gingivalis and spirochetes). An inflammatory response triggered by direct brain infection. They suggested that risk factors like oral infections, genetic predisposition, malnutrition, and the presence of other chronic diseases should be considered. In addition, proper oral hygiene and periodontal disease treatment approaches to modulate Alzheimer's disease risk.

Dominy and colleagues[18] report in Science Advances concluded the association of periodontal disease and pathogenesis of Alzheimer's disease.

Porphyromonas gingivalis, is a key microorganism in periodontitis. Gram-negative anaerobic bacterium, Porphyromonas gingivalis produce virulence factors which plays an important role in periodontitis.[18]

Authors investigated evaluated brain tissue post-mortem from the patients with Alzheimer's disease, and on the control group tissue from healthy brains from patients with no cognitive impairment. Saliva and cerebrospinal fluid (CSF) were taken from patients with Alzheimer's disease. Results were that >90% of samples were positive for Porphyromonas gingivalis gingipains, that are proteases that play an important role in the Porphyromonas gingivalis pathogenicity by colonization of the bacteria, host response to infection neutralizes as well as breakdown of host tissue promoted. Unaffected persons brain tissue has statistically significantly low levels of gingipains. The tau levels, a protein which is found in neurons, increased in patients with Alzheimer's disease.

There was relationship between increased tau and increased gingipains in the brains of Alzheimer's disease. Ubiquitin gives similar results which is also Alzheimer's disease marker. Gingipains are present in the hippocampus which is the area of the brain first to affected by Alzheimer's disease. In the cerebral cortex, Gingipains were also present. In control group, low level gingipains were seen in the brain tissue.

Authors investigated saliva and cerebrospinal fluid in mild/moderate dementia and Alzheimer's disease patients. From 10 Alzheimer's patients, 07 patients showed P. gingivalis by polymerase chain reaction (PCR), and 10 patients had P. gingivalis in their saliva. Cerebrospinal fluid analysis is an approach for brain infections evaluation.

Animal study done in mice that were orally P. gingivalis affected which led to the infection of brain. Increase production of key indicators, this protein is the major content of amyloid plaques which is found in the Alzheimer's patient's brains. After developing a brain infection, administration of new drugs which block gingipain decreased the load of bacteria in the brain of mice, reduced inflammation and less Aβ1-42 production in the brain. Although this drug was only tested in the mice, small-molecule inhibitors of gingipain can treat P. gingivalis associated Alzheimer's disease.

Journal of American Dental Association in 2007, published a study that concluded a link between Alzheimer's and oral disease. Many identified chronic diseases risk factors do not exist. In the study, postmortem neuropathological findings were present. Analysis showed a high dementia risk which was associated with a less remaining teeth (1-9). The drawbacks of this present study was that periodontal disease was not only the cause of loss of teeth but also due to caries and other causes. The association with worsening oral health has been of great interest. Additional epidemiological evidence for an association with worsening oral health from the Taiwan National Database.[20.] Authors evaluated 9,291 patients with chronic periodontitis and 18,672 patients without chronic periodontitis with various variables such as age and sex, and found that People with a 10-year history of chronic periodontitis have been diagnosed with Alzheimer's disease. There were 1.71 people. Patients with chronic periodontitis had complications (hyperlipidemia, history of traumatic brain injury) associated with Alzheimer's disease.

Various studies have a periodontal pathogens role for with respect to periodontitis-specific variables associated with the development of Alzheimer's disease. In the study, cultures of cells of astrocyte (that play a supporting role in brain) absorbed Porphyromonas gingivalis lipopolysaccharide and lysates extracted from the 10 Alzheimer's patients brains were tested. The results showed that 4 out of 10 lysates shows the ability to absorb. Lysate from control (intact) brain showed no uptake. Furthermore, increased antibody titers against many periodontal bacteria (including Porphyromonas gingivalis) were associated Alzheimer's disease risk. Although this study did not correlate with the cognitive decline degree in trial, the periodontitis was present with 6 patients. Increased parity in cognitive decline over the next 6 months.

Reviews and previous studies have correlated a link between Alzheimer's disease and chronic periodontitis. Dominy et al.[18] gives this association of animal models and human brain tissue supports the specific proteases importance that are released from P. gingivalis. These become very important with the aging of the population and the preservation of their teeth and the increasing prevalence of periodontal disease in the elderly.

The dementia research work continues with change in definitions and diagnostic criteria for certain disorders and a better risk factors knowledge for disorders like Alzheimer's disease. Dementia usually exhibits a long preclinical stage, with history occurring over several years. Alzheimer's disease development is the due to direct and indirect risk factors (health status, behavior, genetics and non-communicable diseases).[18]

Human models

1. Porphyromonas gingivalis has been noticed in the brain tissue of human Alzheimer's disease.
2. Gingipain from Porphyromonas gingivalis was detected in Alzheimer's disease patient's brain tissue. It is related to brain pathology.
3. Detects DNA from Porphyromonas gingivalis in the cerebrospinal fluid of Alzheimer's patients.

In Animal models

1. Porphyromonas gingivalis infection of mice causes brain infection and is associated with amyloid production.
2. Gingipain from Porphyromonas gingivalis is noticed in the infected mice brains and it is toxic to brain (neurotoxic).
3. Porphyromonas gingivalis-derived gingipain inhibitor reduced Porphyromonas gingivalis brain colonization, blocked amyloid production and reduced brain inflammation.

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