



## **Informe preliminar**

# **Enfermedad de Alzheimer y enfermedad periodontal. Efecto sobre los pacientes de Alzheimer y sus cuidadores**

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Septiembre 2009

## 1.- La Enfermedad Periodontal (EP) como factor de riesgo de la Enfermedad de Alzheimer (EA):

El Nun Study estudia el efecto de la inflamación periodontal en la demencia y la enfermedad de Alzheimer (EA). Relaciona el número de dientes presentes y otras variables, como la inflamación periodontal y la edad, con la EA[1]. Estudia un grupo homogéneo de hermanas católicas de la congregación de La Escuela de las Hermanas de Notre Dame[2]. Un análisis de datos longitudinales de 144 participantes demostró que **conservar un número reducido de dientes implica un riesgo mayor de incidencia y prevalencia e demencia en los años subsiguientes** [3]. Se estudió la relación entre las restauraciones de amalgama y las funciones cognitivas y no se encontró relación [4].

The thrust of the article is to look at the number of teeth, periodontal conditions, other inflammatory conditions and age in educationally matched patients with extremely similar lifestyles. The nun study is an exceptional arena for gathering data.[1]

The Nun Study is a longitudinal study of 678 Catholic sisters 75 to 107 years of age who are members of the School Sisters of Notre Dame congregation.[2]

Numerous studies have linked dementia to the subsequent deterioration of oral health. Few investigators, however, have examined oral disease as a potential risk factor in the development of dementia. The authors conducted a study to investigate a potential association between a history of oral disease and the development of dementia. **METHODS:** Longitudinal dental records supplemented data collected from 10 annual cognitive assessments of 144 Milwaukee participants in the Nun Study, a longitudinal study of aging and Alzheimer disease, who were 75 to 98 years old. Neuropathologic findings at autopsy were available for 118 participants who died. **RESULTS:** A low number of teeth increased the risk of higher prevalence and incidence of dementia. **CONCLUSION:** Participants with the fewest teeth had the highest risk of prevalence and incidence of dementia. **CLINICAL IMPLICATIONS:** Edentulism or very few (one to nine) teeth may be predictors of dementia late in life.[3]

The authors determined the number and surface area of occlusal dental amalgams in a group of 129 Roman Catholic sisters who were 75 to 102 years of age. Findings from this study of women with relatively homogeneous adult lifestyles and environments suggest that existing amalgams are not associated with lower performance on eight different tests of cognitive function.[4]

**Se cree que la etiología de la EA está relacionada con la inflamación cerebral, y que las infecciones periféricas pueden contribuir a la inflamación en el sistema nervioso central.** La periodontitis es una infección periférica muy extendida en la población, producida por bacterias anaeróbicas capaces de producir infecciones a distancia, localizadas en otras zonas, o generalizadas. Lo importante es que es una condición tratable y en consecuencia un factor de riesgo modificable.[5, 6]

The aetiology and pathogenic mechanisms for AD have not been defined, although inflammation within the brain is thought to play a role. Consistent with this hypothesis, studies suggest that peripheral infections contribute to the inflammatory state of the central nervous system. Periodontitis is a prevalent, persistent peripheral

infection associated with gram negative, anaerobic bacteria that are capable of exhibiting localized and systemic infections in the host. This review offers a hypothetical link between periodontitis and AD and will present possible mechanistic links between periodontitis related inflammation and AD. It will review the pathogenesis of periodontitis and the mechanisms by which periodontal infections may affect the onset and progression of AD. Since periodontitis is a treatable condition, it may be a readily modifiable risk factor for AD.[5]

La enfermedad periodontal está relacionada significativamente con una **alteración de la memoria tardía y de la capacidad de cálculo numérico**. [7]

Third National Health and Nutrition Examination Survey (NHANES-III), a nationally representative cross-sectional observational study among older adults. We included 2355 participants  $\geq 60$  years who completed measures of cognition and Poryphyromona gingivalis IgG. Using SUDAAN, logistic regression models examined the association of P.gingivalis IgG with cognitive test performance. A serological marker of periodontitis is associated with impaired delayed memory and calculation. Further exploration of relationships between oral health and cognition is warranted.[7]

Un análisis de datos longitudinales de 144 participantes del Nun Study demostró que conservar un número reducido de dientes implica un riesgo mayor de incidencia y prevalencia e demencia en los años subsiguientes [3]. Y un estudio sobre población coreana de duración de 2.4 años encontró igualmente una asociación entre **conservar pocos dientes y la aparición de demencia o EA**, especialmente en los pacientes que no usaban dentaduras. Sin embargo, no se encontró asociación entre desnutrición y demencia. Tener pocos dientes puede ser un marcador de demencia, y podría estar relacionado con efectos colaterales de la enfermedad periodontal [8].

BACKGROUND: Dental health is an important determinant of nutritional status, but has not been investigated as a risk factor for dementia. This study aimed to investigate the association between number of teeth, use of dentures and recent-onset dementia. METHODS: This was a cross-sectional analysis nested within a prospective study of community dwelling elderly residents in two areas of Kwangju, South Korea. In a study of 686 community residents aged 65 or over without dementia followed over 2.4 years, measures of dental health were compared between those with and without dementia at follow-up. RESULTS: Fewer teeth were significantly associated with dementia and Alzheimer's disease. This association was strongest in participants without dentures. Strong associations were found between fewer teeth and indices of poor nutrition in this group, but these did not account for the association with dementia. CONCLUSIONS: Having fewer teeth may be a marker of risk for dementia. This might be explained by specific nutritional deficits, or by other side effects of periodontal disease. Further prospective research is indicated.[8]

Se han detectado hasta **10 polimorfismos que afectan al funcionamiento de agentes antiinflamatorios endógenos que están relacionados con la EA**, así como con otras enfermedades relacionadas con desórdenes periféricos de los mecanismos de inflamación, como la artritis reumatoide juvenil, **la periodontitis** o la miastenia gravis, lo que permitiría explicar la posible asociación de ambas enfermedades [9].

The concept of inflammation as a major factor in Alzheimer disease (AD) has heretofore been based on post-mortem findings of autodestructive changes associated with the lesions coupled with epidemiological evidence of a protective effect of anti-inflammatory agents. Now there is evidence that the risk of AD is

substantially influenced by a total of 10 polymorphisms in the inflammatory agents interleukin 1alpha, interleukin 1beta, interleukin 6, tumour necrosis factor alpha, alpha(2)-macroglobulin, and alpha(1)-antichymotrypsin. The polymorphisms are all common ones in the general population, so there is a strong likelihood that any given individual will inherit 1 or more of the high-risk alleles. The overall chances of an individual developing AD might be profoundly affected by a "susceptibility profile" reflecting the combined influence of inheriting multiple high-risk alleles. Since some of the polymorphisms in question have already been linked to peripheral inflammatory disorders, such as juvenile rheumatoid arthritis, myasthenia gravis, and periodontitis, associations between AD and several chronic degenerative diseases may eventually be demonstrated. Such information could lead to strategies for therapeutic intervention in the early stages of such disorders [9].

La **neumonía de aspiración** es la causa de muerte más común en las fases finales de la EA. Dentro de los problemas primarios que predisponen a ella está la **enfermedad periodontal** [10].

Aspiration pneumonia is the most common cause of death in end-stage AD. The primary problems that predispose to aspiration pneumonia include a reduced level of consciousness, dysphagia, loss of the gag reflex, periodontal disease, and the mechanical effects of inserting various tubes into the respiratory and gastrointestinal tracts. The bacterial flora involved include the indigenous oral flora (among which aerobes predominate) and, in the hospital or nursing home setting, nosocomially acquired pathogens such as *Staphylococcus aureus* and various aerobic and facultative gram-negative bacilli that may colonize in patients. In addition to treatment with antibiotics, adequate symptomatic treatment of AD patients with pneumonia is a priority in order to relieve suffering [10].

## **2.- Afeción periodontal y estado médico de los esposos cuidadores de pacientes con EA:**

Los esposos cuidadores de pacientes de EA presentan en un 17% síntomas de EP, mientras que los controles que no cuidan de EA sólo un 8,5%. Los cuidadores de EA tienen además complicaciones médicas, depresión, obesidad o problemas diabéticos. Esto puede estar afectado por el stress crónico al que estos pacientes están sometidos[11].

En pacientes por encima de 50 años los niveles de cortisol están relacionados con el estrés psicológico y con la extensión y severidad de la enfermedad periodontal [12].

La IL-6 es una citoquina proinflamatoria que está relacionada con patología relacionada con la edad como la enfermedad cardiovascular, osteoporosis, artritis, diabetes tipo 2, algún tipo de cáncer, periodontitis, debilidad y declive funcional. En un estudio longitudinal de 6 años se observó que los esposos cuidadores de pacientes con demencia tenían 4 veces más IL-6 que los controles. Estos datos apoyan uno de los mecanismos mediante los cuales los estresores crónicos pueden acelerar el curso de las patologías relacionadas con la edad envejeciendo el sistema inmunológico [13, 14].

Caregivers of spouses with Alzheimer's disease (n = 123) were compared with demographically similar noncaregiver spouses (n = 117). RESULTS: The percentage of caregivers (17%) who reported gingival symptoms was twice that of noncaregivers (8.5%) (p < .05), despite the fact that caregivers and noncaregivers did not differ in oral health care. The relationship between caregiving and gingival symptom reports was mediated by psychophysiologic variables. Caregivers were higher on hassles (p < .05), depressed mood (p < .05), and metabolic risk (insulin, glucose, obesity; p < .05) than were noncaregivers. Greater gingival symptom

reports were also associated with greater hassles ( $p < .01$ ), depressed mood ( $p < .001$ ), and metabolic risk ( $p < .001$ ). Measures of subcutaneous fat, inflammation, and frank diabetes were related to gingival symptom reports but not to caregiver status. **CONCLUSIONS:** A higher percentage of caregivers reported gingival symptoms than noncaregivers. These results have implications for research on aging, psychophysiology, and chronic stress [11].

Periodontitis and its relationship with psycho-neuro-immunological variables, such as psychological stress and cortisol, have been little explored. The objective of this study was to evaluate the extent and severity of chronic periodontitis and its association with the levels of salivary cortisol and the scores obtained with a stress questionnaire in a population aged 50 years and over. We studied 235 individuals in a cross-sectional study. They answered the Lipp's Inventory of Stress Symptoms for Adults, were instructed to collect three saliva samples for cortisol analysis, and were examined for evaluation for periodontitis. Based on logistic regression, cortisol levels were positively associated with the following outcomes: means of clinical attachment level (CAL)  $\geq 4$  mm [OR = 5.1, 95%CI (1.2, 20.7)]; 30% of sites with CAL  $\geq 5$  mm [OR = 6.9, 95%CI (1.7, 27.1)]; and 26% of sites with probing depth  $\geq 4$  mm [OR = 10.7, 95%CI (1.9, 54.1)] after adjustment for confounding variables. The results suggest that cortisol levels were positively associated with the extent and severity of periodontitis[12].

Overproduction of IL-6, a proinflammatory cytokine, is associated with a spectrum of age-related conditions including cardiovascular disease, osteoporosis, arthritis, type 2 diabetes, certain cancers, periodontal disease, frailty, and functional decline. To describe the pattern of change in IL-6 over 6 years among older adults undergoing a chronic stressor, this longitudinal community study assessed the relationship between chronic stress and IL-6 production in 119 men and women who were caregiving for a spouse with dementia and 106 noncaregivers, with a mean age at study entry of 70.58 (SD = 8.03) for the full sample. On entry into this portion of the longitudinal study, 28 of the caregivers' spouses had already died, and an additional 50 of the 119 spouses died during the 6 years of this study. Levels of IL-6 and health behaviours associated with IL-6 were measured across 6 years. Caregivers' average rate of increase in IL-6 was about four times as large as that of noncaregivers. Moreover, the mean annual changes in IL-6 among former caregivers did not differ from that of current caregivers even several years after the death of the impaired spouse. There were no systematic group differences in chronic health problems, medications, or health-relevant behaviours that might have accounted for caregivers' steeper IL-6 slope. These data provide evidence of a key mechanism through which chronic stressors may accelerate risk of a host of age-related diseases by prematurely aging the immune response [13].

Psychoneuroimmunology (PNI) investigates the relations between the psychophysiological and immunophysiological dimensions of living beings. PNI brings together researchers in a number of scientific and medical disciplines, including psychology, the neurosciences, immunology, physiology, pharmacology, psychiatry, behavioural medicine, infectious diseases, and rheumatology. All are scientists with profound interest in interactions between the nervous and immune systems, and the relation between behaviour and health. Despite the variety in domains and approaches to research, the outcome common to all research endeavours is the discovery of new information, of uncovered facts, of novel evidence, which contributes to the continuing generation of knowledge. In this paper we discuss psychoneuroimmune aspects of some conditions that are not routinely immediately associated with immunity, such as the condition of being the caregiver of somebody suffering from dementia; the effect on the brain-body modulations of aluminium, a metal that is not a component of the human body; and insomnia, a fairly common but disturbing disease, that even today lacks an effectual treatment [14].

### 3.- Efecto sobre la salud oral de los pacientes institucionalizados con demencia:

Estudio sobre 125 institucionalizados en Fiji, de los que el 37% tenían problemas cognitivos, médicos y de comportamiento compatibles con demencia. 43% eran desdentados y el resto tenían caries, restos radiculares (DMF 23) y enfermedad periodontal avanzada, siendo este deterioro más marcado en los fumadores y en los más imposibilitados. **La patología de estos pacientes era significativamente superior a una cohorte control de pacientes sin demencia no institucionalizados** [15]

348 pacientes ancianos institucionalizados en Perth. 52% desdentados (45% con patología mucosa), DMF 24,7, el 50% tenía cálculo supragingival y 2 restos radiculares cubiertos de placa. 47% fueron diagnosticados de demencia [16]

326 sujetos ingresados en hospitales psiquiátricos en Gales, el 47% con demencia. 63% desdentados, DMF 19,1, mala higiene oral y enfermedad periodontal moderada, necesitada de raspado y alisado [17]

**En pacientes institucionalizados se encuentra patología oral de importancia, agravada probablemente por las dificultades de autocuidarse de los pacientes. Entre un 43 y 63% de desdentados, DMF entre 19 y 25, mala higiene oral y enfermedad periodontal que necesita tratamiento y restos radiculares que extraer.**

This study provided comprehensive information concerning oral health status and prevalence of oral diseases in institutionalized elderly home residents. The oral health survey included questionnaire and oral examination. Oral examination was carried out by a calibrated examiner. A structured interview on socio-economic status, oral health habits and a clinical evaluation of oral health status and treatment needs were recorded. 37.2 % of the 125 residents from the six nursing homes were medically compromised, functionally dependent, cognitively impaired and behaviourally difficult older adults to caregivers and to dental practitioners. 43% of the study population was edentulous. Dentate residents had a mean DMF of 23 with severe periodontal diseases and treatment need. Oral hygiene was generally poor among the residents and periodontal disease was found to be present in all the dentate subjects examined. The prevalence and experience of coronal and root caries, gingival recession and plaque accumulation was very high in dentate residents especially, those who smoke and those who were severely handicapped. These elderly residents had more retained roots, root caries, missing teeth, mobile teeth, grossly carious teeth and fewer filled teeth when compared with data for community dwelling elderly patients. This study highlighted the poor oral health status of these institutionalized elderly home residents and the great impact of dementia on their high levels of oral diseases [15].

This study aimed to estimate the dental treatment needs and oral health status of a sample of older adults in residential aged care facilities in Perth. **METHODS:** The 348 participants (> or = 65 years) were interviewed and screened in 25 facilities. The screenings were carried out by one examiner using a mirror and a portable light. **RESULTS:** Over half (52 per cent) of the participants were edentulous and 45 per cent of those edentulous participants for whom a recording was made (n=174) had oral mucosal conditions. The 164 dentate participants had a mean of 12 disease-free standing teeth, a mean decayed, missing or filled teeth (DMFT) of 24.7 (mean DT 0.8, mean FT 5.3) and half of them required the removal of supragingival calculus. Of those with root caries experience (n=127), a mean of 1.3 untreated decayed roots and a mean of 1.9 roots covered in plaque were recorded. The majority of the participants (83 per cent) were pensioners eligible for government subsidized dental care and 47 per cent were reported by the Directors of Nursing to have dementia. **CONCLUSIONS:** The data collected here demonstrate poor oral health conditions and a substantial treatment need in a neglected population. More people in nursing

homes and hostels are keeping their natural teeth compared with a similar population studied 13 years ago [16].

Little information is available regarding the oral health of hospitalized psychiatric patients. The aims of the study were: to quantify the oral health status and identify dental treatment needs of hospitalized psychiatric patients in South Wales; and to compare the oral health of subgroups within the population by their age, psychiatric diagnosis, psychotropic medication use, and length of stay. The total patient population of the hospitals involved in the study was 469, and 326 subjects (70%) took part in the study. The mean age of the subjects was 71.1 years, with 265 long-stay and 61 short-stay patients. Forty-seven percent of patients had a psychiatric diagnosis of dementia, 23% of schizophrenia, and 19% of depressive illness. The examination included assessment of oral hygiene, periodontal condition, and prevalence of caries. The treatment needs of the population were also determined. It was found that 63% of the population was edentulous. The mean DMFT score was 19.1 +/- 7.9 (SD). Comparison with the DMFT of the general population showed a similar level of decay, fewer filled teeth, and more missing teeth in the study population. The oral hygiene of the dentate population was poor, and there was little periodontal disease. Treatment needs were mainly for scaling and polishing. There were no significant differences found between subgroups within the population [17].

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