Could periodontitis play a role in the pathogenesis of Alzheimer’s disease?

Periodontitis and Alzheimer’s disease cause totally different symptoms, but there are many similarities in their pathogenesis. Both are chronic, inflammatory, and degenerative conditions that have both familial and sporadic forms, and both are caused by a multifactorial interplay of wider genetic, environmental, and behavioural risk factors. Tanya Cerajewska and Nicola West, researchers at the University of Bristol, explore the links between the two conditions.

Im losing my sense of self, and that is more frightening than anything because that’s all I have – that’s all any of us have’.

This poignant insight, from the recent memoir Somebody I used to know by Wendy Mitchell, casts light on what it is like to live with Alzheimer’s disease (AD), a severely debilitating, incurable, neurodegenerative condition. AD commonly presents with worsening forgetfulness and eventually progresses to gravely affect every aspect of cognitive function. It is often a frightening condition, capable of terrorising those affected and their loved ones.

The most common cause of dementia, AD affects six per cent of the European population over 60 years of age. The chance of developing dementia increases exponentially beyond the age of 60: while fewer than two per cent of Europeans aged between 60 and 64 are living with dementia, the figure rises to nearly 40% of people aged over 90.

The vast majority of people living with AD have sporadic forms of the condition, with autosomal-dominant familial forms of AD accounting for only two or three per cent of all AD diagnoses.

The first case of AD was described in the early 1900s, but the pathogenesis of the condition remains elusive, despite vast amounts of scientific and clinical research. The key discoveries relating to AD, which are relevant to its possible association with periodontitis, are outlined in Figure 1. The pathological hallmarks of AD are recognised as:

1. Neurofibrilllary tangles (NFT) within neurons;
2. Amyloid plaques containing amyloid beta peptides (Aβ).

These hallmarks, along with the symptoms of clinical dementia, are required for a diagnosis of AD. Both NFT and amyloid plaques can predate the onset of dementia symptoms by 10 years or more. It is widely believed that the pathogenesis of AD is related to increased amounts and toxic forms of Aβ within the brain. This can occur as the result of genetic mutations known to play a causal role in the familial forms of the condition. The causation of sporadic AD is not fully understood, yet it seems likely that there is an interplay of factors leading to these same pathological hallmarks.

Aβ is known to disrupt synapse function and cause neuronal death, although the amount of Aβ does not correlate with AD symptoms. Reducing Key –Type of discovery

Pathology
Theoretical
Genetic
Bacterial
Host immune-inflammatory response
Other important findings

1906 Alois Alzheimer reported the case of Auguste Deter. ‘Milliary foci’ (later called amyloid plaques) were found in Auguste’s brain post-mortem
1974 NFTs first isolated from human brain with AD
1984 Aβ identified as main component of amyloid plaques
1986 Hyperphosphorylated tau protein identified as the main component of NFTs
1987 Amyloid Precursor Protein (APP) gene mutations found to cause inherited AD
1990 Aβ found toxic to neurons in vitro
1991 Amyloid cascade hypothesis proposed
1993 Presenilin 1 & 2 genetic mutations found to cause inherited forms of AD via increased toxic forms of Aβ
1995 Apolipoprotein-e4 was the first gene variation found to increase the risk of developing AD, and remains the most significant risk factor for sporadic AD
1999 Pathology of Aβ plaques and NFTs shown to present more than a decade before AD symptoms
2002 Oral spirochaetes isolated from brainstem and cortex of those with AD more readily than controls
2005 Type-2 diabetes mellitus found to increase risk of developing AD
2010 Aβ peptides recognised as having anti-microbial function capable of killing bacteria & fungi
2013 Aβ recognised as capable of inducing inflammation via Inflammasome in AD
2015 LPS from periodontal pathogens is found in human AD brain
2016 Peripherical neutrophils found capable of crossing the blood-brain barrier to influence rate of cognitive decline
2017 Cognitive decline and Aβ in the brains of AD mice were shown to increase after inducing periodontitis with oral Pgingivalis
2018 Neuroinflammation generally accepted to play a role in the development and progression of AD
2019 Bacterial DNA more readily sequenced from post-mortem AD brain than control brain tissue

Figure 1. Timeline of key AD discoveries relevant to the potential association with periodontitis

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cerebral Aβ does not cure or stop the progression of AD, as has been shown by numerous unsuccessful drug trials. Aβ has antimicrobial functions and may be responsive to bacteria, viruses, or fungi, initiating a chain of neuroinflammatory pathological events that, once begun, can continue independently of amyloid levels. Neuroinflammation is now widely recognised as being implicated in AD progression. Recent discoveries, including those related to periodontitis (Figure 1), add weight to the likelihood of an immuno-inflammatory aetiology of AD – which could potentially be influenced by peripheral diseases such as periodontitis. Although periodontitis and AD cause entirely different symptoms, their pathogenesis shares many similarities. They are both chronic, inflammatory and degenerative conditions that have familial and sporadic forms, and which occur as a result of a genetic, environmental and which occur as a result of a combination of factors. Periodontitis has also been significantly associated with an increased rate of cognitive decline in people with mild to moderate AD. The cognitive decline of AD patients, with and without periodontitis, was measured for 52 participants over a six-month period. Those with periodontitis had a six-fold increase in the rate of cognitive decline, independent of the baseline cognitive state. The principle genetic risk factor for late onset AD – APOE4 status – was not statistically different between periodontitis and control groups. Larger studies are required to verify that the results obtained in these smaller studies did not occur by chance. Three case-control studies – which analysed between 6,000 and 28,000 data sets – found that periodontitis may increase the risk of developing dementia. These studies identified those with chronic periodontitis as being 1.16 to 2.54 times more likely to develop dementia in the follow-up period of between one and 10 years. However, the results of these studies need to be interpreted with caution for various reasons. Each of these studies retrospectively analysed the same cohort of patients using information from insurance healthcare records of a Taiwanese population, which may or may not be applicable to other cohorts with dissimilar genetic backgrounds. Little information was provided regarding the diagnostic criteria for periodontitis, while the diagnostic criteria used for dementia is known to select patients with more advanced symptoms. Thus, reverse causality cannot be excluded. In addition, shared risk factors – such as APOE risk – were not controlled for.

Potential mechanisms
The potential mechanisms through which periodontitis could affect the pathogenesis of AD are shown in Figure 2. An interplay between several mechanisms could account for the observed association between periodontitis and AD. A plethora of evidence has come to light which refutes the traditional view of the brain as sterile and isolated from the rest of the body by the blood–brain barrier (BBB). Immune cells and inflammatory mediators involved in the periphery are now known to be capable of crossing the BBB. Many studies have identified microbes, their DNA, and components within brain tissue affected by AD. A variety of microbes, including periodontal pathogens (Figure 2, B), have been identified within the AD brain by numerous researchers using a range of molecular techniques. There are several potential means by which microbes could enter the parenchyma of the brain, shown in Figure 3.

It is well known that periodontal pathogens enter the blood vessels of the systemic circulation and viable periodontal pathogens have also been identified in atherosclerotic plaques. It is therefore possible that oral bacteria could reach the brain via systemic circulation. Porphyromonas gingivalis is capable of disrupting the host’s barrier function, potentially affecting both the junctional epithelial attachment of the gingivae and the BBB. Once within the circulatory system, pathogens may also penetrate the brain via structures not encapsulated by the BBB (e.g. circumventricular organs) or via meningeal channels. Another potential entry portal for peripheral pathogens to reach the brain is via the cranial nerve afferents, particularly as oral treponema have been identified in the trigeminal ganglia, and many of the first changes associated with AD pathology occur in the locus coeruleus within the brainstem, close to the cranial nerve nuclei.

In the 1990s, spirochaetes – including oral pathogens – were identified using microscopy from human post-mortem cerebrospinal fluid from people with AD, but without age-matched controls. Treponema denticola and other spirochaetes were subsequently identified using molecular DNA analysis and immunological techniques. Spirochaetes were identified from more than 90% of AD brains analysed. Lipopolysaccharide (LPS) from P. gingivalis has also been detected in the human AD brain, but not in control samples. Elevated plasma levels of antibodies to the periodontal pathogens Aggregatibacter actinomycetemcomitans, Tannerella forsythia, T. denticola, and P. gingivalis were found in more AD patients than in controls, demonstrating that these bacteria are capable of stimulating a cerebral immune response. Furthermore, a longitudinal study of cognitively unimpaired individuals found that higher baseline serum antibody levels to Prevotella intermedia and Fusobacterium nucleatum correlated with cognitive deficits a decade later. Other bacteria – e.g. Borrelia burgdorferi, Propionibacterium acnei, and Escherichia coli – have also been identified more
frequently from AD brains than from controls. Recent microbiome analyses using multiplex DNA sequencing with reduced bias have provided noteworthy and similar differences in the proportion of bacterial families between AD and control samples. Staphylococcaceae, Burkholderiaceae, and Propionibacteriaceae appear to be present in increased proportions in the AD brain.

Recent findings indicate a direct mechanism whereby bacteria could initiate pathological changes associated with AD and potentially contribute to uncontrolled neuroinflammation. Aβ has antimicrobial functions and, because of this, it potentially increases in response to cerebral infection. LPS from P. gingivalis has been shown to induce Aβ production in neuronal cell cultures.

Spirochaetes were recently shown to form Aβ and amyloid plaques containing both bacterial and host-derived Aβ. Oral inoculation of P. gingivalis in an AD mouse model – which induced periodontitis (determined by alveolar bone loss) – resulted in increased levels of IL-1β, TNFα, and endotoxin in the brain. Cognitive function was significantly impaired in mice affected by periodontitis and they also had increased toxic forms of Aβ in the hippocampus and cortex.

Bacteria are not the only microbes implicated in AD. There are around 100 individual studies that indicate the herpes simplex virus 1 (HSV 1) as a major risk factor for AD. Circulating antibodies to cytomegalovirus (CMV) have also been associated with AD progression, and faster cognitive decline was seen in those infected over the following five years. These viruses have also been isolated from periodontal pockets with greater frequency than from healthy gingival crevices. Similarly, there is evidence that fungi (e.g. Candida albicans) are more commonly associated with brains with AD than with those in control groups.

The immuno-inflammatory response typical of periodontitis may contribute to heightening the neuroinflammation in AD (Figure 2, C) and therefore contribute to AD progression. The central nervous system (CNS) has a specialist immune system that includes numerous glial cells. Microglia, the predominant immune cell within the brain, can change from a benign supporting cell to a pro-inflammatory state when stimulated. Periodontitis is an example of peripheral inflammation that could cause microglia to be primed into a pro-inflammatory phenotype, capable of causing further neurodegeneration. The pro-inflammatory phenotype of peripheral macrophages is also associated with tissue destruction in periodontitis.

Primed peripheral macrophages and inflammatory mediators involved in periodontitis may be implicated in priming microglia. Other glial cells have also been shown to have similar pro-inflammatory responses, which ultimately result in heightened cognitive decline.

Neutrophils, the most prevalent leukocyte in inflamed periodontal tissues, can enter the human brain. Once there, they can contribute towards the pathogenesis of AD to affect the rate of cognitive decline. There is evidence of neutrophils surrounding Aβ plaques with extracellular traps (NETs), which can cause breakdown of the BBB and – once within the brain – could cause pro-inflammatory glial cell activation, with further potential for neuronal damage.

The additional load placed on the CNS as the result of peripheral infection and inflammation (e.g. periodontitis) could lead to an overload of the clearance mechanisms for Aβ, resulting in the build-up of this neurotoxic peptide within the brain. Astrocytes contribute to the clearance of Aβ by direct phagocytosis and control of water channels involved in venous clearance. These mechanisms are efficient when also required to phagocytose other inflammatory mediators or pathogens. Microglia also become less efficient at clearing Aβ when chronically stimulated, thus chronic microglial activation in mice following repeated LPS results in increased Aβ deposition. In animal studies, cytokines (IL-1β, IL-6, and TNFα) have been shown to cross the BBB and influence efflux transporters, leading to the overall increase of cerebral Aβ and cytokines that further drive the neurodegenerative processes.

Periodontitis and AD share several risk factors (Figure 2, A). Genome-wide association studies, which search the genome for small genetic differences associated with particular traits, have identified genes that have single-nucleotide polymorphisms (SNPs) implicated in both periodontitis and AD. At least 25 genes share SNPs associated with AD and periodontitis. These encode for proteins involved in a wide range of cellular functions, membrane transport, and immuno-inflammatory functions.

**Figure 3.** Potential routes for peripheral pathogens and inflammatory mediators to enter the brain.
In addition to this, shared environmental and behavioural risk factors – including diabetes mellitus, atherosclerosis, tobacco smoking, and previous educational attainment – increase the likelihood of developing both periodontitis and AD.

The impact of reverse causation is also an important probable mechanism to explain part of the association between periodontitis and AD (Figure 2, D). As cognitive function deteriorates, so does the patient’s ability to perform effective oral hygiene. For most patients, impaired plaque control increases periodontitis risk. For the patient with AD and periodontitis, this could result in a negative feedback loop, where peripheral pathogens and/or inflammation impact negatively on further neurodegeneration.

**Conclusion**

Recent epidemiologic studies indicate there is an association between AD and periodontitis, but further work is required to describe the nature of this association. Mounting scientific evidence strongly suggests that cerebral microbial infection and neuroinflammation are implicated in the pathogenesis of AD. Oral bacteria and periodontal pathogens are some of the microbes identified from post-mortem AD brains. Despite growing evidence for the potential role of periodontal pathogens and inflammation in the pathogenesis of AD, further research is required across several research spheres to determine whether there is a causal association between periodontitis and AD. These are likely to include clinical, epidemiological, and scientific studies using genomic and proteomic techniques to understand more about the human microbiome interactome.

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**Select Bibliography**


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What impact will new classification have on research?

The new classification of periodontal and peri-implant diseases and conditions, presented formally at EuroPerio9 in June 2018, will have a big impact on clinical research. Mia Rakic, EFP delegate from the Serbian Society of Periodontology, offers an overview of the research implications, highlighting how correct classification of periodontal conditions “is fundamental to successful disease resolution”, while clinicians from across Europe explain what replacing “chronic” and “aggressive” periodontitis with a system based on four “stages” and three “grades” will mean for researchers and clinicians.

The appropriate classification of periodontal conditions is fundamental to successful disease resolution in both clinical and research settings. From the clinical perspective, the diagnosis of periodontal conditions directly impacts appropriate treatment planning and prognosis because the treatment plan is built against pathological conditions and risk factors identified during diagnosis. In the scientific setting, the new classification facilitates future research to address appropriate solutions for clinical concerns and enables researchers to make an accurate case selection, which will ensure the quality of research outcomes.

In developing a new classification, the experts are required to turn state-of-the-art scientific and clinical knowledge into a clinical concept and simplify it so that it is easy for any clinician or researcher to interpret and apply. The main tendency in the evolution of classifications in periodontology has been a constant improvement in the precision of defining periodontal conditions. Given the multifactorial aetiology of periodontitis and an ever-increasing number of discovered contributing factors, the task of updating the definitions was particularly challenging for the World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions in November 2017. The new classification introduces the use of biomarkers as the grading criteria. However, the question marks in the table on grading periodontitis (Figure 1) show that we still lack the necessary standardised biomarkers – as a footnote to the table notes, “Question marks in the last row indicate that specific biomarkers and their thresholds may be incorporated in the table as evidence becomes available.” So, action is needed to identify new biomarkers and standardise them for diagnostic use in the clinical setting. Research is strongly encouraged to identify critical biomarkers and then develop personalised predictive models.

**Aggressive periodontitis**

The most controversial innovation in the new classification system is the removal of aggressive periodontitis as an independent form of the disease. The concept of aggressive periodontitis was introduced in the 1999 classification as a specific biological form of periodontal disease affecting the younger population, characterised by progressive periodontal destruction often located in the incisor-molar group. Such fulminant destruction was considered to result from an excessive host reaction to a low amount of bacterial biofilm associated with specific periodopathogens, led by *Aggregatibacter actinomycetemcomitans*.

However, thanks to the progress of microbiological research and the development of more sensitive microbiological techniques, this specific pathogen-centred hypothesis has been abandoned. It was demonstrated that periodontal microflora is far more diverse than previously thought with a high rate of variability, and it is now considered that the key role in periodontal destruction is played by local dysbiosis rather than by individual pathogens. In relation to *Aggregatibacter actinomycetemcomitans* as a hallmark pathogen, recent microbiological research reveals its presence in fewer than 50% of aggressive-periodontitis cases, in a low concentration before disease onset decreasing to undetectable levels following disease occurrence, and this periopathogen is detectable in healthy and diseased sites in almost the same ratio.

In addition, repeated research studies have failed to profile the specific immunophenotype in patients suffering aggressive periodontitis, so the immunological characteristics of the disease are still not established. Thus, despite the evident clinical characteristics of “aggressive periodontitis”, the lack of intrinsic biological indicators meant that experts had to suspend this category until there is a better biotypology of the disease. By highlighting the lack of accurate indicators of the aggressive periodontitis – which suggests that the previous diagnostic criteria were unreliable – the new classification system raises awareness among researchers and clinicians of the need to resolve this problem.

<table>
<thead>
<tr>
<th>Periodontitis grade</th>
<th>Grade A: Slow rate of progression</th>
<th>Grade B: Moderate rate of progression</th>
<th>Grade C: Rapid rate of progression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Direct evidence of progression</td>
<td>Longitudinal data (radiographic bone loss or CAL)</td>
<td>Evidence of no loss over 5 years</td>
</tr>
<tr>
<td>Primary criteria</td>
<td>% bone loss/age</td>
<td>0.25</td>
<td>0.25 to 1.0</td>
</tr>
<tr>
<td>Indirect evidence</td>
<td>Case phenotype</td>
<td>Heavy biofilm deposits with low levels of destruction</td>
<td>Destruction commensurate with biofilm deposits</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Destruction exceeds expectation given biofilm deposits; specific clinical patterns suggestive of periods of rapid progression and/or early onset disease (e.g., molecular focuser pattern; lack of expected response to standard bacterial control therapies)</td>
</tr>
<tr>
<td>Grade modifiers</td>
<td>Risk factors</td>
<td>Smoking</td>
<td>Non-smoker</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>Normoglycaemic / no diagnosis of diabetes</td>
<td>HbA1c &lt;7.0% in patients with diabetes</td>
</tr>
<tr>
<td>Risk of systemic</td>
<td>Inflammatory burden</td>
<td>High sensitivity CRP (hsCRP)</td>
<td>&lt;1 mg/L</td>
</tr>
<tr>
<td>impact of periodontitis</td>
<td>Indicators of CAL/bone loss</td>
<td>Saliva, gingival crevicular fluid, serum</td>
<td>*</td>
</tr>
</tbody>
</table>

Figure 1. Grading periodontitis according to the new classification
‘It will take time for the new classification to sink in’

While Darko Božić (Croatia) admits to being “emotionally tied to the old classification,” he adds that in many cases he could “never really understand when we could call a case ‘aggressive’ or ‘chronic.’ You would see people aged 45 to 50 who suddenly developed periodontitis and, by examining their older x-rays, you would see that in the course of a few years they suffered significant bone loss. But, if you looked at their age, they were not ‘aggressive’ cases.

“This perplexed me, and I would always ask myself: what’s the difference between these people suffering from severe attachment and bone loss and the younger one? Furthermore, microbiological testing could not distinguish the two entities and gene-arrays. So, there must be something more to it!”

His initial reaction to the new classification was that “it had more logic and was pretty clear” and that it created new opportunities to understand the behaviour of the disease at the same stage and grade in younger patients and older ones. “For example, is there a different response to the same regenerative surgical treatment in younger and older patients with the same attachment loss?” In these cases, he thinks it likely that there will be a difference between the age groups in term of attachment gain and that there will be more data on the treatment possibilities in advanced periodontitis cases (stages III and IV).

“It will take time for the new classification to sink in,” he concludes, “but it gives us new avenues in periodontal research and will give us more information on retaining of extracting ‘hopeless’ teeth.”

For Hady Haririan (Austria), there is a risk that the new classification “might bring some confusion” because “aggressive periodontitis was also linked to a typical distribution of attachment loss in the dentition, which I cannot find in the new system.” However, if what was previously called aggressive periodontitis were linked to “Grade C” in the new classification (defined as “rapid rate of progression”), “ongoing research should not be affected very much.” Nonetheless, “most difficulties will now arise for new research in terms of comparability with previous data based on the old classification.”

This point was echoed by Dominik Hofer (Switzerland), who says “I hope that all the older studies are not automatically made ‘worthless’ by the new classification. Comparison would certainly be very tricky and complex. This will be a huge challenge for scientists.”

Paula Matesanz (Spain) suggests that for research already under way, “I think nothing can be done, because there is no way to adapt the followed inclusion and exclusion criteria once the study has been approved. The results obtained will need to be published based on the later classification, although this may cause a loss of impact of the publication.”

Picking up this point, Peter Eichholz (Germany) says “there will be a transient time while chronic and aggressive periodontitis will still appear in publications. But authors will increasingly have to refer to the new classification even if they started projects with the former system.”

‘Clear definition of stages’

Kristin Kolltveit (Norway) is enthusiastic about the benefits to research from the new classification. “It can be hard to differentiate between aggressive and chronic periodontitis – whereas a stage 2 and 3 periodontitis is clearly defined,” she says. “For future research, the new classification system will facilitate uniform study groups whether in epidemiological or clinical studies. A clear definition of the different stages of periodontitis is making it easier to design study groups, interpret results, perform multicentre studies, and compare studies.”

However, for work already started, depending on how advanced it is, “it might be an idea to redefine the study population in accordance with the new classification.”

Werner Lill (Austria) welcomes the implications of the new classification for research, saying that “the more precise definition and differentiation will additionally increase the sensitivity and specificity of scientific work.”

Virginie Monnet-Corti (France) raises three questions about the implications of the shift from aggressive/chronic periodontitis to a model of the disease based on stages and grades: “Can we extrapolate the results of the studies based on aggressive/chronic periodontitis? Do we have to redo all the clinical and epidemiological trials in the long term? Can we use the former studies for the new meta-analysis?”

She adds that, in terms of research, the new classification may offer two important benefits. “Perhaps it will help us put forward (to highlight) new associated factors to manage and to improve our future patient outcomes.”
PERIODONTAL DISEASES

Periodontal disease and susceptibility to breast cancer: a meta-analysis of observational studies

This meta-analysis was conducted because, while individual studies have suggested an association between periodontal disease and breast cancer, there had not been a formal meta-analysis of this evidence. Relevant studies published until April 2018 were retrieved and screened according to established inclusion criteria. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated to assess the association between periodontal disease and the risk of breast cancer and fixed-effect models were used according to the results of the heterogeneity test. Eight studies, involving 168,111 individuals, were identified as having explored the association between periodontal disease and breast cancer. Summary estimates in view of adjusted data showed that periodontal disease increased susceptibility to breast cancer (RR = 1.18, 95% CI 1.11-1.26, I² = 16%). With robust results confirmed by sensitivity analysis. The results provided evidence of a modest positive association between periodontal disease and breast cancer and the researchers recommended further studies to explore this topic in more detail.

Authors: Tingting Shi, Min Min, Chenyu Sun, Yan Zhang, Mingming Liang, Yehuan Sun.
Published in Journal of Clinical Periodontology Volume 45, Number 9 (September 2018).
Full article: https://www.onlinelibrary.wiley.com/doi/abs/10.1111/jcpe.12982

PERIODONTAL DISEASES

The effects of periodontal treatment on diabetic patients: the DIAPERIO randomised controlled trial

This study sought to assess whether periodontal treatment can lead to improvements in clinical glycaemic control and quality of life in metabolically unbalanced diabetic patients (type 1 or type 2) diagnosed with periodontitis. In this open-labelled, randomised controlled trial, diabetic subjects (n = 91) were given “immediate” or “delayed” periodontal treatment (full-mouth, non-surgical scaling and root planing, systemic antibiotics, and oral-health instructions). The main outcome was the effect on glycated haemoglobin (HbA1c) and fructosamine levels. The General Oral Health Assessment Index and the SF-36 index were used to assess quality of life. Periodontal health significantly improved after periodontal treatment (p < 0.001), but the treatment had no significant effects on glycaemic control based on HbA1c. However, there was significant improvement in oral-health-related quality of life.

Published in Journal of Clinical Periodontology Volume 45, Number 10 (October 2018).
Full article: https://www.onlinelibrary.wiley.com/doi/abs/10.1111/jcpe.13003

PERIODONTAL DISEASES

Effect of two periodontal treatment modalities in patients with uncontrolled type-2 diabetes mellitus: a randomised clinical trial

This randomised controlled clinical trial evaluated the impact of two non-surgical periodontal treatment modalities on metabolic and periodontal clinical parameters in subjects with type-2 diabetes mellitus (T2DM) with poor glycaemic control and chronic periodontitis. Ninety-three T2DM subjects with glycosylated haemoglobin (HbA1c) >7% were randomly assigned to one of two groups receiving scaling with root planing in multiple sessions, quadrant by quadrant (Q by Q), or within 24 hours (one stage). Periodontal parameters, HbA1c, glycaemia blood levels, and C-reactive protein values were assessed at baseline and at three and six months after therapy. At six months, HbA1c had decreased by 0.48% in the Q by Q group and by 0.18% in the one-stage group (p = 0.455). After therapy, subjects with an initial HbA1c <9% showed an increase of 0.31% (p = 0.145), compared with a decrease of 0.88% (p = 0.006) in those with an initial HbA1c >9%. Periodontal parameters improved significantly (p < 0.0001) post-therapy, with similar results for both treatment modalities. Improved HbA1c levels were more apparent among patients who were more severely uncontrolled at baseline.

Authors: Antonio J. Quintero, Alejandra Chaparro, Marc Quirynen, Valeria Ramirez, Diego Prieto, Hélia Morales, Pamela Prada, Macarena Hernández, Antonio Sanz.
Published in Journal of Clinical Periodontology Volume 45, Number 9 (September 2018).
Full article: https://www.onlinelibrary.wiley.com/doi/abs/10.1111/jcpe.12991
IMPLANT THERAPY

Morbidity following transcrestal and lateral sinus floor elevation: a randomised trial

This study sought to make a comparative evaluation of the morbidity following maxillary sinus-floor elevation, according to either the transcrestal (tSFE) or the lateral (lSFE) approach. Outcomes included complete root coverage, recession reduction, keratinised-tissue gain, and dentin hypersensitivity, and were evaluated at six months, one year, and nine years. Multilevel analysis was performed to identify predictors for long-term gingival-margin stability. Baseline gingival recession was 2.4 ± 0.8 mm and 2.4 ± 1.0 mm in the CAF + CTG and in the CAF-treated sites, respectively (p = 0.035).

IMPLANT THERAPY

A randomised controlled study comparing guided bone regeneration with connective tissue graft to re-establish convexity at the buccal aspect of single implants: a one-year CBCT analysis

In a study to compare guided bone regeneration (GBR) with connective tissue graft (CTG) to re-establish convexity at the buccal aspect of single implants, patients with a single tooth gap in the anterior maxilla and horizontal alveolar defect were enrolled in a single-blind, randomised controlled trial. Sites had to demonstrate buccopalatal bone dimension of at least 5 mm before surgery to ensure complete embedding of an implant without the need for bone augmentation. All received a single implant and were randomly allocated to the control group (GBR) or the test group (CTG). Cross-sectional CBCT images before surgery, two weeks after surgery, and one year after surgery were used to evaluate the buccal soft-tissue profile. Secondary outcome variables were buccal bone thickness, buccal soft-tissue thickness, vertical bone loss (VBL), and clinical parameters.

Twenty-one patients were included in each group. After one year, a significant increase in the buccal soft-tissue profile of between 0.7 mm and 1.5 mm was observed in both groups (p < 0.01). Vertical bone loss did not differ significantly between the groups (p > 0.64) and implants demonstrated healthy clinical conditions with no significant differences between the groups for any of the parameters (p > 0.095).


IMPLANT THERAPY

Predictor factors for long-term outcomes stability of coronally advanced flap, with or without connective tissue graft, in the treatment of single maxillary gingival recessions: nine-year results of a randomised controlled clinical trial

This randomised controlled clinical trial assessed the clinical outcomes nine years after the surgical treatment of single maxillary gingival recessions and identified predictors for long-term gingival-margin stability. Twenty-five gingival recessions (Miller Class I and II) were randomly treated with Coronally Advanced Flap (CAF) plus Connective Tissue Graft (CTG) or CAF alone. Outcomes included complete root coverage, recession reduction, keratinised-tissue gain, and dentin hypersensitivity, and were evaluated at six months, one year, and nine years. Multilevel analysis was performed to identify predictors for long-term gingival-margin stability. The chance of gaining and preserving complete root coverage over time is equal to 70% in the CAF + CTG group, while with CTG an increase in keratinised tissue was recorded nine years after the surgery (p = 0.019).

Both treatment modalities demonstrated stability over time, the additional use of CTG provided a greater increase in keratinised tissue, and the presence of non-carious cervical lesions affected both complete root coverage and recession reduction.