Treatment of periodontal disease improves glycaemic control in Type-1 and Type-2 diabetics: a literature review

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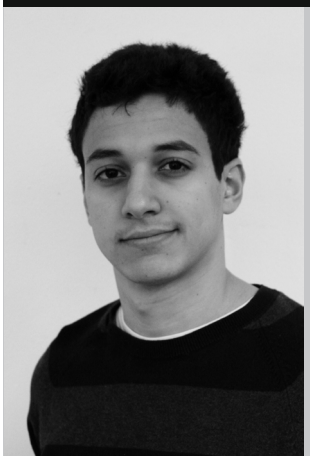

"Two 2011 controlled clinical trials found that periodontal treatment is associated with a decrease in HbA1c levels after 6–8 months in diabetic patients[1,16]."

Abstract:

Periodontal disease and diabetes mellitus are both complex chronic diseases that have a bidirectional intrinsic link. It has been suggested that the chronic inflammation and infection of pre-existing periodontal disease may impair glycaemic control and hasten the development of diabetic complications. Conflicting results have been shown by the limited number of short-term randomised controlled studies carried out to ascertain whether the treatment of periodontal disease contributes to improvement of glycaemic control. High quality reviews have concluded that small but significant improvements can be expected. Glycated haemoglobin (HbA1c), a haematological indicator of hyperglycaemia, is noticeably reduced in Type-2 diabetics who undergo routine scaling/root planing and oral hygiene regimens when compared to such individuals with no periodontal treatment interventions. Regular and appropriate periodontal therapy leading to any improvement in glycaemic control has the potential to make a significant impact on the quality of life for diabetic patients. The aim of this review is to discuss the literature supporting these arguments.

Introduction:

Periodontal disease and diabetes mellitus are two very different but common chronic diseases. The former is a localised infection due to oral bacteria, whereas the latter is a systemic metabolic disorder characterised by abnormal glucose tolerance and hyperglycaemia[1]. A plethora of research has recently been published on the aetiopathophysiological link and bi-directionality of these two diseases, with several hypotheses existing but no definitive mechanisms established as of yet.

The World Health Organization (WHO) estimated that 217 million people worldwide had diabetes in 2005 and that number is set to increase to 366 million by 2030[2]. This growth in diabetes prevalence is principally due to Type-2 diabetes becoming an epidemic[3,4]. It is estimated that between 5–15% of healthy adults from 21–50 years of age and about 30% of those over 50 years of age have severe periodontitis. The prevalence of diabetic patients with periodontitis is estimated to be double or triple these numbers[5].

In the dental profession, it is now widely accepted that controlling diabetes significantly improves the health of the periodontium. However, it is questionable if treating periodontal disease in diabetic patients assists in improving glycaemic control. A reasonable argument based on current evidence may be made for the inclusion of a routine dental health assessment in order to improve metabolic control[6]. This review summarises the relationship between periodontal disease and diabetes and examines the most recent evidence suggesting how successful treatment of periodontal disease can improve glycaemic control.

What is periodontal disease?

Periodontitis is a multifactorial disease defined as inflammation and destruction of the underlying supporting tissues of the teeth[6]. It is characterised by the presence of plaque[7], periodontal pockets, loose teeth, receding gums, bone resorption and eventual teeth exfoliation[5].

Periodontitis is a silent chronic disease that can lead to tooth loss without any prior symptoms. The resultant unaesthetic smile can negatively influence the patient's quality of life. Treatment is aimed at mechanical debridement (scaling and root planing) of plaque and calculus deposits off the affected surfaces of teeth whilst the patient carries out a regimen of oral hygiene measures to prevent the accumulation of the causative factor – dental plaque[5,6]. Success depends largely on patient motivation and compliance. Surgical treatments involve raising gingival flaps to facilitate access to residual

deep pockets or non-responding pockets[6]. Management of periodontal disease requires strict recall visits every 3–6 months.

What is diabetes mellitus?

Diabetes mellitus is defined by WHO as a metabolic disorder of multiple aetiologies characterised by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both[2].

Type-1 diabetes is autoimmune mediated pancreatic ß-cell destruction resulting in the lack of insulin production. The most common type of diabetes is Type-2, which affects approximately 90-95% of the United States diabetic population[7]. It is caused by a disorder in insulin function[8].

Apart from daily blood glucose tests, glycated haemoglobin (HbA1c) is commonly measured to assess blood glucose concentrations over a time period of 6–8 weeks. Higher amounts of HbA1c indicate poorer control of blood glucose levels and an increased risk of diabetic complications[6].

Diabetic complications include retinopathy, nephropathy, peripheral neuropathy and accelerated atherosclerosis[6,7,9]. Oral manifestations include xerostomia, recurrent aphthous ulcerations, burning mouth syndrome and destruction of the periodontium[7].

Effect of periodontal disease on diabetes

Periodontal disease may perpetuate the chronic systemic state of inflammation[10]. Porphyromonas gingivalis (PG) is a negative facultative anaerobe dominant in periodontal disease associated with diabetes. It has been isolated as the main inducer of pro-inflammatory cytokines including interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-1ß (IL-1ß) and tumor necrosis factor-α (TNF-α) in diabetics[4,7,10]. TNF-α has been reported to interfere with lipid metabolism and TNF-α, IL-1, IL-6 are all reported to be insulin antagonists. Also, PG triggers alveolar bone loss in the periodontium[4,7].

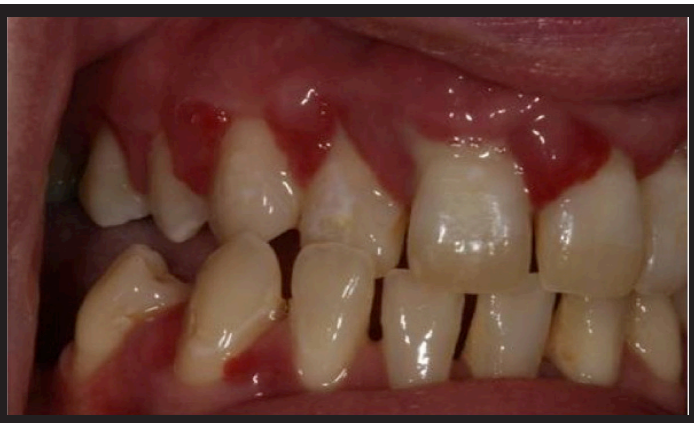

Image 1: 36-year old female patient who presented with obvious plaque, gingival inflammation, suppuration and recession in the Dublin Dental University Hospital. This is a typical presentation of periodontitis in a patient with diabetes. B: Results post non-surgical treatment. The inflammation, ulceration and suppuration have resolved. Photographs courtesy of Dr Omar AlKaradsheh, Department of Restorative Dentistry and Periodontology, Dublin Dental University Hospital, Trinity College Dublin.

Systematic reviews conclude that treating periodontal disease could delay the onset or progression of diabetic complications by restoring insulin sensitivity and improving metabolic control[4,6,10].

Effect of diabetes on periodontal disease

Untreated or inadequately controlled diabetes leading to a hyperglycaemic state exaggerates the inflammatory response to the virulent periodontal pathogenic bacteria[4,5]. Neutrophil adherence, chemotaxis, and phagocytosis are all impaired resulting in more rapid and severe periodontal destruction and inflammation[7,10].

Advanced glycation end-products (AGEs) are formed from non-enzymatic glycation and oxidisation of proteins and lipids under hyperglycemic conditions only[4,5]. These products accumulate in the gingival tissues and delay healing by inducing apoptosis of extracellular-matrix-producing cells, which in turn inhibit osteoblast differentiation and collagen production[4,10,12]. Connective tissue destruction proceeds due to the changed collagen structure and the presence of collagenases called matrix metalloproteinases (MMPs) while bone destruction ensues unopposed[7,8,10].

Hyperglycemia and resultant AGEs formation are considered to be a major causal factor in the pathogenesis of diabetic complications [4].

Mechanisms linking periodontal disease and diabetes mellitus (bidirectional relationship)

Research suggests that systemic inflammation is exacerbated by periodontal inflammation[7], however it is difficult to define the bidirectional relationship exclusively[10].

Periodontal bacteria cause the accumulation of AGEs in periodontal tissues, which results in increased tissue destruction. Furthermore, AGEs stimulate the production of proinflammatory cytokines namely IL-1ß and TNF-α, which exacerbate tissue destruction and decrease the capacity for tissue repair. The lipopolysaccharide released from PG induces IL-1ß and TNF-α, which in diabetic patients impairs glucose transport[5]. A linked aetiopathophysiology can be explained to date as a chronic systemic elevation and continued release of proinflammatory cytokines progressing periodontal destruction and increasing the severity of diabetes[13].

The glucose content of gingival crevicular fluid in diabetics is elevated[7].

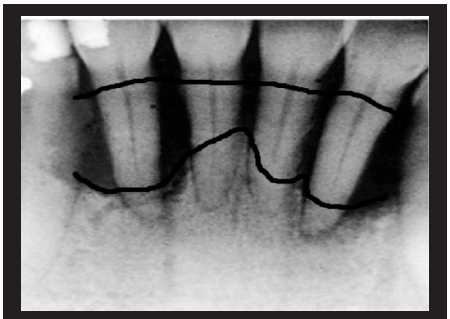

Image 2: Radiograph of mandibular anterior teeth reveals severe bone loss[11]. **A:** Line indicates where bone level in healthy dentition should be located. **B:** Line shows position of bone level due to the destructive effect of periodontitis.

This could provide an altered source of nutrition for periodontal pathogens. Furthermore, the immune response to these pathogens may be compromised in diabetics and leads to the overgrowth of certain species resulting in more severe virulences[7,8] and an increased release of proinflammatory cytokines including IL-6, C-reactive protein (CRP) and TNF-µ.

Genetics has been highlighted as a discernable link between periodontal disease and diabetes[1,14,15]. Both diseases are polygenic disorders with some degree of immunoregulatory dysfunction. A weakened immune system and an altered wound-healing rate in diabetic patients means that repair of periodontal tissues is delayed. Fibroblasts, which are the principle reparative cell in the periodontium, are impaired, resulting in a diminished rate of tissue repair[14].

A bidirectional relationship has been proposed by Mirza *et al*, stating that a pathway exists from the combination of the infection-mediated proinflammatory cytokine cycle and the AGE-mediated cytokine response to periodontal pathogens. This pathway of tissue destruction suggests that control of chronic periodontal infection is essential for achieving long-term control of diabetes[14].

Effect of treatment of periodontal disease on glycemic control in diabetics

Two 2011 controlled clinical trials found that periodontal treatment is associated with a decrease in HbA1c levels after 6–8 months in diabetic patients[1,16]. This result has been substantiated by several well-conducted reviews. Darre *et al* analysed 978 studies and reported a statistically significant mean reduction in HbA1c by 0.79[17]. A 2010 Cochrane review further concluded that there may be a small but significant improvement in glycaemic control from treating pre-existing gum disease in Type-2 diabetics[6]. However, the authors of this review also acknowledge that there are few studies available and individually these lacked the power to detect a significant effect. Most of the participants in the studies had poorly controlled Type-2 diabetes.

The first group to conduct a controlled trial on the response of periodontal therapy to multiple systemic inflammatory markers was O'Connell *et al.* Significant reductions in HbA1c, and multiple inflammatory markers were noted after 3 months follow-up. However, the follow-up time was too short, the sample size was small and their diets were uncontrolled[8].

A well-performed study by Correa *et al* showed that non-surgical periodontal treatment was effective in reducing the levels of IL-1ß, MMP-8 and MMP-9, and the elastase activity in GCF samples from both diabetes and control groups[18]. It should be noted that because the majority of studies were conducted in Type-2 diabetic populations, data suggests that Type-2 diabetics respond to periodontal therapy but in Type-1 diabetics this response is questionable[5]. The Cochrane review suggests that because Type-1 diabetes is an autoimmune disease, these patients may be too young to develop moderate to severe periodontitis[6].

Recommendations for future studies:

Further studies to confirm these findings should be viewed as a public health priority in view of the prevalence of both diabetes and periodontal disease[6].

Studies should also include a sizeable number of Type-1 diabetic participants to determine whether their response to periodontal treatment is similar[6].

Control groups should undergo their usual periodontal treatment regimens as opposed to no treatment which is unethical[6].

Confounding factors including smoking, body mass index, diet and baseline characteristics affecting glycaemic control should be better controlled[19].

Longer follow-up times are needed to properly ascertain the success of periodontal treatment in controlling periodontal disease and simultaneously improving glycaemic control.

Conclusion:

Diabetes is associated with an increased prevalence of periodontal disease and periodontal disease itself is associated with poorer glycaemic control in diabetic patients. Long-term glycaemic control is considered to be of critical importance in preventing and delaying the progression of diabetic complications.

The authors of this review recommend that all Type-2 diabetic patients should be screened for periodontal disease. The loss of teeth and an unaesthetic smile can negatively affect the quality of a person's life as much as systemic diseases themselves. The majority of short-term studies have proven that treating periodontal disease may assist in improving glycaemic control; thus improving a diabetic patient's overall health. However, these results need to be corroborated over a longer time-frame in more controlled studies.

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Clinical points:

- Periodontal disease is a destructive inflammatory condition of the periodontium increasing the mobility and subsequent loss of teeth.
- Diabetes mellitus is a metabolic disorder characterised by hyperglycaemia.
- Recent studies show that diabetes and periodontal disease exacerbate the effect of pro-inflammatory cytokines, thus worsening the clinical presentation of the other.
- All patients who with diabetes should be screened for and educated about gum disease.
- Treating periodontal disease helps to improve glycaemic control, which in turn helps prevent the progression of diabetic complications.

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