

From the Division of Periodontology, Department of Dental Medicine Karolinska Institutet, Stockholm, Sweden

PERIODONTAL CONDITIONS AND TREATMENT OUTCOMES FOR SUBJECTS WITH DIABETES MELLITUS: SPECIAL EMPHASIS ON HBA1C LEVELS AND T-CELLS

AKADEMISK AVHANDLING som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Hörsal **4**U plan 4 Alfred Nobels allé 8, Huddinge.

Fredagen den 16 December 2016, kl. 09.00

av

Murad Altamash BDS

Huvudhandledare:

Docent Per-Erik Engström

Karolinska Institutet Department of Dental Medicine Division of Periodontology

Bihandledare:

Professor Björn Klinge

Karolinska Institutet
Department of Dental Medicine
Division of Periodontology
Professor, Department of Periodontology,
Faculty of Odontology, Malmo University

Professor Karl-Gösta Sundqvist

Karolinska Institutet Department of Laboratory Medicine Division of Clinical Immunology Fakultetsopponent:

Professor Palle Holmstrup

University of Copenhagen Department of Odontology Section of Periodontology

Betygsnämnd:

Docent Eva Toft

Karolinska Institutet Department of Medicine

Docent Per Ramberg

PR Dental

Professor Mats Remberger

Karolinska Institutet Department of Oncology and Pathology

ABSTRACT

A two way relationship between periodontal disease (PD) and diabetes mellitus has previously been reported. This thesis was aimed to further analyze the influence of PD on blood glucose levels of subjects with (T2D) mellitus (T2D) and vice versa. Periodontal conditions (bleeding on probing [BOP], plaque index [PI], periodontal pocket depth [PPD] [4mm < 6mm and \geq 6mm]) and marginal bone levels) were investigated in subjects with pre-diabetes as well as those with or without diabetes mellitus. HbA1c levels in individuals with periodontal disease and diabetes mellitus were analyzed after non-surgical and surgical treatments. This thesis also assessed the influence of diabetes on infiltration of inflammatory cells, T lymphocytes and B lymphocytes in gingiva and the effect of glucose control on T-cell motility.

AIMS

Study I aimed to evaluate the difference in periodontal conditions between subjects with pre-diabetes, well or poorly controlled diabetes mellitus and non-diabetes. Hemoglobin A1c levels, BMI and WC were also measured. Study II aimed to study the effect of periodontal treatment (non-surgical and surgical) on HbA1c levels in subjects with or without PD and with or without diabetes mellitus. HbA1c, BOP, PI and PPD 4mm <6mm; ≥6 mm were recorded.

Study III aimed to investigate the infiltration of T and B lymphocytes in gingival biopsies of diabetic and non-diabetic subjects with or without periodontal disease.

Study IV examined the influence of D-glucose on T cell motility.

RESULTS

In *study I*, thirty seven percent of all individuals who reported to be non-diabetics were pre-diabetics. An increase in the number of PPD \geq 6mm was seen in subjects with poorly controlled diabetes as compared to pre-diabetics and non-diabetics (P<0.05).

In *study II*, periodontal inflammatory conditions in all groups improved with non-surgical and surgical treatment. Subjects with diabetes mellitus showed decreased levels in HbA1c over a period of 3 and 6 months. No changes were detected in PPD 4mm <6mm in diabetics after treatment. Subjects with diabetes require periodontal treatment for at least 6 months to reduce blood sugar levels.

In *study III*, the number of gingival CD4 and CD19 positive cells was reduced in diabetic individuals suggesting that diabetes inhibits lymphocyte entry into gingival tissues.

In *study IV*, it was demonstrated that D-glucose, at a high concentration, intially stimulated T-cell motility while subsequently causing inhibition. These effects were associated with increased cell surface expression of TSP-1 and LRP-1.

In conclusion,

This thesis shows that diabetes mellitus influences the periodontal conditions and treatment of periodontal disease has an influence on blood sugar status. Furthermore, diabetes mellitus influences the immunological status where high blood glucose sugar levels influence T cells. Overall, this thesis strenghtens the bidirectional relationship between PD and diabetes mellitus from both a pre-clinical and a clinical aspect.