Periodontal Disease and Chronic Diseases: Emerging Science and Programs

Periodontal Disease and Diabetes

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Overview

- Conceptual model for relationships involving periodontal infection, systemic inflammatory burden and diabetes
- Supporting empirical evidence, periodontal infection and/or its treatment and …
  - chronic systemic inflammatory burden
  - glycemic control
  - complications of diabetes
  - incidence of diabetes
  - medical care costs
- Conclusions
Chronic inflammation
Visceral obesity

Proinflammatory state
Chronic overexpression of cytokines

Insulin resistance

Pancreatic beta cell damage

Glycemic Control

Conceptual Model: Adapted from Richard Donahue, 2001
Supporting empirical evidence

- Periodontitis and systemic inflammatory burden
**Periodontal therapy: effects on systemic inflammation**

- Improved endothelial function
  - Seinhost et al., 2005
  - Elter et al., 2006
  - Tonetti et al., 2007

- CRP level reduced
  - Offenbacher et al., 2009
  - Seinost et al., 2005
  - D’Aiuto et al., 2005
  - Ebersole et al., 1997

- IL-6 levels reduced
  - D’Aiuto et al., 2005
  - Iwamoto et al., 2003

- TNFα levels reduced
  - Iwamoto et al., 2003
Supporting empirical evidence

- Periodontitis and insulin resistance
Prevalence of insulin resistance (HOMA 80\textsuperscript{th}) in U.S. adults, ages 18+, by periodontal status*  
Unadjusted odds ratio=2.3 (95%CI: 1.6, 3.4)

* Sev. Perio=1+ site w LPA 6 mm+, gingival bleeding

### Logistic regression model
**Response: HOMA 80\textsuperscript{th} (n=1574/5313)**

<table>
<thead>
<tr>
<th>COVARIATE</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe perio.</td>
<td>1.74</td>
<td>1.01, 3.0</td>
</tr>
<tr>
<td>BMI (&gt;27)</td>
<td>4.77</td>
<td>4.1, 5.6</td>
</tr>
<tr>
<td>HDL (≤40)</td>
<td>2.2</td>
<td>1.7, 2.9</td>
</tr>
<tr>
<td>TRIG (&gt;200)</td>
<td>2.7</td>
<td>2.0, 3.6</td>
</tr>
<tr>
<td>CRP</td>
<td>1.3</td>
<td>1.1, 1.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4.72</td>
<td>2.6, 8.4</td>
</tr>
</tbody>
</table>

Other covariates controlled in model were age, race/ethnicity, exercise, white blood cell count, fibrinogen.
Periodontal Infection and Glycemic Control: Intervention Studies
Locations of clinical therapeutic studies
Non-surgical periodontal therapy studies: Organizing the evidence (as of 2009)

- Randomized clinical trials (RCT)
  - Non-treated control group: 1 positive/3 studies
  - Positive control group: 5 positive/6 studies
  - Usual source of care: 0 positive/1 study

- Non-randomized clinical treatment studies (non-RCT)
  - Non-treated control group: 1 positive/2 studies
  - No control group: 11 positive/19 studies
Systematic Review and Meta-analysis

Source: SUNY - http://library.downstate.edu/EBM2/2700.htm
Non-surgical periodontal therapy: a meta-analysis.
Darré et al. Diabetes and Metabolism, 2008

![Forest plot](image)

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldridge I et al.</td>
<td>0.30 (-1.11, 1.71)</td>
<td>5.38</td>
</tr>
<tr>
<td>Aldridge II et al.</td>
<td>-0.80 (-2.74, 1.14)</td>
<td>3.05</td>
</tr>
<tr>
<td>Calbacho et al.</td>
<td>0.30 (-1.85, 2.45)</td>
<td>2.51</td>
</tr>
<tr>
<td>Jones et al.</td>
<td>0.14 (-0.31, 0.59)</td>
<td>23.29</td>
</tr>
<tr>
<td>Kiran et al.</td>
<td>1.17 (0.13, 2.20)</td>
<td>8.85</td>
</tr>
<tr>
<td>Mansouri et al.</td>
<td>0.20 (-1.39, 1.79)</td>
<td>4.38</td>
</tr>
<tr>
<td>Promsudthi et al.</td>
<td>0.31 (-0.18, 0.80)</td>
<td>21.79</td>
</tr>
<tr>
<td>Stewart et al.</td>
<td>1.10 (0.59, 1.60)</td>
<td>21.07</td>
</tr>
<tr>
<td>Yun et al.</td>
<td>0.19 (-0.79, 1.17)</td>
<td>9.67</td>
</tr>
</tbody>
</table>

Overall SMD: 0.46 (0.11, 0.82) P = 0.01

Glycaemic control after periodontal treatment
(Standardized Mean Difference)
Non-surgical periodontal therapy: a meta-analysis.
Teeuw et al. Diabetes Care, 2010
Periodontal Disease and Complications of Diabetes
Periodontal disease and diabetes complications
The major diabetic complications

- Eyes (retinopathy)
- Brain and cerebral circulation (cerebrovascular disease)
- Heart and coronary circulation (coronary heart disease)
- Kidney (nephropathy)
- Lower limbs (peripheral vascular disease)
- Peripheral nervous system (neuropathy)
- Diabetic foot (ulceration and amputation)
Landmark clinical trials demonstrating the significance of improving of glycemic control

- **Diabetes Control and Complications Trial (DCCT)**
  - Intensive blood glucose control in type 1 diabetes
  - 35% to 70% reduction in risk of retinopathy, nephropathy and neuropathy

- **UK Prospective Diabetes Study (UKPDS)**
  - Intensive blood glucose control in type 2 diabetes
  - 12% to 33% reduction in risk of retinopathy and nephropathy
Periodontal infection and complications of diabetes

- Thorstensson et al., 1996; J Clin Periodontol.
  - 39 case-control pairs, type 1 and type 2 diabetes
  - Six years median follow-up period
  - Cases (severe periodontal disease) had greater risk for
    - Proteinuria
    - Cardiovascular complications: stroke, TIA, angina, myocardial infarction, and intermittent claudication
Periodontal infection and complications of diabetes

- Saremi et al., 2005; Diabetes Care.
  - Prospective cohort study of n=628, type 2 diabetes
  - Severe periodontal disease: 3.2x greater risk for cardiorenal mortality (ischemic heart disease and nephropathy)
  - Controlled for established risk factors: age, sex, duration, BMI, hypertension, blood glucose, cholesterol, ECG abnormalities, macroalbuminuria, and smoking
Periodontal infection and complications of diabetes: Overt nephropathy and ESRD

- Shultis et al., 2007; Diabetes Care.
  - Prospective cohort study of n=529, type 2 diabetes
  - Severe periodontal disease associated with incidence of macroalbuminuria and ESRD adjusted for age and sex

(n = 529). □, none/mild periodontitis; ■, moderate periodontitis; ■, severe periodontitis; □, edentulous.
**Periodontal infection and complications of diabetes:**

*Overt nephropathy and ESRD*

Shultis et al., 2007; Diabetes Care

<table>
<thead>
<tr>
<th>Macroalbuminuria</th>
<th>ESRD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HRR</strong></td>
<td><strong>HRR</strong></td>
</tr>
<tr>
<td>Mod Perio: 2.0 (1.2-3.5)</td>
<td>Mod Perio: 2.3 (0.6-8.1)</td>
</tr>
<tr>
<td>Sev Perio: 2.1. (1.2-3.8)</td>
<td>Sev Perio: 3.5 (0.96-12.4)</td>
</tr>
<tr>
<td>Edent: 2.6 (1.4-4.6)</td>
<td>Edent: 4.9 (1.4-17.4)</td>
</tr>
<tr>
<td>n=193/529</td>
<td>n=68/529</td>
</tr>
</tbody>
</table>

Proportional Hazards Model: Adjusted for Age, Sex, Diabetes Duration, BMI, and Smoking
Periodontal Disease As a Risk Indicator for Complications of Diabetes: NHANES III

- **Study design**: cross-sectional (1988-94)
- **Population**: U.S. adults with diabetes, ages 40+ (N=1,135)
- **Exposure**: PDz score: proportion of teeth with 4+mm attachment loss and bleeding and accounted for tooth loss
- **Comparison group**: Lowest quartile of PDz score
- **Outcome**: Quartiles 2, 3, & 4 had 2 x greater odds for having 1+ diabetes complications
  - Controlled for age, sex, race/ethnicity, income, smoking, health care visits, HTN, macroalbuminuria, cholesterol, HbA1c, and CRP
Periodontal Infection As a Risk Factor for Type 2 Diabetes: Emerging Evidence (Demmer et al., 2008)

- **Study design**: cohort, NHEFS, 1971 – 1992
- **Population**: U.S. adults (N=7,168), followed for 17 years (mean)
- **Exposure**: Periodontal disease at baseline
- **Comparison group**: No or mild periodontal disease at baseline
- **Outcome**: Periodontal disease at baseline independently associated with 50-100% greater risk for type 2 diabetes incidence
  - Controlled for demographics, SES, smoking, exercise, adiposity, hypertension, cholesterol, diet and WBC
Periodontal Treatment and Medical Care Costs in People with Diabetes
Specific Aims

◆ To determine the association between periodontal treatment for people with diabetes and …
  ◆ AIM 1: **Total medical care costs**
  ◆ AIM 2: Costs for medical care **specifically related to diabetes** and its complications
  ◆ AIM 3: Costs for medical care related to **specific complications and combinations of complications**
Study population (N=2,674)

- Age 18 to 64 years
- Diagnosis of diabetes for at least 6 months
- Simultaneous, continuous enrollment in following product lines for at least one year of the 2001-2005 study period:
  1) Blue Cross Blue Shield
  2) Pharmaceutical insurance plan
  3) Dental insurance plan
Principal exposure: Non-surgical Periodontal Treatment and Prophylaxis Procedures (NSPP)

◆ Rationale:
  ◆ Procedures likely to have an effect on reducing gingival and periodontal inflammation
  ◆ Gingival and periodontal inflammation hypothesized to have an adverse effect on glycemic control
◆ Procedures types included
  ◆ Adult prophylaxis
  ◆ Scaling and root planing
  ◆ Periodontal maintenance procedures
  ◆ Debridement
◆ Exposure variable description
  ◆ Number of non-surgical periodontal and prophylaxis procedures over entire enrollment period of study
Other Predictor Variables

- **Member characteristics**
  - Age in 2001
  - Gender
  - Presence of diabetes complications
  - HbA1c test during coverage period
  - Year of enrollment for member’s record (i.e. 2001, … , 2005)

- **Contextural characteristics**
  - % African American in member’s county
  - % Hispanic/Latino in member’s county
  - Income per capita in member’s county
GEE Regression Model of Costs

Outcomes
1. Total medical costs
2. Total medical and Rx costs
3. Diabetes-related costs
4. Diabetes compl. costs
5. Diabetes compl. combination costs

Predictor Variables (i.e. Covariates)

\[ \text{Intercept} + \beta_1 \times \text{NSSPcat1} + \beta_2 \times \text{NSSPcat2} + \]
\[ + \beta_3 \times \text{NSSPcat3} + \beta_4 \times \text{Age2001} + \beta_5 \times \text{Female} + \]
\[ + \beta_6 \times \text{Compl} + \beta_7 \times \text{AnyHbA1c} + \beta_8 \times \% \text{AfrAm} + \]
\[ + \beta_9 \times \% \text{Hisp/Latino} + \beta_10 \times \text{Income} + \]
\[ + \beta_11 \times \text{Year (01-05)} \]
### AIM 1: Total medical expenditures

% Lower expenditures

<table>
<thead>
<tr>
<th>Type of Cost</th>
<th>N</th>
<th>1-2 / year</th>
<th>3-4/ year</th>
<th>&gt;4/ year</th>
<th>0 / year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical only</td>
<td>2674</td>
<td>-11.6%</td>
<td>-11.9%</td>
<td></td>
<td>referent</td>
</tr>
<tr>
<td>Medical and Rx</td>
<td>2674</td>
<td>-10.0%</td>
<td>-9.1%</td>
<td>-18.5%</td>
<td>referent</td>
</tr>
</tbody>
</table>
### AIM 2: Diabetes-related costs: % Lower expenditures

<table>
<thead>
<tr>
<th>Type of Cost</th>
<th>N</th>
<th>1-2 / year</th>
<th>3-4/ year</th>
<th>&gt;4/ year</th>
<th>0 / year</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM medical</td>
<td>2506</td>
<td>-14.3%</td>
<td>-19.4%</td>
<td></td>
<td>referent</td>
</tr>
<tr>
<td>DM medical &amp; Rx</td>
<td>2565</td>
<td>-9.3%</td>
<td>-11.6%</td>
<td></td>
<td>referent</td>
</tr>
</tbody>
</table>
**AIM 3: Diabetes complications: % Lower expenditures**

<table>
<thead>
<tr>
<th>Type of Cost</th>
<th>N</th>
<th>1-2 / year</th>
<th>3-4/ year</th>
<th>&gt;4/ year</th>
<th>0 / year</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD</td>
<td>1913</td>
<td>-28.2%</td>
<td>-37.6%</td>
<td>-50.9%</td>
<td>referent</td>
</tr>
<tr>
<td>PVD</td>
<td>380</td>
<td>-58.4%</td>
<td>referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>895</td>
<td>-34.5%</td>
<td>-52.4%</td>
<td>referent</td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>190</td>
<td>-54.1%</td>
<td>-72.2%</td>
<td>referent</td>
<td></td>
</tr>
</tbody>
</table>
**AIM 3: Diabetes complications, con’t.: % Lower expenditures**

<table>
<thead>
<tr>
<th>Type of Cost</th>
<th>N</th>
<th>1-2 / year</th>
<th>3-4/ year</th>
<th>&gt;4/ year</th>
<th>0 / year</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD</td>
<td>298</td>
<td>-48.3%</td>
<td>-71.5%</td>
<td></td>
<td>referent</td>
</tr>
<tr>
<td>Retinop/Eye disorders</td>
<td>940</td>
<td>-30.2%</td>
<td>-30.3%</td>
<td></td>
<td>referent</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>607</td>
<td></td>
<td></td>
<td></td>
<td>referent</td>
</tr>
<tr>
<td>CVD&amp; CKD</td>
<td>278</td>
<td>-34.8%</td>
<td>-66.3%</td>
<td></td>
<td>referent</td>
</tr>
</tbody>
</table>
Conclusions

- Evidence that chronic periodontitis may contribute to insulin resistance

- Evidence that treating periodontal infection may:
  - Lead to improved glycemic control
  - Possibly contribute to lower medical care costs

- Evidence that periodontal infection
  - Contributes to the risk for complications of diabetes
  - Contributes to the development of diabetes itself
Acknowledgements

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- National Institute of Dental and Craniofacial Research
- Blue Cross Blue Shield Foundation of Michigan
Thank you for your attention

- Please feel to contact me

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University of Michigan School of Dentistry
National Diabetes Education Program

Awareness Campaigns

Community Interventions

Partnership Network

Special Populations

Health Systems

A joint initiative of CDC and NIH
NDEP structure

- Joint initiative of CDC and NIH
- Partnership with over 200 organizations
  - Public and private organizations
  - Traditional (e.g., American Diabetes Association) and non-traditional (National Urban League) partners
- Diabetes Prevention and Control Programs
- Program goal: To reduce the morbidity and mortality associated with diabetes and its complications by changing the way diabetes treated
NDEP Campaign Materials: Control & Prevention
PPOD is NOT a Vegetable: It is an NDEP Resource
WORKING TOGETHER TO MANAGE DIABETES

A GUIDE FOR PHARMACISTS, PODIATRISTS, OPTOMETRISTS, AND DENTAL PROFESSIONALS
PPOD Primer

- Focus on comprehensive, interdisciplinary diabetes care
- Section on “What You As A Health Care Provider Care Do” for all HCP
- Educate PPOD providers so they can educate patients in turn
- Sections specific to each discipline:
  - Key issues in each PPOD discipline
  - Recommendations RE referrals
  - Expanded information on PPOD provider’s role
CONTROL THE ABCs OF DIABETES

ABC - Americans with diabetes are at increased risk of:
A - Angiopathies - changes in small blood vessels
B - Neuropathies - changes in nerves
C - Retinopathies - changes in blood vessels of the eye

Talk to your health care provider for more information on how to control your diabetes.

MEDICATION MANAGEMENT

- Use a pill box or planner to manage medication.
- Set alerts and reminders for medication times.
- Keep a record of all medications and dosages.
- Consult with your healthcare provider about medication changes.

FOOTCARE

- Use a footbath and check your feet regularly.
- Inspect your feet daily for any changes.
- Wear shoes that fit well.
- Consult with a podiatrist or foot doctor.

EYE CARE

- Use a Q-tip and clean your eyes daily.
- Avoid rubbing your eyes.
- Consult with an eye doctor if you have any issues.
- Wear glasses or contact lenses as prescribed.

DENTAL CARE

- Use a toothbrush and floss regularly.
- Visit a dentist regularly for checkups.
- Consult with your dentist if you have any issues.

OTHER THINGS YOU CAN DO

- Eat a healthy diet.
- Exercise regularly.
- Manage stress.
- Get enough sleep.

Talk to your provider to learn more.

For more information, call 1-800-345-6789.
How do I get NDEP materials?

All NDEP materials are copyright-free. Download from www.ndep.nih.gov
www.YourDiabetesInfo.org

Visit all of the NDEP Web sites:

www.ndep.nih.gov
www.betterdiabetescare.nih.gov
www.cdc.gov/diabetes/ndep
www.diabetesatwork.org