Periodontal Diseases: Effects on Diabetes Control and Complications

Clinical Directors Network-Community Health Centers-
University of Michigan School of Dentistry Collaboration
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Overview

- Overview of diabetes and periodontal diseases
- Conceptual model of chronic periodontal inflammation and insulin resistance
- Periodontal infection and insulin resistance: empirical evidence
- Periodontal infection and glycemic control: empirical evidence
  - Observational studies
  - Treatment studies
- Significance of improving glycemic control
- Periodontitis and complications of diabetes
- Current collaboration with CDN and CHC’s
Diabetes Mellitus
Insulin: action, production, or both

Hyperglycemia and other metabolic abnormalities

Chronic Complications

- Atherosclerosis
- Retinopathy
- Nephropathy
- Neuropathy
- Perio diseases
- Impaired wound healing
Diabetes Overview

- Prevalence: 20.8 mil; 7.0% of U.S. pop.
  - Diagnosed: 14.6 mil
  - Undiagnosed: 6.2 mil
- Incidence: 1,300,000 /yr
- Prevalence by age
  - 60+: 20.9%
  - 20+: 9.6%
  - <20: 0.22%

Source: [http://www.cdc.gov/diabetes/pubs/estimates05.htm#fig2](http://www.cdc.gov/diabetes/pubs/estimates05.htm#fig2), Feb, 2006
Diabetes Overview (con’t.)

- Prevalence by race/ethnicity (20 yrs+)
  - Non-Hispanic whites: 8.7%
  - Non-Hispanic blacks: 13.3%
  - Hispanic/Latino Americans: 9.5%
  - Native Amer. and Alaska Natives: 15.1%
  - Asian Amer. & Pacific Islanders: up to 2.5x nHwhite

http://www.cdc.gov/diabetes/pubs/estimates05.htm#fig2, Feb, 2006
Age-Standardized Prevalence of Diagnosed Diabetes per 100 Adult Population, by State, United States

What is periodontal disease?
Periodontal disease

- Chronic inflammatory disease
- Bacterial etiology
  - Gram negative anaerobes are prominent
- Destruction of periodontal tissues
  - Formation of pathologic pockets around teeth
  - Loss of connective tissue attachment
  - Loss of alveolar bone
- Can lead to tooth loss
Gingivitis

- Bacterial plaque
- Initial periodontal disease
- Inflamed gingiva
- Reversible
- Can progress if untreated
Periodontitis

- Bacterial plaque
- Advanced periodontal disease
- Connective tissue loss
- Periodontal ligament loss
- Supporting bone loss
Measuring periodontal status

Clinical

Radiographic
How prevalent is periodontal disease?
Gingivitis and severe periodontal disease prevalence (1+ sites with LPA 6+ mm)

Severe Periodontitis by race/ethnicity: U.S. population (attachment loss > 6mm)

Diabetes and periodontal health
Children and adolescents with 1+ sites with periodontal attachment loss ≥ 2mm. (Lalla E et al. 2006)
Incidence of Alveolar Bone Loss after ~2 yrs Follow-up in the Pima Indians

Source: Taylor et al., 1998
Why do we think periodontal disease can have an adverse effect on glycemic control?
Periodontitis and Chronic Systemic Inflammation

Relationship to Insulin Resistance
Response to Bacterial Plaque in Disease

Fatty acids
FMLP
LPS

Low
IL-10
TGF-β
IL-1ra
TIMPs

High
TNFα
IL-6
IL-1β
IFN-γ
PGE2
MMPs
Chronic inflammation
Visceral obesity

Proinflammatory state
Chronic overexpression of cytokines

Insulin resistance

Pancreatic beta cell damage

Glycemic Control

Liver

Acute Phase Response (CRP, Fibrinog., PAI-1)

Il-6
TNFα

Conceptual Model: From Richard Donahue, 2004
What empirical evidence do we have to link periodontal disease to insulin resistance and glycemic control?
Supporting epidemiologic evidence: cross-sectional and longitudinal studies

- Inflammation and insulin resistance
- Insulin resistance and diabetes
- Inflammation and diabetes
- Periodontitis and the acute-phase response
Periodontitis and Insulin Resistance: Epidemiologic Evidence of an Association
Periodontitis and Insulin Resistance in U.S. Adults, NHANES III, Preliminary Results

To evaluate the association between severe periodontitis and insulin resistance in a representative sample of U.S. adults, ages 17-90 years old.
MAJOR EXPOSURE

- Severe periodontitis
  - At least 1 site with 6 mm or more of attachment loss
  - Gingival bleeding at the teeth with 6+ mm of attachment loss

OUTCOME

- Insulin Resistance
  - HOMA formula
    - Fasting insulin (FI)
    - Fasting glucose (FG)
  - $\frac{FI \times FG}{22.5}$
  - Dichotomous variable using the 80th percentile as the cutpoint
Prevalence of insulin resistance in U.S. non-smoking adults, ages 17+, by periodontal status* (N=5313)

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

Association between severe periodontitis and insulin resistance (HOMA 80th): crude odds ratio

- Total study group: N=5313 individuals

- Severe periodontitis: n=281 (5.3%)

- Insulin resistance
  - No severe periodontitis: n=1474 (24.6%)
  - Severe periodontitis: n=100 (38.7%)

- ASSOCIATION: Crude Odds Ratio: 2.3 (1.58, 3.39)
Logistic regression model
Response: HOMA 80th ($n=1574/5313$)

<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.
Epidemiologic Evidence: Incidence of poor glycem. control at ~2-yr follow-up in the Pima Indians

Source: Taylor et al., 1996

N for bone loss < 50% = 56
N for bone loss 50%+ = 49
Prevalence of poorer glycemic control in U.S. adults, ages 45+, by periodontal status*

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

Association between severe periodontitis and glycemic control: $N=535$

**Crude Odds Ratio:** $3.20 \ (1.47, \ 6.98)$

<table>
<thead>
<tr>
<th>Periodontal Status</th>
<th>Glycemic Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Better</strong></td>
</tr>
<tr>
<td>HbA1c $&lt;8%$</td>
<td>270 (61%)</td>
</tr>
<tr>
<td>HbA1c $\geq 8%$</td>
<td>39 (41%)</td>
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</tbody>
</table>

Sev. Perio: NO

Sev. Perio: YES
Logistic regression model: poor glycemic control in U.S. adults, ages 45+, non-smoking, NHANES III

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<th>COVARIATE</th>
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<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe perio.</td>
<td>4.9</td>
<td>2.0, 11.9</td>
</tr>
<tr>
<td>Taking Diab med</td>
<td>3.4</td>
<td>1.7, 5.8</td>
</tr>
<tr>
<td>BMI (≥ 27)</td>
<td>2.6</td>
<td>1.2, 5.4</td>
</tr>
<tr>
<td>TRIG (&gt;200)</td>
<td>2.7</td>
<td>2.0, 3.6</td>
</tr>
<tr>
<td>CRP (&gt;1.0)</td>
<td>2.6</td>
<td>0.5, 13.8</td>
</tr>
<tr>
<td>Exercise</td>
<td>1.0</td>
<td>0.99, 1.01</td>
</tr>
</tbody>
</table>

Other covariates controlled in model were age, race/ethnicity, sex, education, poverty income ratio, and MD and DDS visits.
Periodontal Infection
Its Effect on Glycemic Control:

Non-surgical Periodontal Treatment Studies
Locations of clinical therapeutic studies
Non-surgical periodontal therapy studies: organizing the evidence AKA “sorting the apples and oranges”

- Randomized clinical trials (RCT)
  - Non-treated control group: 1 positive/3 studies
  - Positive control group: 3 positive/3 studies

- Non-randomized clinical treatment studies (non-RCT)
  - Non-treated control group: 1 positive/2 studies
  - No control group: 5 positive/8 studies
Non-surgical periodontal therapy: a meta-analysis.
Janket et al. J Dent Res, 2005
Treating Periodontal Infection: Effects on Glycemic Control

- University of Michigan
- SUNY at Buffalo
- University of North Carolina at Chapel Hill
- NIH/NIDCR
SPT = supportive periodontal therapy, including ssrt
ssrt = site specific rescue therapy
Preliminary results: Improvement in Hemoglobin A1c N=16, 15, 15

Visit: months of follow-up after treatment
HbA1c difference from tx visit
delay
doxy
metro

Visit: months of follow-up after treatment
Study Design

Group 1
- Perio tx + Doxy.
- Month: 0, 3, 6, 9, 12, 15

Group 2
- Perio tx + Metron.
- Month: 0, 3, 6, 9, 12, 15

Controls
- Prophy + Placebo.
- Perio tx.
- Month: 0, 3, 6, 9, 12, 15

SPT = supportive periodontal therapy, including ssrt
ssrt = site specific rescue therapy
Overview

- Global overview of diabetes and periodontal diseases prevalence
- Conceptual model of chronic periodontal inflammation and insulin resistance
- Periodontal infection and glycemic control
  - Observational studies
  - Treatment studies
- Significance of improving glycemic control
- Periodontitis and complications of diabetes
- Conclusions
Significance of improving of glycemic control

- Any sustained lowering of blood glucose helps delay the onset and progression of microvascular complications of diabetes

Medical complications of diabetes

- Neuropathy – 50%
- Any cardiovascular disease – 38%
- Coronary heart disease – 22%
- Stroke – 21%
- Visual Impairment – 23%
- Kidney disease – 40% of new cases of renal failure due to diabetes
Landmark clinical trials demonstrating the significance of improving 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
  - Cases (severe periodontal disease) had greater risk for
    - Proteinuria
    - Cardiovascular complications: stroke, TIA, angina, myocardial infarction, and intermittent claudication

- 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
Conclusions

- Evidence that treating periodontal infection can:
  - Lead to improved glycemic control
  - Possibly prevent, delay, or reduce severity of complications
TREATING PERIODONTAL INFECTION: EFFECTS ON GLYCEMIC CONTROL IN COMMUNITY HEALTH CENTERS

Our Collaboration, funded by NIH/NIDCR
Specific Aims

1. Identify and characterize the population of patients with type 2 diabetes, ages 18+ years, who are listed in the diabetes registry.

2. Select a probability sample (n=200) from each center’s list to review medical and dental records and the CHC’s electronic databases to determine the degree to which information is available and accessible for assessing eligibility.

3. Test feasible mechanisms of contacting potential study participants, including telephone, U.S. mail, and face-to-face contact in the medical and dental departments of the CHCs to determine study eligibility and willingness to participate in a clinical examination and interview session, and the yet-to-be planned full-scale RCT.
Specific Aims, con’t.

4. Determine proportion of the 50 sampled patients from each Center who will present for a clinical examination and interview session.

5. Characterize the patients who present for the dental appointment with regards to:
   a. meeting the clinical periodontal disease and medical eligibility criteria,
   b. responses to a set of self-report questions designed to estimate periodontal disease status,
   c. willingness to participate in the full-scale RCT, and
   d. other characteristics influencing periodontal disease status and glycemic control status, including current HbA1c status.
Inclusion criteria

- 18+ years old
- Registered patient at one of the four participating CHCs
- Type 2 diabetes, at least 6 months duration
- At least 6 natural teeth
- Willingness to participate in the pilot clinical examination and interview session
Exclusion criteria

- Blood dyscrasias
- Pregnancy or breast feeding
- Presence of severe cognitive or communicative impairment
- HIV+ positive
- Cardiac pacemaker
- Requiring prophylactic antibiotics before dental treatment
- Medically unstable
  - {(e.g. accelerated angina, undergoing medical diagnostic evaluation, and current or recent severe illness or surgery (e.g. end-stage renal disease or terminal cancer)
Diabetes registry
Ages 18; N=all w/ dm 6mos

Initial CHC data base.
Send to UM

UM eval. elig., selects strat. sample
N=200, List 1
UM prioritizes for contacting

Study intro letter sent to List 1

CDN contacts List 1: recruitm. script,
track contacts, schedule appointment. n=50/clinic

Consent visit and, if at all possible, study visit: n=50/clinic

Review medical records for excl. criteria

Other data sources for dx and procedure info (ICD9, PECs)

Dental records
Review???

Age, gender,
Race/ethn, HbA1c,
ICD 9 exclus. criteria
Other med condition info.
Informed consent

Screening interview (screening form and script)

Study visit

Brief Phys. Exam:
- Ht.
- Wt.
- BP
- HbA1c

Interview

Dental exam:
- EO & IO soft tissue
- # teeth
- Caries status
- Perio (Pck, BOP)

Participant Advise and $25 pymt
Outcomes anticipated for our project

- Evaluation of feasibility of conducting randomized clinical trial (RCT)
- Prelim data for planning grant (R-21) to plan multi-center RCT (Feb 1 or June 1, 2007 submission)
- Prelim data for multi-center RCT proposal (U-01)
Thank you for your attention

◆ Please feel to contact me:

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