Development of Noninvasive Procedure for Monitoring Blood Glucose Level Using Gingival Crevicular Bleeding

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SUMMARY
Introduction Diabetes mellitus (DM) and chronic periodontitis are common chronic diseases in adults. It is usually necessary to provide a sample of capillary blood to measure blood glucose level in diabetics. However, it is possible to obtain blood during periodontal probing without any discomfort. The aim of the study was to evaluate accessibility of chair side noninvasive screening method for blood glucose level in DM during routine periodontal examination.

Material and Methods 15 non diabetics and 15 newly onset type 2 diabetic patients with moderate to severe periodontitis were selected for the study after meeting inclusion and exclusion criteria. Periodontal pocket probing was performed using Williams Graduated periodontal probe. Blood oozing from gingival sulcus of anterior teeth following periodontal pocket probing was collected with a stick of glucose self monitoring device. As control, finger stick capillary blood was taken.

Results Statistically significant correlation was observed between the blood glucose level in gingival crevicular blood (GCB) and peripheral fasting blood (PFB) in diabetic subjects. The mean GCB glucose level in diabetic subjects was 172.27±5.02 mg/dL while mean PFB glucose level was 167.80±8.87 mg/dL. The correlation coefficients for diabetic and non diabetic subjects were r=0.715 and r=0.619, respectively.

Conclusion The results suggested that blood oozing during routine periodontal examination may be used for DM screening in dental office without the need for any extra procedure.

Keywords: type 2 diabetes; chronic periodontitis; gingival crevicular fluid; noninvasive method; probing

INTRODUCTION
Diabetes mellitus (DM) and chronic periodontitis are common chronic diseases in adults. DM is a complex disease with both metabolic and vascular components characterized by hyperglycemia due to defects in insulin secretion, insulin action or both, as well as dysregulation of protein and lipid metabolism [1]. DM is associated with a wide range of complications such as retinopathy, nephropathy, neuropathy, micro and macro vascular disease and altered wound healing [2]. Also, as per American Diabetes Association (ADA) in 1993, periodontal disease is sixth most common complication in patients who have DM [3]. Moreover, DM and periodontitis seem to interact in bidirectional manner [4].

Periodontitis is defined as an infectious disease which considers inflammation of teeth supporting tissue that leads to progressive attachment and bone loss. Periodontal infections are mixed infections characterized by complex microbiota. Microscopic examination of sub-gingival plaque samples obtained from sites with periodontitis has revealed elevated levels of Gram-negative anaerobes and Bacteroides [5]. These microbial species have even been shown to affect endocrine metabolic status in diabetic patients. Research about the relationship between DM and periodontal disease has been conducted since 1960s [6]. The incidence and severity of periodontal disease has been shown to be influenced by DM and blood glucose level. An improvement in serum glycemic control has also been noticed after PDL therapy [7, 8, 9].

Due to close relationship between DM and periodontitis, it can be assumed that dental practitioners are extremely likely to encounter high number of patients having both, DM and periodontitis. Early diagnosis of DM, however, may help to prevent its long term complications responsible for high morbidity and mortality of diabetic patients [10]. Periodontitis is also likely to be more severe in diabetic individuals with advanced systemic complications because of poorly controlled, persistently high blood sugar levels known as sustained hyperglycemia [11].

The release of bio-inflammatory cytokines in both cases explains their bidirectional relationship. The mechanism associated with periodontitis found in diabetic patients is accumulation of advanced glycation end products

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(AGEs), which affects migration and phagocytosis of polymorphonuclear cells, producing sub-gingival flora with predominance of Gram-negative anaerobes [12]. This triggers secretion of various mediators that facilitate connective tissue destruction and bone resorption and cause insulin resistance in tissues. At the same time periodontal infections induce resistance to insulin in tissues, which contributes to accumulation of AGEs.

A lot of diabetic patients undergoing dental treatment need to be examined for existing blood sugar level, so appropriate treatment can be provided to each patient individually. Therefore, they need to provide blood sample after a small puncture. However, in such patients, small amount of blood can also be obtained simply by probing periodontium without any discomfort.

The aim of the present study was to evaluate feasibility and accuracy of gingival cervicular blood test in dental office to screen blood glucose level as compared to conventional method of peripheral blood sampling.

**MATERIAL AND METHODS**

The study was approved by ethical committee of the institution and an informed consent was obtained from all subjects prior conducting study. A total of 15 diabetic (type 2, previously undiagnosed) and 15 non diabetic patients in the age group of 40-55 years with untreated moderate to severe periodontitis, having probing depth in the upper anterior teeth ≥5 mm, were selected from Diabetes Care and Research Centre, S.P. Medical College, Bikaner. Patients that required premedication or prophylactic drug regime, and suffered from any other systemic infection/diseases or sites with suppuration were excluded from the study.

Periodontal probing depth was assessed by Williams graduated periodontal probe. Contamination with saliva was prevented using gauze and air drying. Teeth were probed mesially and distally. Blood oozing from gingival sulcus/ pocket was collected by placing glucometer diagnostic strip at the entrance of gingival sulcus. In addition, finger stick capillary blood was collected. Both samples, 3 µL each were analyzed using a glucose self monitoring device (Quicktest, Braun Company, Germany), according to the manufacturer’s recommendations.

Statistical analysis was performed by Student (paired and unpaired) t-test or coefficient correlation test in SPSS 10.0 (SPSS, Inc., Chicago, IL, USA).

**RESULTS**

Results of this study revealed a strong correlation (r=0.715, p<0.001) of blood glucose levels between gingival cervicular blood (GCB) and peripheral capillary blood (PFB). The mean blood glucose level from GCB in diabetic group was 172.27±5.02 mg/dL while mean blood glucose level from PFB was 167.80±8.87 mg/dL. The correlation coefficients of diabetic and non diabetic subjects were r=0.715 and r=0.619, respectively. There was significant difference between peripheral capillary and cervicular blood glucose level in diabetic and non diabetic subjects (Table 1).

**DISCUSSION**

ADA recommends screening for DM from age 45 every 3 years in persons without risk factors and more frequently in those with risk factor for DM [9]. In our study, correlation between PFB and GCB glucose readings for diabetic group participants was high i.e. r=0.715. Contrary to that, for participants in non diabetic group, correlation between glucose readings was lower (r=0.619).

A lot of research has been done to develop painless and noninvasive methods to measure blood glucose levels [13]. Sites with periodontal inflammation have been shown to produce adequate amount of blood during routine periodontal examination [14]. Therefore, there is no need for an extra procedure (finger puncture with sharp needle) to obtain blood samples for the assessment of blood glucose level. There is also added advantage in cases with low gingival cervicular bleeding as low amount of blood (3 µL) is necessary to perform the analysis.

Although gingival bleeding is an indicator of inflammation, it may also be possible that vascular changes in DM result in increased gingival bleeding. The relation between controlled DM and development of vascular changes was studied by Tchobroutsky, who observed less vascular changes in well controlled DM [15]. Comparing diabetic and healthy children Bernick et al. [16] found gingival inflammation more frequently in diabetic group. Kjellman et al. [17] came to conclusion that diabetics with poor cooperation had gingivitis more frequently than those with good cooperation. Poorly cooperating group also showed higher levels of blood glucose suggesting poor control of the disease.

According to our findings, there is significant correlation between fingerstick capillary blood and gingival cervicular blood glucose levels. The present study is in agreement with another study that demonstrated strong correlation between gingival cervicular and fingerstick capillary blood [18]. Moreover, in this study, correlation between fingerstick and cervicular gingival blood glucose

**Table 1.** Mean blood glucose level measured in gingival cervicular and peripheral blood (X±SD; mg/dL) in diabetic and non diabetic patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Peripheral fasting blood</th>
<th>Gingival cervicular blood</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic patients</td>
<td>167.8±8.87</td>
<td>172.27±5.02</td>
<td>5.15</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Healthy patients</td>
<td>106.9±3.80</td>
<td>109.8±5.11</td>
<td>6.48</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Zdrave osobe</td>
<td>6.72</td>
<td>6.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* statistically significant difference
* statistički značajna razlika

**Table 1.** Srednja vrednost nivoa glukoze u gingivalnoj sulksnoj i perifernoj krvi (X±SD; mg/dL) osoba sa dijabetes melitusom (DM) i zdravih ispitanika
levels measured in laboratory analyzer was found to be highly statistically significant ($r=0.715, p<0.001$).

Cohen et al. [19] found that diabetics had increased degree of inflammatory changes in their periodontium compared to healthy controls. In the same study it was found that the amount of soft deposits was lower in diabetic group while the amount of hard deposits was equal in both groups. Belting et al. [20] found severe periodontal changes in diabetic patients. Schenkein et al. [21] and Sheridan et al. [22] showed that pocket formation, presence of calculus, increased tooth mobility and tooth loss occurred with greater frequency in patients with decreased glucose tolerance. Patients with confirmed or possible DM also showed increased alveolar bone loss and marginal periodontal membrane widening.

The results of the present study indicate that gingival crevicular blood can be an excellent source for measuring blood glucose level during diagnostic periodontal examination. However, the study was carried out in a small number of respondents and the technique to obtain acceptable blood sample from gingival crevices was not always feasible and reliable which could limit its application in clinical practice. Further studies should be carried out in large group of subjects to obtain confirmatory diagnosis and establish benchmark GCB glucose levels for both diabetic and non diabetic patients.

CONCLUSION

The results of the current study suggest that gingival crevicular blood is a reliable and definitive indicator for the analysis of glycemic status. However, further studies are required to isolate uncontaminated blood and ascertain ratio of contamination. Also, greater number of respondents is required for better comparison of gingival crevicular blood glucose levels and variations with peripheral capillary blood levels.

REFERENCES


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Neinvazivni postupak za utvrđivanje nivoa glukoze u krvi pomoću krvarenja iz gingivalnog sulkusa

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čeno 15 osoba sa DM tip 2 (prethodno nedijagnostikovan) odabranih u instituciji Diabetes Care i istraživački centar, S.P. Medicinskog fakulteta u Bikaneru, i 15 zdravih osoba starosti od 40 do 55 godina s unerijenim do teškim periodontitismom i dubinom parodontalnih džepova na gornjim prednjim zubima od najmanje 5 mm. Bolesnici kojima je bila potrebna premedička ili profilaktička terapija, oni koji su patili od sistemskih infekcija, odnosno oboljenja, ili su imali neko mesto sa supuracijom isključeni su iz studije.


Statistička analiza je urađena Studentovim t-testom i koeficijentom korelacije u programu SPSS 10.0 (SPSS, Inc., Čikago, Illinois, SAD).

REZULTATI

Rezultati su pokazali korelaciju (r=0,715; p<0,001) između nivoa glukoze u krvim iz gingivalnog sulksusa iiperfiran kapilarnim krvim. Srednja vrednost glukoze u krvim iz gingivalnog sulksusa ispitanika sa DM bila je 172,27±5,02 mg/dl, a iz periferne krvim 167,80±8,87 mg/dl. Koeficijenti korelacije ispitanika sa DM i zdravih ispitanika bili su r=0,715, odnosno r=0,619. Utvrđena je statistička značajna razlika između količine glukoze u krvim gingivalnog sulksusa i krvim perifirnih kapilara i kod bolesnika sa DM, i kod zdravih ispitanika (Tabela 1).

DISKUSIJA

ADA preporučuje preventivni pregled za DM osobama starijim od 45 godina, kao i ponavljanje testa svake tri godine ako ne postoji povećani rizik, odnosno ranije i češće ako postoji povećan rizik za obolevanje od DM [9]. U našem istraživanju korelacija između nivoa glukoze u krvim gingivalnog sulksusa i perifirnoj krvim kod ispitanika sa DM bila je visoka (r=0,715). Kod zdravih ispitanika, pak, korelacija je bila niža (r=0,619).

Dosta istraživanja je urađeno kako se razvila bezbolna i nein pazivna metoda za merenje nivoa glukoze u krvim [13]. Mesta na gingivi gde postoji upala daju dovoljnu količinu krvki tokom rutinskog sondiranja periodontalnih džepova [14]. Na taj način se sprećava dodatno uzimanje krvki (npr. iz prsta), kada treba probiti kožu oštrim iglom da bi se dobio uzorak za održivanje nivoa glukoze. Prednost ovakvog uzimanja krvki je u tome što je potrebna mala količina krvki (3 μl), koju je moguće dobiti čak i u slučajevima s oskudnim krvenjem iz sulksusa.

Iako je krvenje iz gingive pokazatelj postojanja upale, ono takođe može nastati zbog vaskularnih promena koje se razvijaju kao posledica DM. Odnos između DM i vaskularnih promena proučavao je Čobrucki (Tchobroucksky), koji je uočio slabije izražene vaskularne promene u dobro kontrolisanim DM [15]. Upoređujući zdravu i decu sa DM, Bernik (Bernick) i radnici [16] su ustanovili izraženiju upalu desni kod dece sa DM. Kjelman (Kjellman) i radnici [17] su zaključili da osobe obeole od DM koje loše rade sa bolestima imaju izraženiji gingivitis od onih bolesnika koji pokazuju dobru radnju. Grupa bolesnika s kojom nije ostvarena dobra radnja imala je više nivoa glukoze, što ukazuje na lošu kontrolu bolesti.

Prema rezultatima naše studije, postoji značajna korelacija između nivoa glukoze u kapilarnoj krvim iz prsta i krvim iz gingivalnog sulksusa, što su potvrdila i druga istraživanja [18]. U našoj studiji korelacija nivoa glukoze u kapilarnoj krvim iz prsta i krvim iz gingivalnog sulksusa izmerena u laboratorijskom analizatoru bila je statistički značajna (r=0,715; p<0,001).


Rezultati ovog istraživanja pokazuju da se krv iz gingivalnog sulksusa može koristiti za merenje nivoa glukoze u krvki tokom dijagnostičkog pregleda periodoncijuma. Međutim, istraživanje je izvedeno na malom broju ispitanika, a tehniku za dobijanje prihvatljivog uzorka krvki iz gingivalnog sulksusa nije uvek moguće pouzdanije provenijencu, što bi ograničavalo njeno upotrebu u kliničkoj praksi. Treba uraditi dalja istraživanja na većem uzorku i uspostaviti referentne vrednosti glukoze u krvki gingivalnog sulksusa kod osoba sa DM i zdravih ljudi.

ZAKLJUČAK

Krv iz gingivalnog sulksusa je pouzdan pokazatelj glikemijeskog stanja pojedinca. Međutim, potrebna su dalja istraživanja kako bi se dobila nekontaminirana krv i utvrdio nivo kontaminacije. Takođe, potrebna je veći broj ispitanika da bi se bolje uporedile vrednosti nivoa glukoze u krvki gingivalnog sulksusa i varijacije u odnosu na vrednosti u krvki perifirnih kapilara.