

THE IMPACT OF PERIODONTAL THERAPY ON PERIODONTAL PATIENT WITH TYPE 2 DIABETES MELLITUS.

ABSTRACT:

Diabetes is a common disease with many oral manifestations; persistent poor glycemic control has been associated with the incidence and progression of diabetes related complications including gingivitis and periodontitis which the most common cause of tooth loss, evidence suggests that periodontitis affects glucose control in diabetes.

The periodontitis induced bacteremia will cause elevation in serum pro inflammatory cytokines leading to hyperlipidemia and ultimately causing an insulin resistance syndrome and contributing to destruction of pancreatic beta cells. Treating chronic periodontal infections is essential for managing diabetes. Aim of this literature review is to examine the effect of periodontal therapy on glycemic control in type II diabetic patients.

Comment [PERI1]: key findings are not clear

INTRODUCTION:

Type 2 diabetes mellitus and obesity are the severe nutritional disorders of multifactorial nature, which altered almost over 100 million population. (Gursoy UK, Marakoglu, Ersan S.) Patient with diabetes have increased incidence and severity of periodontal disease not accounted for by differences in the sub gingival microbial infection poor glycemic control has been consistently associated with periodontal disease severity. Also recent evidence suggests that hyper glycemia may induce inflammatory cytokine production. (Engebretson SP, Hey-Hadavi J, Ehrhardt FJ, Hsu D, Celenti RS, Grbic JT, Lamster IB.) Deep pockets were closely related to current glucose tolerance Engebretson SP, Hey-Hadavi J, Ehrhardt FJ, Hsu D, Celenti RS, Grbic JT, Lamster IB.) Deep pockets were closely related to current glucose tolerance status and the patient with glucose

intolerance has more deep pockets. Further studies suggested that periodontitis affects glucose control in diabetes. (Saito T, Shimazaki Y, Kiyohara Y, Kato I, Kubo M, Iida M, Koga T.) . Diabetes had fewer caries and plaque, lower salivary flow rates and buffer effect, and more frequent growth of yeasts than their non-diabetic control. (Siudikiene J, Machiulskiene V, Nyvad B, Tenovuo J, Nedzelskiene I.) Periodontal disease is most common cause of tooth loss. It has insidious onset, chronic course and commonly result due to cumulative effect of dietary habits, oral hygiene methods and oral habits practiced over the years. (Shah N, Sundaram KR.)

Diabetes is a group of infections and lesions affecting the periodontal tissues that form that attachment apparatus of a tooth. (Stegeman CA.)

Laminin 5 (ln-5) is involved in the apical migration of epithelial cells during the development of periodontal pockets. Low-dose doxycycline (LDD) can therapeutically modulate the host response with its non-anti microbial properties. (Emingil G, Atilla G, Sorsa T, Savolainen P, Baylas H.) Taylor GW.

In addition, evidence supports the observation that periodontal infections contribute to problems with glycemic control (Taylor GW.)

for e.g.: adults with diabetes who received ultrasonic scaling curettage in combination with systematically administered at three months, significant reduction in mean HbA1c nearly 10% from pretreatment value. (Grossi SG, Skrepcinski FB, DeCaro) Evidence suggests that periodontitis induced bacteremia will cause elevation in serum pro inflammatory cytokines, leading to hyperlipidemia and ultimately causing an insulin resistance syndrome and contributing to destruction of pancreatic beta cells. (Iacopino AM.) Treating chronic periodontal infections is essential for managing diabetes.

Literature REVIEW:

Type 2 diabetes mellitus patient were 2.8 times more likely to have destructive periodontal disease (Emrich LJ, Shlossman M, Genco RJ (1991). and 4.2 times more likely to have alveolar bone loss progression. (Taylor G, Burt B, Becker M, Genco RJ,

Comment [PERI2]: does not use the methodology?

Shlossman M (1998a). periodontal disease has been considered to be another complication of diabetes mellitus and evidence (Loe & H (1993). also support poorer glycemic control contributing to poorer periodontal health. (Ainamo J, Lahtinen A, Uitto V 1990; Unal T, Firatli E, Sivas A, Meric H, Oz H 1993; Novaes AJ, Gutierrez F, Novaes A 1996; Taylor G, Burt B, Becker M 1998b)

Recent studies illustrated the synergistic relationship between diabetes and periodontics. severe periodontics was associated with poor glycaemic control and exacerbated diabetes included hyperglycaemia. Although it has been (Taylor, G. W., Burt, B. A., Becker, M. P.,

Genco, R. J., Shlossman, M., Knowler, W. C. & Pettitt, D. J. (1996) . Although it has been reported that improved metabolic control may lead to improved periodontal health, (Sastrowijoto, S. H., van der Velden, U., vanSteenbergen, T. J., Hilleman, P., Hart, A. A., de Graff, J. & Abraham-Inpijn, L. (1990) It is still unclear whether the control of periodontal infection may improve the metabolic control of diabetes. The aim of the present study was to investigate the effect of improved periodontal health on metabolic control in type 2 DM patients. It is known that infections are often accompanied by tissue insulin resistance Viki-Jarvinen, H., Salmakorpi, K., Koivisto, V. & Nikkila, E. (1989) A recent study has demonstrated that during the acute phase of a bacterial infection, insulin resistance increased by 33% whereas during the convalescence period it increased by 28% (Salmakorpi 1989). moreover, Grossi, S. G., Skrepcinski, F.B., DeCaro, T., Zambon, J.J., Cummin, D. & Genco, R. J. 1996) have suggested that chronic gram-negative infections and chronic endotoxemia, such as is seen in periodontal disease could also induce insulin resistance and a worsening of metabolic control in diabetic patients. In view of these facts, it has been hypothesized that control of periodontal infections improves metabolic control of diabetes.

one study investigated several microbial treatments in type 2 diabetics, to determine their efficacy compared to conventional non surgical therapy. (Grossi 1996) Another report examined the correlation between gingival bleeding and blood glucose levels in 9 diabetics with moderate to severe periodontitis (Miller LS, Manwell MA, Newbold D,

Reding ME, Rasheed A, Blodgett J, Kornman KS. 1992) In this study, glycated hemoglobin (HbA1c) and glycated albumin were determined prior to periodontal therapy, and 4 and 8 weeks after therapy. Periodontal therapy consisted of 1 and 2 sessions of root planning, oral hygiene instructions, doxycycline 100 mg for 14 days, and polishing at 2 weeks. A nonsignificant decrease in HbA1c from 9.44% to 9.01% was observed in the 9 subjects. Glycated albumin levels did not change after therapy. 5 to 9 subjects had a consistent reduction in bleeding on probing (reduced at 4 to 8 weeks). In these 5 subjects, HbA1c was reduced from 8.7% to 7.8%, which was statistically significant. Therefore, this small, short-term pilot study suggested that controlling periodontal inflammation may improve metabolic control of diabetes. (Grossi S. G., Skrepcinski, F.B., DeCaro, T., Zambon, J.J., Cummin, D. & Genco, R. J. 1996).

Study of 85 type 2 diabetes mellitus Native Americans (Grossi S. G., Skrepcinski, F.B., DeCaro, T., Zambon, J.J., Cummin, D. & Genco, R. J. 1996). It was found that fasting blood glucose did not significantly improve after periodontal treatment, but a statistically significant decrease in HbA1c was observed. This improvement was attributed to be a possible effect of doxycycline inhibition of glycation of hemoglobin. These findings were discussed in further detail in a subsequent report (Grossi, S.G., Skrepcinski, included an additional 28 subjects). In the treatment group which exhibited the greatest improvement, baseline HbA1c level was 10.5% and decreased to 9.6% 3 months after periodontal treatment. However, by the 6 months examination, HbA1c levels returned to baseline, in spite of continuing improvement in periodontal probing depths and attachment levels. In this report, periodontal therapy, in addition to doxycycline, was credited for the improvement in HbA1c.

There is strong evidence to suggest that the incidence and severity of periodontics is influenced by the presence or absence of diabetes mellitus, as well as the degree to which the disease is controlled by patients (. Bacic M, Plancak D, Granic M 1988 Emrich IJ, Shlossman M, Genco RJ. 1991, Lalla E, Lamster IB, Schmidt AM 1998, Nelson RG, Shlossman M, Budding IM, Pettit DJ, Saad MF, Genco RJ, Knowler WC 1998 Novaes AB Jr, Gutierrez FG, Novaes AB. 1996. Oliver RC, Tervonen T 1993, Ringelberg ML, Dixon

DO, Francis AO, Plummer RW 1977, Shlossman M, Knowler WC, Pettitt DJ, Genco RJ. 1990, Ternoven T, Oliver R. 1993) other report indicate that the existence severe generalized periodontitis may adversely influence the control of underlying systemic disease (Grossi SG, Genco RJ. 1998 Grossi SG, Skrepinski FB, DeCaro T, Zambon JJ, Cummins D, Genco RJ. 1996, . Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A, Blodgett J, Kornman K. 1992 Sammakorpi K. 1989. . Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M, Kinder WC, Pettitt DJ 1998, William R, Mahan C. 1960, . Yki-Jarvinen, H., Sammakorpi, K., Koivisto, V. & Nikkila, E. (1989)). Epidemiological data indicate the growing elderly population has a far higher incidence of type 2 diabetes mellitus than do younger age groups (Gottsegen R. 1990, Mealey BL 1998, Nathan DM, Dale DC, Federman DD, 1996, United States Pharmacopeia Drug Information 1998).

Certain systemic disease, such as diabetes mellitus (DM), are known to increase this risk (.Grossi, S., Zambon, J, Ho, 1994) Page, R. C. & Beck, J. D. (1997c). Less research attention has been paid to roll that chronic oral disease may play in systematic disease, despite the possibility that the morbidity and mortality rates of some diseases might be reduced by an improvement in periodontal health. (Beck, J. D., Garcia, R., Heiss, G., Vokonas, P.S. & Offenbacher, S. (1996), Offenbacher, S., Katz, V., Fertik, G. (1996) Grossi & Genco RJ, 1998, Scannapieco, F.A. & Genco R, J, 1999). Periodontitis as a chronic localized oral infection that triggers a systematic as well as local host immune-inflammatory response and that can be a source of bacteraemia, because of the large epithelial surface with ulcerated periodontal pockets (Ebersole, J.L. & Cappelli, D. 2000). Periodontitis, especially in its severe clinical form, is currently considered to influence the pathogenesis or increase the risk of some systematic diseases (Garcia R, Henshaw, M. & Krall, E. 2001). the biological relationship between DM and periodontal disease is well documented (Mattson J. S. & Cerutis, R. (2001) , Soskoline, W.A. & Klinger, A. 2001). Periodontal disease and DM are closely associated and are highly prevalent chronic diseases with many similarities in pathobiology. Inflammation is a critical player in the association, & its importance is just now coming to light (Mealey, B. L., & Oates,

T.W. (2006) 2006)DM,the most common human endocrinal disease,is characterized as a metabolic disorder associated with a chronic highper glycaemic state.It was first demonstrated that DM was a risk factor for periodontitis and substiquently the inverse relationship was proposed,i.e. that periodontitis may be a risk factor for diabetic decompensation, and this hypothesis has been supported by various studies (. Grossi, S.G.2001, Iacopino AM. 2001, Lalla E, Lamster IB, Stern DM, Schmidt AM2001, Taylor GW. 2001, Katz, J, Bhattacharyya, I, Farkhondeh- Kish, F, Perez, F.M, Caudle, R.M.&Heft, M. W. (2005), Takeda, M, Ojima, M, Yoshioka, H. Inaba, H, Kogo, M, Shizukuishi, s, Nomura,M.& Amano,A (2006) Lim, L.P, Tay, F.B.K, Sum, C.F.& Thai, A.C.&2007 Rea). Several recent experimental studies have addressed the mechanisms underlying the interaction in between DM and periodontitis. All reported a strong inflammatory response characterized by a large secretion of inflammation mediators, mainly pro-inflammatory cytokines, which can have both local (periodontal destruction) and systemic (impaired glycaemic control) effects(Grossi ,S.G.(2001) Iacopino ,A.2001, Lalla ,E,Lamster, I, Stern, D.& Schmidt, A.M.(2001), Nishimura ,F, Iwamoto, Y., Mineshiba, J., Shimizu, A., Soga, Y. & Murayama, Y. 2003, Genco ,R.J., Grossi, S.g., Ho, A., Nishimura, F.& Murayama, Y.2005). Various studies have been published on the effect of periodontal treatment on DM control. Although some authors found (Miller,L. S., Manwell, M.A., Newbold, D. 1992, . Grossi, S. G., Skrepcinski, F.B., DeCaro, T., Zambon, J.J., Cummin, D. & Genco, R. J. 1996, Grossi SG, Skrepcinski FB, DeCaro 1997, Iwamoto, Y., Nishimura, F., Nakagawa, M.2001, Rodrigues, D., Taba, M., Novaes, A., Souza, S. & Grisi, M. 2003, Kiran , M., Arpak, N., Unsal, E.& Erdogan, M.F.2005) that periodontal therapy may have a beneficial effect on glycaemic controlo, not allreported this improvement (seppala ,B., Seppala, M.& Ainamo, J.1993, Seppala & Ainamo ,J.1994, Aldrdge,J. P., Lester, V., Watts, T.L.P, Collins, A., Viberti, G.& Wilson, R. F. 1995, Smith,G.T., Greenbaum, C.J., Johnson, B. D. & Persson, 1996, westfelt ,e., Rylander, H., Blohme, G., Jonasson, P. & Lindhe,J.1996, Christgau, M.,Palitzsch, K-D., Schmalz, G., Kreiner,U.&Frenzel, S.1998, Hagiwara et al 2002, Jones, J. A., Miller, D. R., Wehler, C. J., Rich, S. E., Krall-Kaye, E. A., McCoy, L. C., Christiansen, C. L.,

Rothendler, J.A.& Garcia, R. I. 2007). Even now, at the beginning of 21st century, the scientific evidence remains inadequate and inconclusive. With this background, a cynical study was designed to determine whether an improvement in the periodontal status of type 2 diabetic subjects is accompanied by an improvement in their metabolic control

Microbial dental plaque is the initiator of periodontal disease. Systemic factors modify all forms of periodontitis principally through their normal effects on the normal immune and inflammatory defences. Periodontal disease has been characterized as the sixth complication of diabetes. (Loe H. 1993) .A 1995 report (Aldridge JP, Lester V, Watts TL, Collins A, Viberti G, Wilson RF. 1995) confirmed that metabolic control may be the most important factor between periodontal health and IDDM. These data support the hypothesis that diabetes and the level of metabolic control are important modifiers of periodontitis.

Data on the efficacy of periodontal care on improving glycaemic control in poorly controlled diabetes are equivocal (.. Taylor GW 1999,2001,2003,US Department of Health and Human & Services. 2000) .A two way relationship between diabetes and periodontitis has been postulated (Grossi, S.G., & Genco, R J, 1998; Iacopino, A. 2001), but supporting data are sparse. Several studies suggest that improvements in periodontal condition will improve glycaemic control (Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A,Blodgett J,Kornman KS 1992,Taylor, G. W., Burt, B. A., Becker, M. P.,Genco, R. J., Shlossman, M., Knowler, W. C.& Pettitt, D. J 1996, Grossi SG, Skrepickinski FB, DeCaro 1997; St Iwamoto ,Y., Nishimura, F., Nakagawa, M. Sugimoto, H., Shikata, K., Makino, H., Fukuda, T., Tsuji, T., Iwamoto, M. & Murayama, Y.2001. Stewart, J.E., Wager, K.A., Friedlander, A. H. & Zadeh, H. H. 2001).

Epidemiological studies have demonstrated an association between both types of diabetes and periodontal disease (Emrich LJ, Shlossman M, Genco RJ. 1991, Moore PA, Weyant RJ, Mongelluzzo MB, Myers DE, Rossie K, Guggenheimer J, Block HM, Huber H, Orchard T.1999). However increased periodontal risk is often related to duration and adequacy of control of the diabetic state. For example, it has been noted that individuals with non-insulin-dependent diabetes mellitus have a three-fold increased risk of

developing periodontal disease that can not otherwise be explained on the basis of age, sex or oral hygiene (Emrich LJ, Shlossman M, Genco RJ. 1991). Study (. Sastrowijoto, S. H., van der Velden, U., van Steenberghe, T. J., Hillemans, P., Hart, A. A., de Graff, J. & Abraham- Inpijn, L. 1990) that showed that individuals with poor metabolic control had increased attachment loss compared to well-controlled subjects, despite similar oral hygiene levels. It is also well documented that diabetic patients have a compromised ability to respond to bacterial infections, and it has been proposed that it is this compromised host response that in part may increase diabetics risk of periodontal disease. Interestingly, the reverse possibility that the periodontal infection may exacerbate the diabetic condition is now beginning to receive increasing attention (Grossi, S. G. & Genco, R. J. 1998) . The presence of glycated hemoglobin in the circulation and in tissues, resulting from the hyperglycemia of diabetes, is believed to be a contributing factor to the degenerative micro vascular and arterial changes that are common sequelae of diabetes. A study of the Gila river Indian community, a population having a prevalence of non-insulin-dependent diabetes mellitus of about 50%. Has recently tested the hypothesis that severe periodontitis in individuals with non-insulin-dependent diabetes mellitus increases the concentration of glycated hemoglobin. (Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M1998) The results showed that severe periodontitis at baseline was associated with increased risk of having poor glycaemic control at follow-up 2 or more years later. If periodontal disease does affect diabetic status, we would expect that treating periodontal disease would reduce the severity of diabetes. A recent systematic review of the literature by Grossi, S. G. & Genco, R. J. 1998). Concluded that the effect on diabetic status was dependent upon the treatment modality. Studies that investigate the effect of only mechanical debridement were unable to demonstrate any effect on blood glucose level or glycated hemoglobin level regardless of periodontal disease severity or degree of diabetes control Aldridge JP, Lester V, Watts TL, Collins A, Viberti G, Wilson RF, 1995, O'Neil TC 1979, Seppala B, Ainamo J. 1994). However, all three studies that added systemic antibiotics to mechanical debrident demonstrated improved metabolic control of diabetes 2. (Miller LS, Manwell MA,

Newbold D, Reding ME, Rasheed A, Blodgett J, Kornman KS 1992, O'Neil TC 1979, Williams RC Jr, Mahan CJ 1960). Results indicate that all subjects that were treated with doxycycline experienced a reduction in glycated hemoglobin (Grossi SG, Skrepcinski FB, Dcaro T, Zambon jj, Cummins D, Genco RJ 1996) These results suggest that periodontal antimicrobial treatment may reduce the level of glycated hemoglobin in diabetic subjects and may ultimately hold the potential to reduce diabetic sequelae.

There is an extensive body of literature that point to an emerging "two-way relationship" between diabetes/poor glycaemic control and periodontal disease. Specifically, the severity of the diabetic condition, whether insulin-dependent diabetes mellitus is related to the incidence and severity of periodontal disease (Soskolne WA, Klinger A. 2001 Taylor GW 2001, Tsai C, Hayes C, Taylor GW 2002). Conversely, there is evidence that the severity of periodontal disease may affect the level of glycaemic control in diabetic patients (Grossi SG. 2001, Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A, Blodgett J, Kornman KS, Stewart JE, Wager KA, Friedlander AH, Zadeh HH. 2001, Taylor GW. 2001). It has been proposed that this effect may be due in part to the role of the chronic bacterial load and chronic inflammation that is characteristic of periodontal disease. Products of the bacterial load and products of the inflammatory response could enter the systemic circulation, leading to an increase in the resistance to insulin. This would result in an elevated blood glucose, which in turn could react with haemoglobin to form glycosylated hemoglobin. Further glycation and oxidation of proteins and lipids would then lead to formation of advanced glycation end products that could promote sequelae of diabetes such as local destructive inflammatory responses and tissue damage (Stewart JE, Wager KA, Friedlander AH, Zadeh HH 2001)

Conclusion ;

For the dental practitioner, an important area of clinical research centers on improving glycemic control (as measured by the glycosylated hemoglobin) through periodontal therapy. Studies using combinations of debridement, local irrigation, and/or systematic antibiotics on both NIDDM and IDDM patients have shown small, but in some cases significant, reductions in glycosylated hemoglobin after periodontal treatment (Grossi SG

2001, .Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A, Blodgett J, Kornman KS 1992, .Stewart JE, Wager KA, Friedlander AH, Zadeh HH 2001, .Taylor GW 2001). We concluded that periodontal therapy itself improves metabolic control and reinforces that T2DM is a risk factor for periodontitis.

Comment [PER13]: What is the key finding?

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