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HbA1c, And Blood Glucose, Changes When Treating Periodontal Disease with the Perio Protect Method™

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ABSTRACT

Periodontal disease is a chronic wound resulting in host elevated local and systemic inflammatory markers in response to the microorganisms of the periodontal biofilm. Separately from its importance as an oral ailment, chronic periodontitis has gained relevance since it can develop into a systemic condition characterized by hyper-inflammation, disruption of the innate and adaptive immune system, and other system-wide alterations. There is compelling evidence that inflammation and chronic infection play an essential role in the development of inflammatory markers and of type 2 diabetes. Studies in humans suggest that circulating inflammatory marker levels may predict type 2 diabetes years in advance of the onset of the disease.

Local and systemic expression of inflammatory cytokines, such as TNF-alpha and IL-6, increase in individuals with periodontitis. TNF-alpha and IL-6 impair intracellular insulin signaling, which may lead to insulin resistance and are significantly associated with cardiovascular events and stroke. This case study demonstrates treating periodontal disease with a direct medication delivery method (Perio Protect Method™) manages the patient's periodontal disease and lowers daily blood glucose and HbA1c levels.

Keywords

Periodontal disease, Diabetes, Diabetic markers, Perio Protect Method, HbA1c, Blood glucose.

Introduction

Research supports possible cause/effect associations between type 2 diabetes and periodontal disease [1-3]. Both are chronic inflammatory host responses and appear related, but not fully explained. Diabetic patients have a higher risk of developing periodontal disease [4]. Managing diabetes appears to have a positive affect for controlling periodontal disease and treating periodontal disease appears to improve glycemic control [5].

There is a greater recurrence of periodontal disease expected in diabetic individuals because periodontal treatments provide short-term benefits as compared to non-diabetic patients [6]. Severe periodontitis is associated with poorly controlled glycemia, higher HbA1c levels and systemic complications [7]. Periodontitis is associated with a slight elevation of HbA1c in non-diabetic subjects (periodontitis may potentially increase the incidence of diabetes); although a clear-cut association is not established [8].

Although the probable associations between diabetes and periodontal disease are evident, it is not clear if treating periodontal disease with conventional methods like scaling and root planing affect diabetic management. This case study demonstrates managing patient's periodontal disease with the Perio Protect Method™ significantly improves daily blood glucose and HbA1c levels. The patients signed informed consent forms regarding the use of the Perio Protect Method™ for treating their periodontal disease.

Materials and Methods

Inflammation and chronic infection play an essential role in the development of inflammatory markers and of type 2 diabetes. In periodontal disease, there is a shift from health to disease when a greater number (10^4-10^5) of Gram-negative anaerobic

microorganisms [9] replaces a low number of bacteria (10^2-10^3) that are mostly Gram-positive aerobic and facultative anaerobes.

Gram-positive and Gram-negative bacteria equally induce IL-1 beta, but Gram-positive bacteria generate twice as much TNF-alpha. Gram-negative bacteria induce at least twice as much IL-6 and IL-8 [10]. Gram-negative bacteria produce lipopolysaccharides (LPS) that up-regulates endothelial cell adhesion molecule expression and increases the secretion of interleukin-1 (IL-1), tumor necrosis factor alpha (TNF-alpha) and thromboxane, which increases platelet aggregation and adhesion, causing the formation of lipid laden foam cells and deposits of cholesterol and cholesterol esters [11].

Studies in humans suggest that circulating inflammatory marker levels may predict type 2 diabetes years in advance of the onset of the disease [12]. Local and systemic expression of inflammatory cytokines, such as TNF-alpha and IL-6, increase in individuals with periodontitis. TNF-alpha and IL-6 impair intracellular insulin signaling, which may lead to insulin resistance and are significantly associated with cardiovascular events and stroke [13].

Treatment of Type 2 diabetic patients with non-surgical periodontal treatments provides a variety of results. Non-surgical periodontal therapy significantly lowers HbA1c levels in type 2 diabetics [14], but studies show non-surgical therapy alone significantly reduced HbA1c levels only in well-controlled diabetics [15,16]. Other studies refute the benefit of periodontal therapy in helping diabetic patients manage their blood glucose levels [17,18]. According to these findings, the use of nonsurgical periodontal treatment to reduce levels of HbA1c is not justified.

Controlled clinical trials demonstrate the Perio Protect Method™ (PPM™) helps patient's manage periodontal disease [19,20]. Studies have shown using the PPM™ lowers patient's systemic inflammatory marker LpPLA2 [21] and HsCrp [22], but the effects on diabetic markers is unknown.

This study reports on diabetes marker changes for patients adding direct medication delivery (Perio Protect Method™) as the only change in the dental/medical treatment. The Perio Protect Method™ uses a custom formed medical device (Perio Tray™) that has received FDA clearance to deliver medications (Perio Gel™ 1.7% hydrogen peroxide) deeper into periodontal pockets than other dental tray devices. The method is used in accordance with the patient's conditions to manage the pathogens that cause periodontal disease [23]. The patients' diabetic markers were taken before, during and after treatment.

There is no randomization or blinding as the unexpected diabetic results appeared during the periodontal treatment. The sample size is small and shows promising results but needs to be further evaluated with studies that are more extensive.

Case One

The patient has advanced periodontal disease and a history of unstable diabetes not well controlled by 500 mg Metformin BID and a family history of cardiovascular disease (CVD). Periodontal probing demonstrates generalized periodontitis and some areas with severe bone loss and pocket formation and 100% bleeding upon probing.

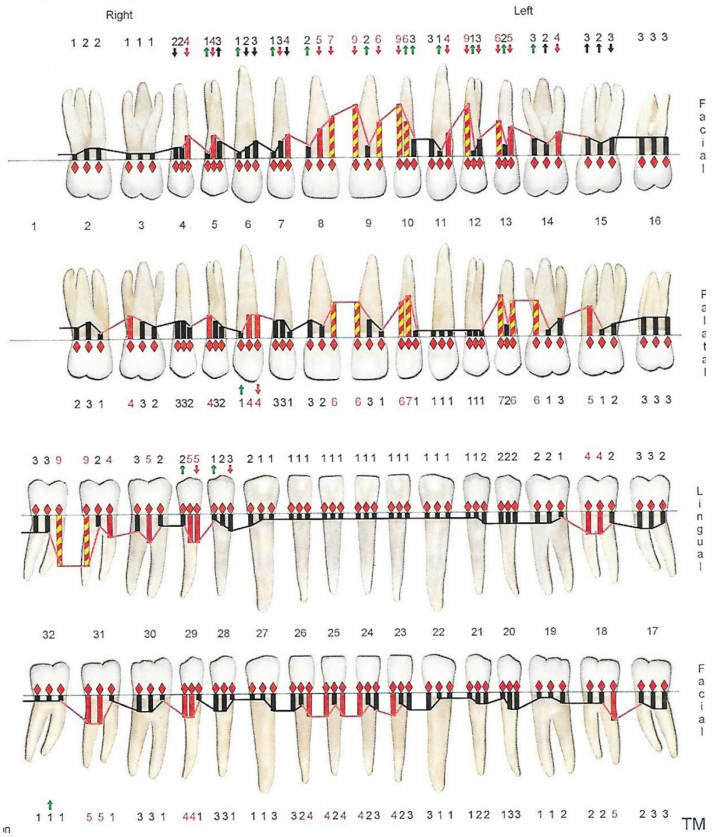

Figure 1: Red diamond represent bleeding upon probing (BOP at 100%) along with the numerical pocket probing depth (3mm is normal). The patient experienced multiple periodontal pockets from 4-9 mm.

Perio Trays™ are fabricated in accordance with the periodontal conditions and are delivered prior to any oral mechanical treatment in accordance with the American Medical Association (AMA) Wound Healing Society Chronic Wound Guidelines [24].

Figure 2: Custom formed maxillary and mandibular Perio Trays™ with customized peripheral seals and extensions deliver 1.7% hydrogen peroxide gel (Perio Gel™) subgingival and interproximal and maintain the medication in place for a sufficient time to manage the periodontal pathogens.

The treatment plan consisted of:

- Initial Examination and impressions for Perio Tray™
- Perio Tray™ Delivery to Treat the Cause of Infection
  - chemical debridement
- Mechanical debridement
  - scaling and root planing
  - laser surgery if indicated
- Impression for second set of Perio Trays™
- Maintenance and Prevention of Reoccurrence

The Perio Trays™ are used initially to control the etiology of disease before mechanical intervention as advocated by the Chronic Wound Care Guidelines of the AMA Wound Healing Society. The results of the microbial management are shown in figure 3. The areas that did not respond completely (return to 3mm or less with no bleeding) are treated with scaling and root planing and the treatment plan is further modified to include laser surgery for the maxillary anterior region. A second treatment tray is fabricated after tissue improvements to maintain the delivery of the medications as the tissues heal.

Prior studies show usage of the PPM results in a shift in the composition of the oral biofilm from a greater number of predominantly Gram-negative obligate anaerobes before treatment to a lesser number of Gram-positive aerobes and Gram positive and negative facultative anaerobes and aerobic bacteria after treatment. This modifies the biofilm from a greater number of virulent bacteria to a lesser number of less virulent bacteria as determined by DNA analysis [25]. This shift in the oral biofilm from virulent to less virulent and the decreased number of pathogens relate to improvements in the oral health conditions found in the probing and examination results (Figure 3).

Results following tray usage

Although significantly improved, the results are not maintainable with the pockets and granulomatous tissues. Site specific laser surgery was used to treat the area with remaining pockets. The results following laser surgery show normal probing depth with one 4mm probing (Figure 4 -distal #13) in an area that did not receive laser therapy. A final maintenance tray is sometimes necessary if the tray seals no longer maintain the medications due to tissue healing.

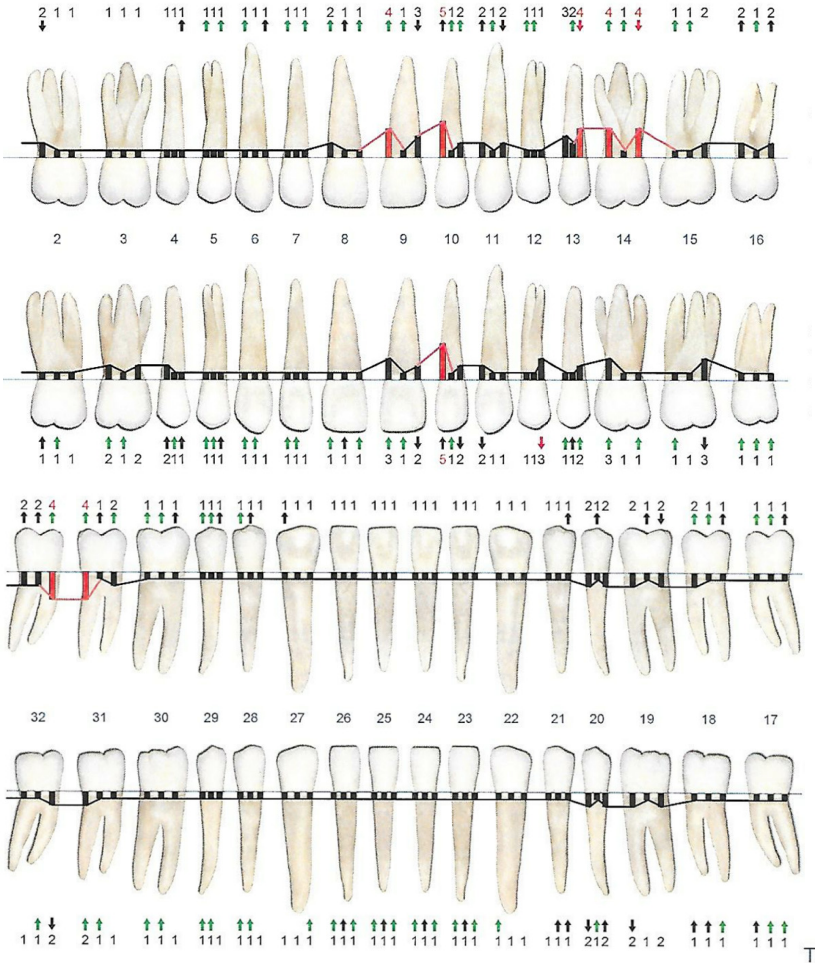

Figure 3: Results following the first set of Perio Trays™ where BOP and PPD decrease. Scaling and root planning are completed after wearing the Perio Trays™ to control the cause of infection. There is no BOP, but some areas require further treatment with laser surgery to control granulomatous tissue as a new Perio Tray is fabricated for the improved conditions..

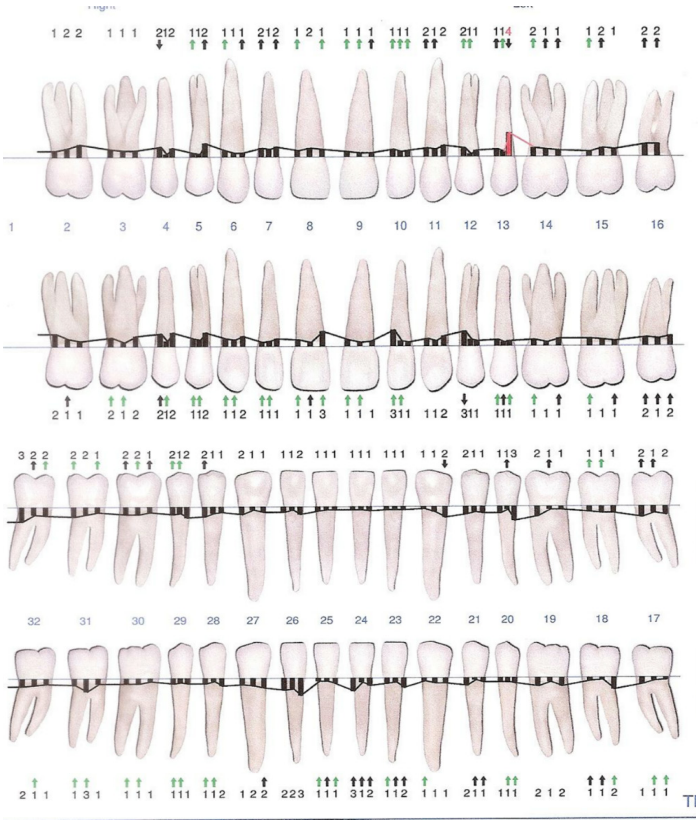

Figure 4: Results following the scaling and root planing and laser surgery around the maxillary right anterior quadrant. One probing depth is greater than 3mm and there is no BOP.

Daily blood glucose levels are taken before and during treatment. The initial blood glucose level is 179, which decreased to 141 during treatment and is 130 at the end of active treatment. The patient remains a diabetic with lower blood glucose levels.

Figure 5: The composite of daily blood glucose levels demonstrates the blood sugar level decreases during the Perio Protect Method usage.

This case is important as it demonstrates a possible association between changes in the patient's blood glucose levels as the inflammatory markers are managed and appears associated with a decrease in the periodontal disease [26]. The improvement may enable the patient to decrease diabetic medications in the future, but a further evaluation will be necessary to determine these factors.

Case Two

Dr. Patricia Stoker, DMD. treats the second patient. The patient is an uncontrolled diabetic allergic to insulin with an HbA1c level of 12. Dr. Stoker prescribes the Perio Protect Method™ to treat the advanced periodontal disease for this uncontrolled diabetic. The patient's HbA1c level is monitored by her treating physician.

Figure 6 shows the pocket probing depths and bleeding upon probing prior to the PPM. Previously, the patient received conventional periodontal intervention (prophylaxis, scaling and root planing), which did not alter her HbA1c.

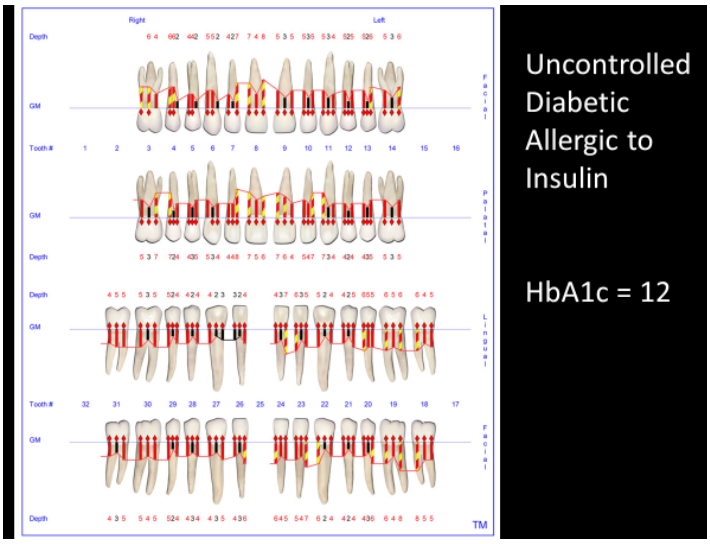

Figure 6: The periodontal charting showed pockets up to 8mm periodontal pockets and 97% bleeding on probing prior to the use of the Perio Protect Method™.

The Perio Trays™ are delivered in November 2011 and the patient uses Perio Gel™ four times / day and Vibramycin 50 mg/ml three drops / tray. The Perio Gel™ alters the micro-environment of the pockets by the introduction of oxygen under pressure, which modifies the biofilm [27]. The Vibramycin is used at a subclinical dose to serve as an antioxidant to decrease inflammation and alter osteoclastic and osteoblastic activity [28].

The patient has 97% bleeding upon probing and periodontal pockets up to 8mm prior to treatment. The Perio Protect Method™ manages the biofilm resulting in decreasing bleeding upon probing from 97% to 23% by April 4, 2012. Full mouth scaling and root planing are done April 4, 2012. The HbA1c level is 7 when she visits her family physician on July 11, 2012.

This case is significant as the patient is not able to use insulin to help manage her diabetes, but the HbA1c marker decreases significantly, as the periodontal disease is managed with the PPM. This may relate to an association between diabetes and periodontal disease, but additional studies will be needed to confirm or refute this possibility.

Case Three

Dr Tim Pranger initiates treatment for this patient on April 25, 2016 where he prescribes the Perio Protect Method™ after an initial visit and Perio Tray™ impressions. During the examination, he found the patient is a diabetic and suffered a previous myocardial infarction. The treatment summary is demonstrated in the following (Figure 8).

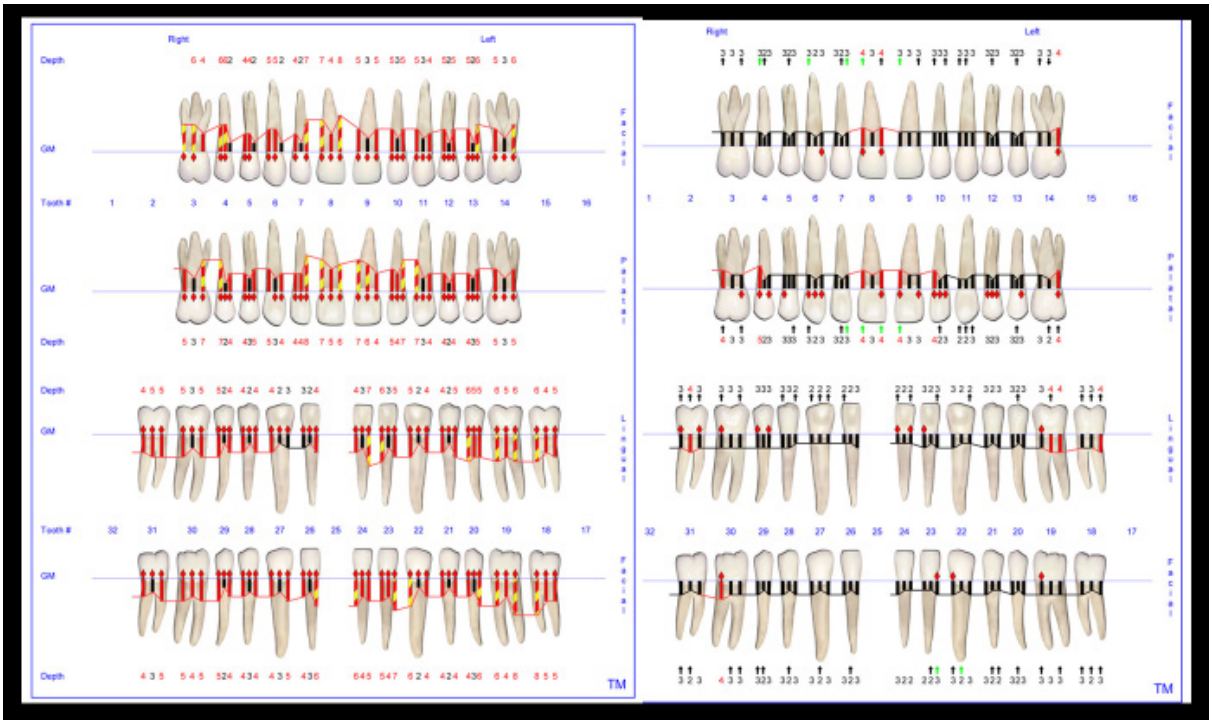

Figure 7: Comparison of before and after Perio Protect Method™ usage show pocket probing depths improve throughout the mouth and bleeding upon probing goes from 97% to 23% in 6 months.

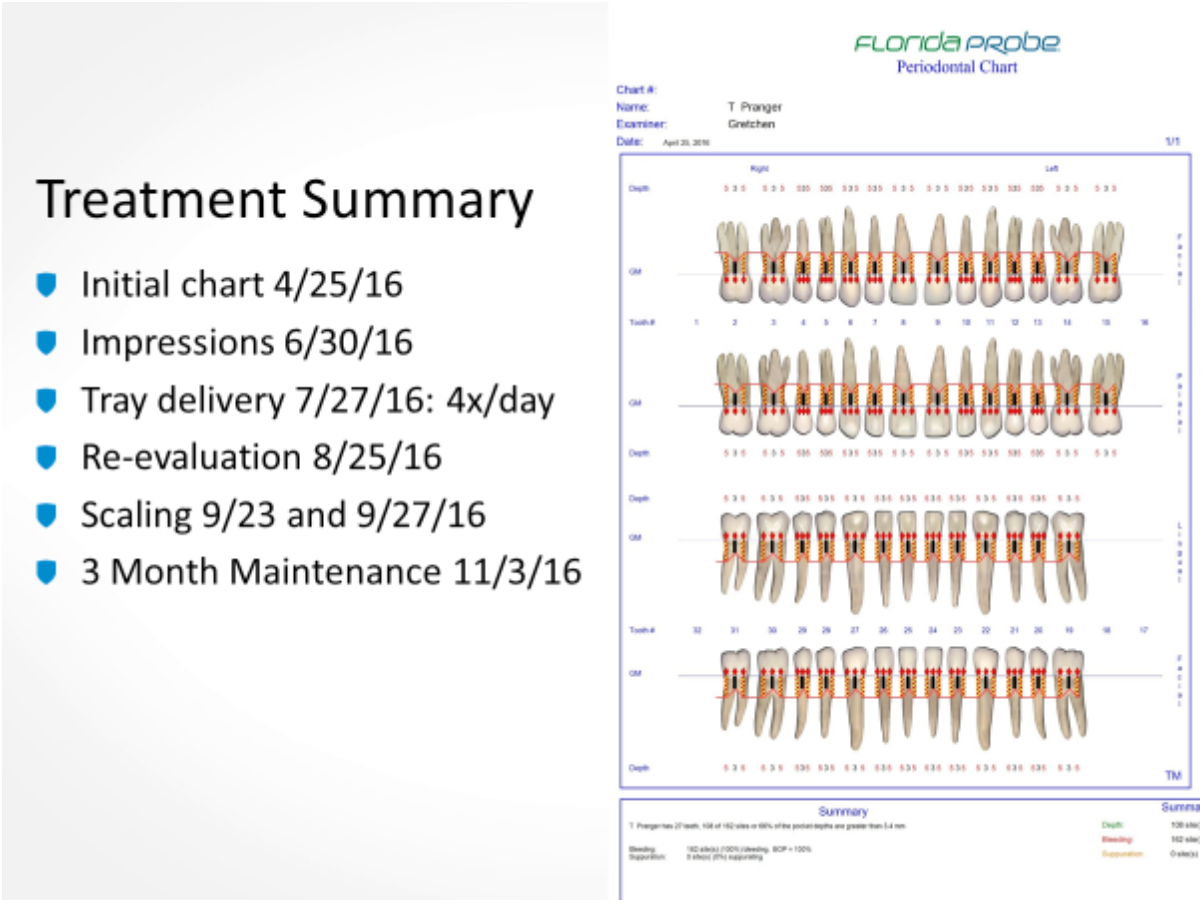

Figure 8: The treatment summary and initial conditions are recorded. The Perio Tray delivery of Perio Gel enables managing the periodontal pathogens prior to mechanical intervention as recommended by the AMA Chronic Wound Care Guidelines

Perio Trays™ are delivered and the patient uses the Perio Protect Method™ with 1.7% hydrogen peroxide (Perio Gel™) and three drops per tray doxycycline 50 mg/ml. The medications delivered by the Perio Protect Method™ manage the pathogens and this decreases the inflammation and edema within the first month (Figure 9).

Figure 9: The images above show the conditions before treatment and following one month of Perio Tray™ usage prior to scaling and root planing. This regimen follows the AMA Chronic Wound Guidelines to treat the cause of disease as the initial step in chronic wound therapy. Tissue swelling and redness decrease, and the calculus and tartar are modified by the hydrogen peroxide (Perio Gel™) along with the anti-inflammatory results of hydrogen peroxide and doxycycline.

Use of the PPM prior to S&RP follows the Chronic Wound Guidelines to manage the cause of disease, when possible, before mechanical debridement. Hydrogen peroxide through it reactive oxygen species (ROS) is thought to be proinflammatory, but is shown to result in anti-inflammatory effects as it relates to neutrophil activity [29]. Likewise, doxycycline has anti-inflammatory properties when used to mitigate pathogen activity [30].

The patient's HbA1c markers before treatment are compared to 2 months during treatment. The HbA1c decreases from 9.3 to 5.8. Studies demonstrate reducing patient's HbA1c is associated with a corresponding decrease in relative risks for microvascular events associated with eye disease, heart disease, kidney disease, nerve damage, and stroke [31]. This patient is followed for almost 18 months where the patient uses the Perio Protect Method™ to manage the periodontal pathogens. The HbA1c level remains controlled.

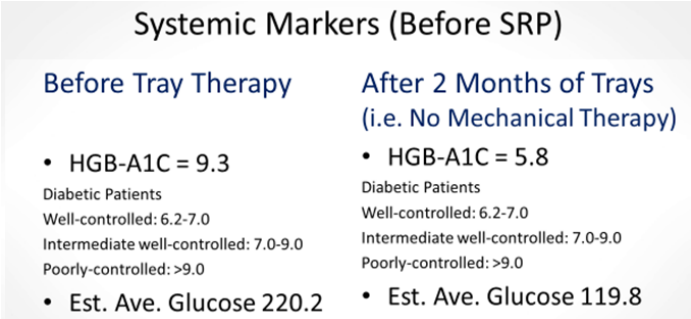

Figure 10: The HbA1c levels before and during treatment with the Perio Protect Method™ show a decrease from 9.3 to 5.8, which equates to a daily blood glucose level from 220.0 to 119.8.

Name *Standard Range*	2/9/16	9/23/16	3/14/17	8/15/17
Est Average Glucose *mg/dL*	220.2	119.8	131.2	116.9
HGB-A1C *4.4 - 6.4 %*	9.3	5.8	6.2	5.7

Figure 11: The patient is followed for 18 months. The HbA1c level remains controlled during this time as the patient continues using the PPM to manage the periodontal disease.

HbA1c Levels Over 18 Months

Initial and final periodontal probing demonstrate a significant improvement in periodontal conditions with the Perio Protect Method™.

There are no changes in the patient's medications during these studies as the introduction of the Perio Protect Method™ is the only change in the treatment. The periodontal disease is managed with the Protect Method™ and the HbA1c level decreases to normal and remains controlled for 18 months.

This case is important as the patient has a history of cardiovascular events and type 2 diabetes. The decrease in his HbA1c may be an indication of systemic alterations in response to managing periodontal disease and possible associated cause/effect relationships, but a larger study is needed to confirm or refute these possibilities.

Discussion

An association between type 2 diabetes and periodontal disease has been recognized. There is a greater recurrence of periodontal disease expected in diabetic individuals because conventional periodontal treatments provide short-term benefits as compared to non-diabetic patients. These case reports demonstrate treating patient's periodontal conditions with the Perio Protect Method provide long lasting periodontal results and the patient's diabetic markers decrease for up to 18 months. This study is important in

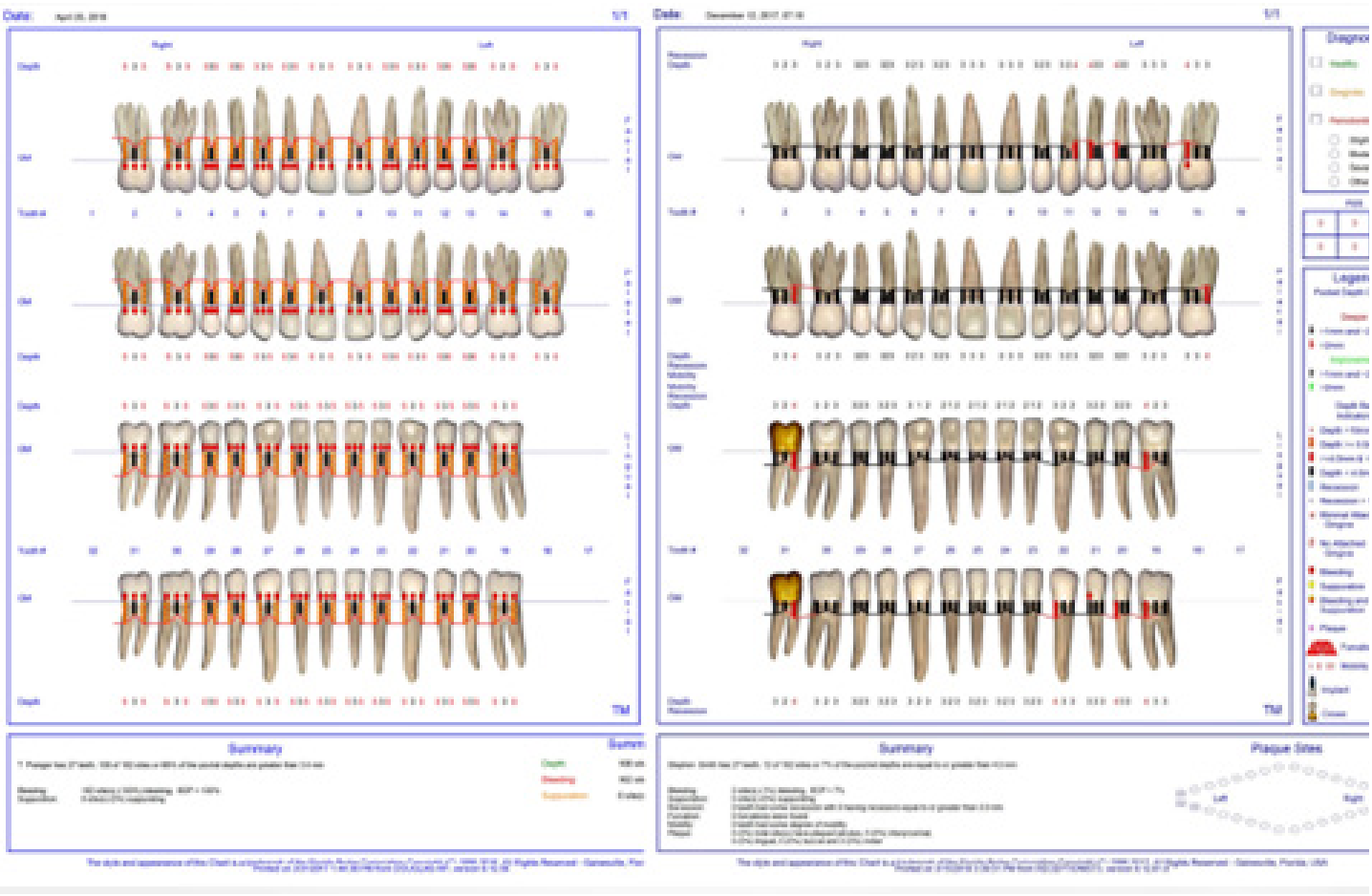

Figure 12: The periodontal charting before and after using the Perio Protect Method™ show significant improvements in pocket probing depth and bleeding upon probing.

demonstrating diabetic marker levels decrease as the periodontal conditions are managed. A more comprehensive study is needed to evaluate these possible associations in greater depth.

Conclusions

The Perio Protect Method™ enables the patients to manage their periodontal disease and this appears to help decrease their daily blood glucose and HbA1c levels. These case reports are important in demonstrating ways to assist diabetic patients in maintaining their periodontal health and in lowering their systemic diabetic markers. This may have implications for other systemic inflammatory relationships, but this will require a more detailed investigation to determine these associations.

Competing Interests

Dr Duane Keller was one of the treating doctors and is the President and Chief Scientific Officer of Perio Protect LLC.

Acknowledgements

Dr. Patricia Stoker dentist treating patient 2.
Dr. Tim Pranger dentist treating patient 3.

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