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PROFESSIONAL AND HOME-MANAGEMENT IN NON-SURGICAL PERIODONTAL THERAPY TO EVALUATE THE PERCENTAGE OF GLYCATED HEMOGLOBIN IN TYPE 1 DIABETES PATIENTS

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ABSTRACT

Objectives: To evaluate the decrease of Glycated Hemoglobin (HbA1c), patients affected by Type 1 Diabetes Mellitus were treated by non-surgical periodontal therapy, involving professional dental hygiene every three months and monthly checks to apply ozonated water; furthermore, to patients, were given domiciliary supply, such as "Biorepair Plus" mouthwash and "Biorepair Plus Parodontgel" paste to use daily.

Materials and Methods: 36 Type 1 diabetic subjects were enlisted and randomly allocated in 2 several groups following different therapies: Group 1 followed the main therapy above mentioned; Group 2 followed only professional dental hygiene every three months and monthly checks to apply ozonated water. In each group were taken the periodontal indices (PPD, BOP and PI) monthly and, furthermore were asked to patients, to bring in vision the lasts Glycated Hemoglobin tests to evaluate the decrease of that. Both groups were followed for six months and, at the end of every operative season, the periodontal indices were prepared and summarized.

Results: At the begin of the study there was initial difference between the groups in every index examined particularly the Trial Group's HbA1c average value was 6,9% vs an initial average value equal to 7,4% of Control Group; Trial Group's PPD average value was 2,3mm vs 2,8mm of Control Group, for BOP the average value was equal to

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8,7% in Trial Group vs 6,2% of Control Group; finally the Trial Group's IP average value was equal to 64,9% vs 54% of Control Group. In both groups we have seen a decrease of periodontal indices: the PPD passed to a value equal to 1,9mm in Trial Group, while in control group passed to a value equal to 2,5 mm; the BOP passed to a value of 3%, while passed to 1,6% in Control Group; the PI passed to 17,5% in Trial Group, while in Control Group the value passed to 39,1%; however the most important result is the decrease of Glycate Hemoglobin that has been noticed in Trial Group, indeed the average value passed to 6,4% vs the same index the remained unchanged in Control group.

Conclusion: Frequent recalls of oral hygiene, associated with the use of ozonated water and home therapy with "Biorepair Plus" mouthwash and "Biorepair Plus Parodontgel" paste, it would seem to reduce the periodontal indices, which lead to reduce the Glycated Hemoglobin index.

1. INTRODUCTION

There are many studies that confirm the existence of a link between periodontal infections and certain number of systemic conditions. Among these, important are cardiovascular and cerebrovascular diseases, pregnancy conditions and Diabetes Mellitus; at the same time, it is considered that periodontal disease can be a risk factor for them, thus establishing a two-way relationship [1-13].

Diabetes Mellitus and Periodontitis are currently the subject of several studies aimed at verifying the relationship existing between these two pathologies. Both are among the most common disease in the general population. Often Diabetes Mellitus and Periodontitis can be present simultaneously in many people and are able to condition each other, as to be called "the diabolic duo" [14]. Periodontal disease has also been considered as one of the multiple complications of Diabetes Mellitus; furthermore, in 1997, the report of the commission of experts for the diagnosis and classification of Diabetes Mellitus defined periodontal disease as a pathology with very high prevalence in diabetic patients [15], in fact, the susceptibility to onset of periodontitis is three times greater in patients with Diabetes Mellitus. This would also seem to be linked to poor metabolic control. A loss of periodontal attachment was found more frequently in those people with poor metabolic control [16]. The scientific evidence of the last 15-20 years supports a significant association between periodontal inflammation and glycemic status. However, it has been suggested that adequate periodontal treatment in diabetic patients may be useful in reducing diabetic complications [12].

Chronic Hyperglycemia, as well as periodontitis, induced the hyperactivation of immune system with consequent hyper-production of pro-inflammatory molecules (TNF-gamma, IL6, IL1). These ones, entering in systemic circle, can negatively affect the organism [2]. Interleukin (IL)1a, Interleukin (IL)1b and gamma tumor-necrosis (TNF-gamma) stimulate bone resorption and inhibit bone formation, thus this relationship must be considered of a two-way nature. A further aspect linked to chronic periodontitis is the alteration of the immune system in terms of the balance between antioxidant agents and reactive oxygen species in favour of the latter.

As "oxidative stress" we can describe a pathological condition of the organism in which there is no balance between the production and elimination of chemical oxidizing species and, in the case of a diabetic patient, it can aggravate the clinical conditions

of the same. On the other hand, diabetes is in turn a cause of oxidative stress and this may justify how periodontitis pictures are particularly aggressive in diabetic patients [13]. This persistence of systemic oxidizing substances result in the activation of different pathways that contribute to the onset of diabetic complications, an example that must be taken in consideration is the activation of protein Kinase C8 and the increase of the formation of AGEs (Advanced Glycation End-products). The latter are products that are formed by an irreversible reaction of non-enzymatic glycosillation of numerous proteins (link between a protein and a sugar, without a catalytic action of an enzyme), which is triggered by prolonged systemic hyperglycemic conditions [17]. Precisely, regarding to the immune system, AGEs can bind macrophages and monocytes leading them to a destructive phenotype, with an increase in sensitivity to stimuli, whose result represented by an excessive cytokine release. This condition is able to contribute to the delay in wound healing that is observed in diabetic patients. With regard to the connective tissues, o the other hand, a hyperglycemic environment causes a reduction in the extracellular matrix synthesis by fibroblasts and osteoblasts and an inhibition of differentiation of the latter; moreover the accumulation of AGEs can alter the functions of the various components of the intercellular matrix, including the collagen of the vascular walls, with important consequences: thickening of the vascular membrane of the capillaries which in turn causes a slowing down of the gaseous exchanges and the elimination of substances of rejection, vasoconstriction and microthrombi.

According to above mentioned, the reduction of bacteria species could be useful to diabetic patients to improve their lifestyle. An innovative method is represented by the Ozone: it is an allotropic form of oxygen and it's used in medicine from a long time. Only recently, however, the ozone entered in the dental field and in the last years a lot of studies have proven the antibacterial action of ozone; in fact, the addition of rinses using water with percentage of 0,1ppm of ozone can be a valid addition to the daily brushing and use interdental aids for the control and removal of the oral bacterial biofilm [18].

The periodontium pathologies have been classified by means of the new classification of periodontitis elaborated in the last Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions [19].

2. MATERIALS AND METHODS

The study included 36 older patients suffering from Type 1 Diabetes Mellitus; they were enrolled in the Department of Clinical Surgical, Diagnostic and Pediatric, and Diabetology of the IRCCS Policlinic San Matteo Foundation following the release of their free consent to participate in the study.

Were not considered patients that:

- Has taken oral or intravenous bisphosphonate therapy in the last 12 months
- Has low participation or insufficient motivation to participate in this study
- Have been irradiated to the head or neck in the last 12 months
- Were in pregnant or lactating status

- Abuses drugs and alcohol
- Has psychiatric problems that contraindicate the intervention

Patients that joined to the study were random allocated in two groups. Patients were, furthermore, invited to read an informative module to interaction of periodontitis and Diabetes Mellitus and complete a questionnaire regarding them home oral hygiene habits. Research has shown that 37,5% of the examined patients brushed their teeth with an average of 1-2 times a day, 50% 2-3 times a day, while 12,5% brushed their teeth more than 3 times a day. 4,2% of patients said that they stopped brushing their teeth after a few seconds, 45,8% said they spend between 1-2 minutes, while 50% took more than 2 minutes. Regarding the type of toothbrush used, it emerged that 41,7% used the manual toothbrush, while 58,3% preferred the electric toothbrush, but none of the patients examined used the sonic toothbrush. Furthermore, 16,7% of patients made a vertical movement with toothbrush, 75% reported performing a mixed movement, nobody uses a horizontal brushing, but 8.3% report not making any movement, since it uses an electric toothbrush (equivalent to 14.3% of patients using an electric toothbrush). Considering the use of interdental tools the 37.5% used interdental subsidies daily, the same percentage of patients use them sporadically, while 25% declared that they do not use them. 29,2% of patients declared brushed daily the tongue, 33,3% declared that brushed that sporadically, but 37,5% said they did not brush the tongue. The 8.3% of patients examined reported noticeable gingival bleeding during brushing, 58.3% reported it sporadically, while 33.3% said they did not suffer from gingival bleeding. The 70.8% of the examined patients had all natural elements in their mouth, 29.2% had one or more prosthetic elements, while no patient has total or partial removable prostheses. The 8.3% said they suffered from halitosis, while the remaining 91.7% said they did not suffer from it. The 66.6% carry out regular visits about once a year, 16.7% once every two or three years and with the same percentage patients declare not to undergo periodic checks. At the end the 50% of patients do not undergo a professional oral hygiene session for more than a year, 8.3% are not recognized by hygiene for about a year, while 41.7% state that they have subjected to a professional oral hygiene session within 6 months.

- Trial Group: following the main therapy involving monthly check to apply ozonated water, a home use of “Biorepair Plus” mouthwash 2 times a day and “Biorepair Plus Parodontgel” toothpaste to replace with the conventional toothpaste, and professional dental hygiene recalls every three months.
- Control Group: following a secondary therapy involving monthly check to apply ozonated water and professional dental hygiene recalls every three months.

Monthly, at the time of the recall, were asked to patients, to bring in vision the lasts Glycated Hemoglobin tests which has been collected and filed in data collection sheets. At the same time has been evaluated the periodontal indexes, such as Periodontal Probing Depth (PPD), Bleeding On Probing (BOP) and Plaque Index (PI). At the end of the operative season, the indexes were grouped and processed.

The study, therefore, was structured as follows:

- **T0**, first operative season; acquisition of: personal data, anamnestic data, intra and extra-oral exams, dental charting, periodontal indexes (PPD, BOP, PI), HbA1c value. Initial motivation, instructions for oral hygiene (tooth brushing maneuvers, interproximal hygiene aids, tongue cleaning), removal of overgrowth hard and soft deposits from both dental arches, by means of professional instrumentation, such as sonic/ultrasonic scaler with traditional tip, scaler, air-polishing (glycine or bicarbonate), final polishing with prophylaxis paste, final irrigation of periodontal pocket by means of ozonated water (Aquolab) [20]. Motivational reinforcement, prescription of home offices ("Biorapair Plus" mouthwash and "Biorepair Plus Parodontgel," only for Trial Group).
- **T1,** first control recall: revaluation of periodontal indexes (PPD, BOP, PI), HbA1c value, irrigation of periodontal pocket by means of ozonated water (Aquolab). Motivational reinforcement, prescription of home offices ("Biorapair Plus" mouthwash and "Biorepair Plus Parodontgel," only for Trial Group).
- **T2**, second control recall: revaluation of periodontal indexes (PPD, BOP, PI), HbA1c value, irrigation of periodontal pocket by means of ozonated water (Aquolab). Motivational reinforcement, prescription of home offices ("Biorapair Plus" mouthwash and "Biorepair Plus Parodontgel," only for Trial Group).
- **T3**, second operative season: revaluation of periodontal indexes (PPD, BOP, PI), HbA1c value, removal of overgrowth hard and soft deposits from both dental arches, by means of professional instrumentation, such as sonic/ultrasonic scaler with traditional tip, scaler, air-polishing (glycine or bicarbonate), final polishing with prophylaxis paste, final irrigation of periodontal pocket by means of ozonated water (Aquolab). Motivational reinforcement, prescription of home offices ("Biorapair Plus" mouthwash and "Biorepair Plus Parodontgel," only for Trial Group).
- **T4,** third control recall: revaluation of periodontal indexes (PPD, BOP, PI), HbA1c value, irrigation of periodontal pocket by means of ozonated water (Aquolab). Motivational reinforcement, prescription of home offices ("Biorapair Plus" mouthwash and "Biorepair Plus Parodontgel," only for Trial Group).
- **T5**, fourth control recall: revaluation of periodontal indexes (PPD, BOP, PI), HbA1c value, irrigation of periodontal pocket by means of ozonated water (Aquolab). Motivational reinforcement, prescription of home offices ("Biorapair Plus" mouthwash and "Biorepair Plus Parodontgel," only for Trial Group).

The monthly application of ozonated water, has been effectuated for a minute and half for each dental arch.

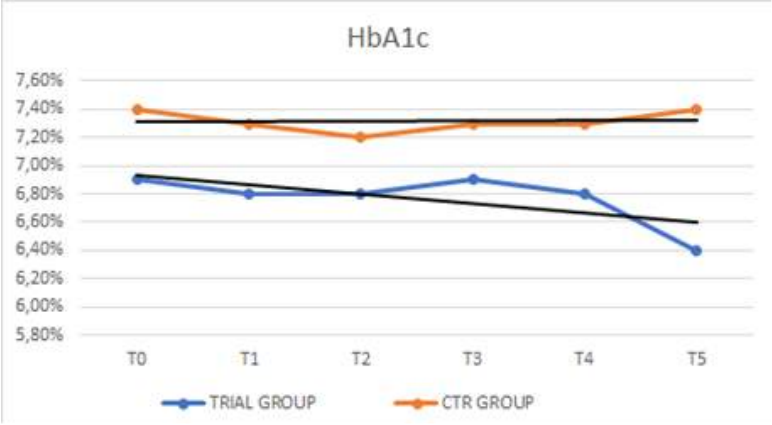
3. RESULTS

At the end of each recall and operative season, indices have been grouped and processed in comparative tables, furthermore, to make the results more understandable, graphs have been developed with respective trend lines.

- Glycated Hemoglobin (HbA1c)

Table 1. Variation of Glycated Hemoglobin values

HbA1c (%)	T0	T1	T2	T3	T4	T5
TRIAL GROUP	(±0,006) 6,90%	(±0,005) 6,80%	(±0,005) 6,80%	(±0,005) 6,90%	(±0,005) 6,80%	(±0,003) 6,40%
CTR GROUP	(±0,009)7,40%	(±0,004)7,30%	(±0,004)7,20%	(±0,001)7,30%	(±0,001)7,30%	7,40%

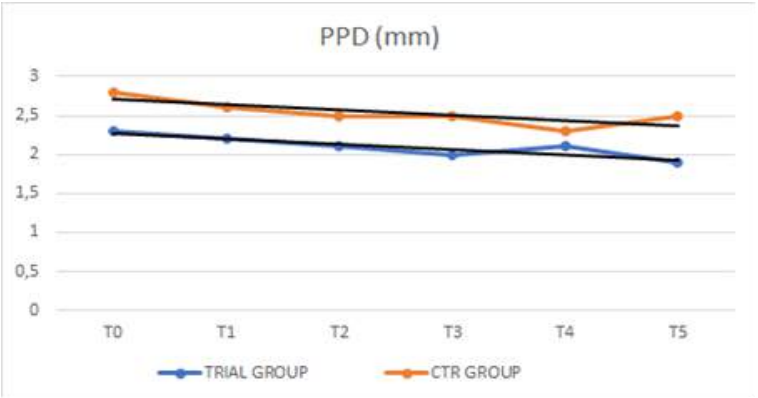


Graph 1. Variation in Glycated Hemoglobin values.

- Periodontal Probing Depth (PPD)

Table 2. Variation of Periodontal Probing Depth values

PERIODONTAL PROBING DEPTH (mm)	T0	T1	T2	T3	T4	T5
TRIAL GROUP	(±0,4) 2,3	(±0,5) 2,2	(±0,3) 2,1	(±0,2) 2	(±0,2) 2,1	(±0,1) 1,9
CTR GROUP	(±0,5) 2,8	(±0,8) 2,6	(±0,7) 2,5	(±0,7) 2,5	(±0,4) 2,3	2,5

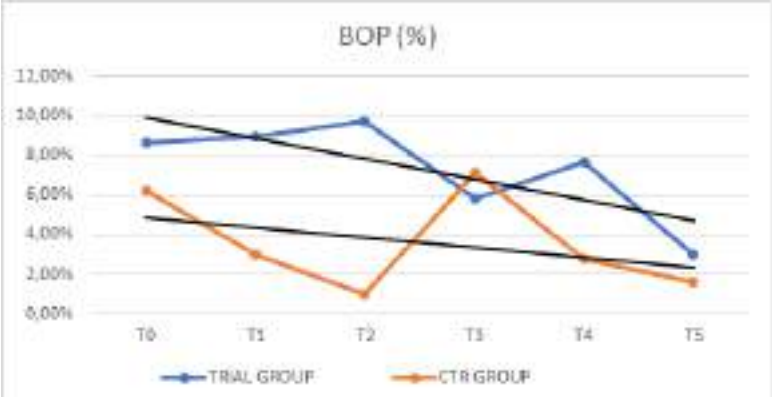


Graph 2. Variation of Periodontal Probing Depth values.

- Bleeding on probing

Table 3. Variation of Bleeding on Probing values

Bleeding On Probing (%)	T0	T1	T2	T3	T4	T5
TRIAL GROUP	(±0,09) 8,70%	(±0,09) 9%	(±0,10) 9,70%	(±0,04) 5,80%	(±0,08) 7,70%	(±0,04) 3%
CTR GROUP	(±0,09) 6,20%	(±0,02) 3%	1%	(±0,08)7,10%	(±0,006)2,80%	1,60%



Graph 3. Variation of Bleeding on Probing values.

- Plaque Index

Table 4. Variation of Plaque Index values

IP (%)	T0	T1	T2	T3	T4	T5
TRIAL GROUP	(±0,3) 64,90%	(±0,3) 49,70%	(±0,2) 49,20%	(±0,1) 44,70%	(±0,2) 43,70%	(±0,07)17,50%
CTR GROUP	(±0,3) 54%	(±0,3)38,80%	(±0,14)31,50%	(±0,14)53,10%	(±0,08)31,60%	39,10%

Graph 4. Variation of Plaque Index values.

DISCUSSIONS

In each group, we can find a reduction of the indexes evaluated more or less evident, precisely:

HbA1c: it's evident an initial and equal decrease of 0,1% in both groups at T1, however, as regards the Trial Group, there is a constant period up to T2, where the average of HbA1c remain unchanged at 6,8%, while it would seem that the Control Group continue to improve, reaching a value of HbA1c equal to 7,2% at T2.

On the fourth recall (T3), both groups showed a slight increase in values (0,1%), which brings the Trial Group back to the starting value of 6,9%, while the Control Group at 7,3%. At T4 a regression of HbA1c value of 0,1% can be seen again in the Trial Group, bringing it back to an average value of 6,8%, while, regarding the Control Group we can see a stalemate period which remain stable with average value of 7,3%.

Only in T5 we can highlight a significant decrease in the values in the Trial Group of around 0,4%, which leads the average value to 6,4%, while the Control Group, not only doesn't remain stable, but rather increase further by 0,1% returning to the average initial value of 7,4%.

PPD: it's immediately evident a decrease in the probing depth in both groups, in fact, in T1 can be seen a decrease of 0,1% in the Trial Group, which results, therefore, in an average probing depth of 2,2 mm. At the same time in Control Group is evident a decrease of 0,2 mm, which leads the average value to 2,6 mm. In T2 there is a fair 0,1% improvement in the average value in both groups. We can note, in fact, an average probing depth of the Trial Group equal to 2,1 mm, while the Control Group shown an average probing depth that drops to 2,5 mm. In T3 it's observable a constant decrease in the probing depth value of the Trial Group of 0,1mm, leading it to an average value of 2 mm, at the same time, the same index remains constant in the Control Group (2,5 mm). In T4 there is a slight increase in the average probing depth value in Trial Group, in fact, it returns to a value of 2,1 mm as in T2, instead, it is possible to se a 0,2 mm reduction of the same value inn the Control Group arriving at 2,3 mm. in T5, however, we can find a significant decrease of 0,2mm in the Trial Group reaching an average value of 1,9mm, while the Control Group re turns to an average value of 2,5 mm, as in T3.

BOP: in both study groups can be seen that the bleeding indexes are below the theoretical value of 10%, indicative of a pathological inflammatory state (gingivitis), during the months of study. In T0 different BOP value are noted, Trial Group is represented by an average value equal to 8,7%, while the other Group it's represented by 6,2% as average value of the same index. At the first monthly recall (T1) there is a slight increase in the bleeding index of 0,3% in the Trial Group, which appears to reach the average value of 9%, unlike, in the Control Group, there is a significant reduction of the same index, which drops at 3%. Paradoxically, in T2 we can see a further increase in BOP in Trial Group reaching a value of 9,7%, while in the Control Group there is a further reduction in the index which reaches the value of 1%. In T3, finally, in Trial Group, it is observable a significant reduction in BOP, which leads the value below 6% (5,8%), unlike, in the Control Group, we note a significant increase, reaching a value equal to 7,1%. In T4 BOP returns to an average value of 7,4% in Trial Group, while in Control Group we can find a further reduction in the index, which is brought back to 2,8%.

At the last recall, it is possible to observe that the BOP index decreases in both groups, reaching a value of 3% in Trial Group and a value of 1,6% in Control Group.

PI: only for this index we can find values far superior to the physiological parameter (20%) for a periodontal health. In T0, in fact, an average plaque index of about 65% can be observed in Trial Group, and in the Control Group the same index reaches the 54%. After one month from the first non-surgical periodontal treatment session, it is observable an important decrease in PI, which lead Trial Group to 49,7% and the Control Group to 38,8%. In following month, we can find a constant phase in both groups almost, in fact, the Trial Group reduces his PI by only 0,5% (a negligible percentage), while Control Group reaches a value of 31,5%. In T3 there is a slight reduction in the average of PI in the Trial Group which drops to 44,7%, in contrast, in Control Group we can find a significant increase which leads the PI average back to 53,1%, a value comparable with the starting value of the same group. In following recall, a slight decrease in PI can be seen in Trial Group, which reaches 43,3%, while in Control Group it is observable a significant decrease that leads the same index to 31,6%. Only in T5, however, we can see a drastic decrease in PI in Trial Group which reach 17,5%, thus falling within the physiological range, while Control Group shown a slight increase again (39,1%).

Although plaque index is the last parameter that has been considered, it is the index that has a fundamental role for reduction of all other periodontal indexes. After the procedures of professional oral hygiene and those education and motivation for oral home-hygiene, positive feedback has been obtained from patients who, reducing oral bacterial biofilm, made possible reaching periodontal tissues healing. In this way the average value of glycated hemoglobin, periodontal probing depth and bleeding on probing were reduced.

The results of the present report are in agreement with the existing literature.

The oral hygiene control is crucial aspect in oral health, as it prevents from caries and periodontal disease. This importance is greater diabetic patients that presents higher periodontal disease risk. Previous reports showed that the use of chlorhexidine mouthwashes has a significant effect in the reduction of periodontal parameters [21]. However chlorhexidine cannot be applied continuously, but needs a cyclic use. During treatment suspension, a relapse of the parameters has been demonstrated [22]. Therefore the use of chlorhexidine-free agents has been tested showing promising results [23, 24]. Similar results have been reported in this study. The present report tested a new experimental mixture of ialuronic acid, biomimetic nano hydroxyapatite, E vitamin, lactoferrin and tyndallized probiotics. The main difference between the presented protocol and previous chlorhexidine-free agents is the presence of biomimetic nano hydroxyapatite that is particularly active with erosive and decalcified lesions [25].

The use of the proposed mouthwash and dentifrice, matched with ozonized water as non surgical periodontal therapy, has been demonstrated to be efficient in maintenance of the Glycated Hemoglobin values under acceptable limits. Therefore, the present protocol could be suggested in Type 1 diabetes patients. However, the importance of dietary habits is crucial for complete periodontal prevention. The acidic environment (inducted by acidic drinks and foods) is strictly correlated with dentin [26] and enamel damage [27]. Additionally, degradation of restorative [28] and prosthodontic [29] materials has been reported. These factors should be carefully considered for prevention promotion, by stressing more the importance of dietary education for a complete patient care.

CONCLUSION

According to the descriptive analysis performed it is now possible to draw the final evaluations regarding the study conducted.

In both groups, the secondary objective of study was reached, in fact, we have seen an improvement in the periodontal indexes, particularly:

- PPD: a 0,4mm decrease in periodontal probing depth was found in Trial Group, against 0,3mm in Control Group between T0 and T5.
- BOP: there was a decrease in that values, from T0 to T5 equal to 34,5% within the Trial Group, against 25,8% of the entire Control Group.
- PI: there was a reduction in Plaque Index of 47,4%, from T0 to T5, within the Trial Group, against a decrease of 14,9% in the Control Group.

It is evident that regarding to the Plaque Index there is an important difference between the two study groups which, as explained above, has allowed the reduction of the periodontal inflammatory state and therefore led to an improvement in the indexes. Although improvements were found also in Control Group it is fair to consider that only in Trial Group, subjected to non-surgical periodontal treatment every three months, monthly application of ozonated water and home use of “Biorepair Plus” mouthwash and “Biorepair Plus Parodontgel” toothpaste, it was possible to reachthe primary objective of study, finding a decrease, equal to 0,5%, in the average values of Glycated Hemoglobin in Type 1 diabetic patients.

Using frequent calls for oral hygiene combined with the professional use of ozonated water (by means of Aquolab) and home use of “Biorepair Plus” mouthwash and “Biorepair Plus Parodontgel” toothpaste seems, therefore, to have a positive impact on the decrease in the value of Glycated Hemoglobin in diabetic patients, thus improving the health status of the patients themselves and their lifestyle.

ETHICAL COMPLIANCE

The authors have stated all possible conflicts of interest within this work. The authors have stated all sources of funding for this work. If this work involved human participants, informed consent was received from each individual. If this work involved human participants, it was conducted in accordance with the 1964 Declaration of Helsinki. If this work involved experiments with humans or animals, it was conducted in accordance with the related institutions’ research ethics guidelines.

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PREPARATION AND CHARACTERIZATION OF NANO-ZINC PHOSPHATE CEMENT

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ABSTRACT

Purpose: The aim of the current study was to measure the pH changes, the final setting time and the cytotoxicity in experimentally prepared nano-zinc phosphate cement as compared to conventional zinc phosphate cement when used in a base consistency.

Methods: Nano-zinc phosphate powder was prepared by the sol-gel chemistry according to the results obtained from the X-ray fluorescence chemical analysis for the conventional zinc phosphate powder. Optimum P/L ratio of the nano-zinc phosphate cement was determined according to a pilot study. The pH changes were measured at different time periods by the pH meter. The Final setting time was measured according to ISO 9917-1 specifications. The Cytotoxicity effect was evaluated against epithelial cell line MA-104 according to ANSI/ADA no. 41. Data were statistically analyzed by Kolmogorov-Smirnov, Shapiro-Wilk, Mann-Whitney, Independent sample t, Repeated measure ANOVA and Paired sample t tests. The significance level was set at $P \leq 0.05$.

Results: The pH values of the nano-zinc phosphate cement were significantly higher than those of the conventional zinc phosphate cement at all tested time periods. Additionally, the nano-zinc phosphate cement revealed a faster rise in the pH values until the neutrality level was reached. The final setting time of the nano-zinc phosphate cement was significantly lower than that of the conventional zinc phosphate cement but still within the practical limits stated by the ISO 9917-1 specifications. The cytotoxicity results of both cements were non-significantly different and ranged from mild to moderate cell response.

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