NON-SURGICAL TREATMENT OF PERIODONTAL INTRABONY DEFECTS WITH ADJUNCTIVE CROSS-LINKED HYALURONIC ACID. A SINGLE-BLINDED RANDOMIZED CONTROLLED CLINICAL TRIAL.

Blasi A[1], Iorio-Siciliano V[1], Mauriello L[1], Salvi GE[2], Ramaglia L[1], Sculean A[2].

[1]*Department of Periodontology, School of Dental Medicine, University of Naples Federico II, Italy.*

[2] *Department of Periodontology, School of Dental Medicine, University of Bern, Switzerland*

SIdP – Premio H.M. Goldman – lavoro vincitore ex aqueo sessione CLINICA

ABSTRACT

Aim: to compare the 6-months outcomes of intrabony defects treated with minimally invasive non-surgical technique (MINST) alone or with adjunctive delivery of cross-linked hyaluronic acid (xHyA) gel.

Materials and methods: Forty-two patients with 42 interdental intrabony defects were randomly assigned to test (MINST+xHyA) or control procedures (MINST). At baseline, 3 and 6 months, probing depth (PD), clinical attachment level (CAL), gingival recession (GR) and sites with bleeding on probing (BOP) were assessed. At baseline and 6 months, full mouth plaque score (FMPS) full mouth bleeding score (FMBS), radiographic defect depth (RDD) and radiographic defect angle (RDA) were recorded. The primary outcome was PD change.

Results: Thirty-eight patients completed the trial. At 6 months a significant improvement (p<0.05) of all clinical parameters was noted with exception of GR (p>0.05). Significant differences between test and control sites were observed at 3 months (p<0.05) but not at 6 months (p>0.05). After 6 months a significant RDD reduction was noted in both groups. The RDD change was significant between test and control groups at 6 months (p<0.05) while RDA did not change significantly (p>0.05).

Conclusions: Within limitations of this study, the adjunctive use of xHyA gel failed to yield better results than MINST alone.

Obiettivo: Valutare la guarigione di difetti infraossei trattati mediante tecnica non chirurgica minimamente invasiva (MINST) con o senza l'aggiunta di acido ialuronico reticolato (xHyA).

Materiali e metodi: Quarantadue pazienti con 42 difetti infraossei interdentali sono stati assegnati random ai gruppi test (MINST+xHyA) o controllo (MINST). PD (variabile principale), CAL, GR e siti con BOP sono stati valutati al baseline, 3 e 6 mesi. Il FMPS, il FMBS, la profondità (RDD) e l'angolo radiografico del difetto (RDA) sono stati registrati al baseline e dopo 6 mesi.

Risultati: Trentotto pazienti hanno completato lo studio. Dopo 6 mesi, è stato registrato un miglioramento significativo (p<0,05) dei parametri clinici, fatta eccezione per GR (p>0.05). Dopo 3 mesi, la differenza tra i due gruppi è stata significativa (p<0.05), tuttavia nessuna differenza è stata riportata a 6 mesi di follow-up (p>0.05). Tra il baseline e 6 mesi si è assistito ad un miglioramento significativo della variabile RDD (p<0.05) per entrambe le procedure. A 6 mesi la comparazione tra i gruppi ha dato una differenza statisticamente significativa (p<0.05) per RDD e non per RDA (p>0.05).

Conclusioni: Nonostante i limiti dello studio, l'associazione di MINST e xHyA non ha determinato risultati superiori rispetto alla sola procedura MINST.

INTRODUCTION

Periodontitis is a chronic multifactorial inflammatory disease caused by supra- and sub-gingival biofilm and characterized by progressive loss of the tooth-supporting structures (Belibasakis,2023).

Subgingival biofilm removal using different instruments represents a crucial step in periodontal treatment and often re-establishes periodontal health avoiding periodontal surgery (Lang,2019) independently of the protocols applied or the instruments used. Data from systematic review (Suvan, 2020) reported a proportion of closed pockets (i.e. PD ≤ 4mm) of 74% at 6 months. Nevertheless, in deep periodontal pockets associated with intrabony defects mechanical removal of subgingival biofilm is frequently incomplete (Rabbani,1981). The residual pockets associated to intrabony defects represent a risk factor for disease progression and require additional surgical therapy (Matuliene,2008, Papapanou,1991). However, in the last years several authors proposed treatment of intrabony defects by means of a minimally invasive non-surgical technique (MINST) based on the use of mini and micro instruments in combination with magnification loops (Barbato, 2020). The MINST approach potentially reduces the postoperative trauma, gingival recessions and preserves the aesthetic (Riberio, 2023), and it determines a considerable clinical and radiographic improvement for the treatment of intrabony defects (Nibali,2015, Nibali,2018). In addition, similar PD reduction and CAL gain were noted when MINST was compared to minimally invasive surgical approach without regenerative procedures in the treatment of intra-osseous defects (Riberio,2011, Nibali,2019). Data for a systematic review reported additional benefits of local application of hyaluronic acid (HA) on the clinical outcomes following non-surgical periodontal therapy (Eliezer,2019).

Recently, a formulation of cross-linked hyaluronic acid gel of non-animal origin with high molecular weight (xHyA) was proposed to improve the wound healing and to regenerate the periodontal tissues (Mendes,2008).

Hence, the aim of present study was to evaluate clinical and radiographic outcomes at 6 months following treatment of intrabony defects using MINST with or without adjunctive delivery of cross-linked hyaluronic acid gel (xHyA).

The null hypothesis of no statistically significant differences with respect to PD change was tested.

MATERIAL AND METHODS

Study design

The study was designed as a superiority, parallel arm, single-blinded, randomized controlled trial (RCT) with a 6-month follow-up. In each patient, one intrabony defect was selected for the investigation. The intrabony defects were randomly assigned at test or control procedure. Defects of test group were treated by means of MINST and adjunct of xHyA gel, while in control group MINST alone was performed. The study was conducted at the Department of Periodontology, University of Naples Federico II from October 2021 to March 2023. The Research Protocol was submitted to and approved by the Institutional Review Board (IRB) of the University of Naples Federico II, Italy (Approval Number: 141/21) and the study protocol was registered at ClinicalTrial.gov (N°NCT05188898). Furthermore, written

consent was obtained from all patients before the investigation. The study was reported according to CONSORT Statement, and it was conducted in observance to the Principles of the Declaration oh Helsinki on experimentation involving human subjects.

Patients' sample

From the patient pool of the Department of Periodontology, University of Naples Federico II, patients diagnosed with periodontitis according to Tonetti et al. 2018 were invited to participate in the study.

After initial screening, an accurate periodontal exam confirming the diagnosis of periodontitis was made. Patients who met the eligibility criteria were enrolled in the study.

Inclusion criteria

- Males and females aged ≥18 years.
- Patients with diagnosis of periodontitis (Stage III or IV).
- Single-rooted and multi-rooted teeth in both arches.
- Presence of interdental periodontal defects with PD ≥ 5 mm associated to an intra-bony component ≥ 2 mm at single-rooted teeth or to an intra-bony component ≥ 2 mm at molars with ≤ class I furcation involvement.

Exclusion criteria

- Patients with systemic diseases
- Pregnant or lactating females
- Tobacco smokers (≥ 10 cigarettes per day).
- Third molars.
- Teeth with grade III mobility.
- Peri-apical pathology and acute abscess
- Non-surgical or surgical periodontal treatment in the past 12 months
- Prolonged antibiotic treatment or anti-inflammatory treatment within 6 months prior to periodontal therapy.
- Patients without adequate level of oral hygiene (FMPS ≥ 20%) following step 1 of periodontal therapy or at follow-up visits (FMPS ≥ 20%).

The initial periodontal screening occurred from October 2021 to December 2021, while the trial was conducted from January 2022 till March 2023.

Clinical and radiographic outcome measures

Primary outcome

The primary outcome was the change in probing depth (PD) measured from the gingival margin to the bottom of the pocket.

Secondary outcomes

The following secondary clinical and radiographic outcomes were assessed:

-Full mouth plaque score (FMPS) (O'Leary,1972).

-Full mouth bleeding score (FMBS) (Claffey,1990).

-Clinical attachment level (CAL) measured from the CEJ to the bottom of the pocket.

-Gingival recession (GR) measured from the CEJ to the gingival margin.

-Radiographic Defect Depth (RDD) measured from the alveolar bone crest to the most apical extension of the bone defect.

-Radiographic Defect Angle (RDA) defined as angle between the line connecting the CEJ of the tooth presenting the intrabony defect to the most apical point of the defect and the line connecting the most apical point of the defect and the point where the bone crest touched the neighboring tooth (Steffensen,1989).

All clinical variables were recorded using a manual periodontal probe (PCP-UNC 15®, Hu-Friedy, Chicago, IL, USA), applying a probing force of 0.2 N. The radiographic examination was performed at baseline and at the 6-month follow-up, using a parallel-cone technique with a Rinn holder. The radiographic measurements were performed using a computer software (VistaSoft© 2.4.3. Durr Dental Italia S.R.L). Additionally, information on gender, age and smoking habits was also collected. All data were collected in the Department of Periodontology, University of Naples Federico II, Naples, Italy.

Sample size calculation

The sample size calculation was performed using a computer software (IBM-SPSS, IBM Inc). Based on data presented in a previous study (Rajan,2014), to detect a statistically significant difference of 1.12 mm with a power of 0.80 for the primary outcome (i.e. PD change at 6 months) between test and control procedures, a sample size of 11 patients with 1 intrabony defect was required in each group.

Investigators' calibration

All parameters were recorded by two expert periodontists (B.A. and M.L.).

Examiners attended a training and calibration session on a total of 40 patients (20 patients for examiner) not involved in the trial.

Furthermore, calibration on radiographic measurements was also performed on 20 x-rays of patients not enrolled in the study.

A contingency coefficient was used to test the agreement between examiners. A value of 0.954 was observed for clinical variables, while a value of 0.814 was found for the radiographic parameters.

Randomization and blinding

The patients were randomly assigned to test or control procedures by means of a simple randomization without restrictions and using 1:1 allocation ratio. Minimization and stratification were not done. Randomization was made using a computerized random number generator. The allocation concealment was performed associating even numbers to the test group and odd numbers to the control group. The cards with numbers were closed in opaque envelopes and treatment allocation was performed after subgingival instrumentation of the intrabony defect selected for the study by opening the envelope containing the number. The random allocation sequence was generated by a clinician not involved in the investigation. The examiners of outcome measures were masked with respect to test and control procedures, while the periodontist performing the treatments and

patients were not masked. Clinical and radiographic parameters were recorded at baseline by A.B and at follow-up examinations by L.M.

Intervention

Pre-treatment

Prior to the pre-treatment phase, the FMPS and FMBS were assessed. On the first step of periodontal therapy (Sanz,2020), all participants received full-mouth supragingival scaling in combination with oral hygiene instructions and motivation. After 4 weeks the clinical parameters of the intrabony defects selected for the trial were assessed (i.e., PD, CAL, GR, and BOP).

Treatment

All patients received step 2 of periodontal therapy based on a quadrant-wise approach. Teeth with degree 2 mobility were splinted before the subgingival instrumentation. All periodontal pockets of each quadrant were treated by means of subgingival instrumentation using an ultrasonic scaler under local anesthesia and only the periodontal pocket associated with intrabony defect selected for the investigation was treated by means of experimental procedure. MINST was applied by means of subgingival application of thin ultrasonic tips (Instrument PS® EMS Electro Medical System S.A., Nyon, Switzerland). Additional subgingival instrumentation using Gracey mini-curettes (Hu-Friedy®, Chicago, IL, USA) was also performed to achieve biofilm removal in aeras with difficult access. Subgingival rinses were not used. All therapies were performed using 4.0 x magnification loupes (Univet®, Italy). After completion of MINST the defects were randomly assigned to test or control groups. In the patients of the test group, at the end of subgingival instrumentation, the pockets associated with intrabony defects were filled using xHyA gel (Hyadent BG®, Regedent AG, Zürich, Switzerland). The defects of control group received only MINST approach. No antiseptic mouthwashes and no antibiotics were prescribed in both groups. All clinical procedures were performed by the same expert operator (V.I.S.).

Post-operative follow-up

All patients were recalled at 1-, 3- and 6-months following treatment for professional supragingival tooth cleaning and motivation.

Statistical analysis

All data were collected and analyzed at Department of Periodontology, University of Naples Federico II. Statistical analysis of data, with patient as statistical unit, was performed using a statistical software package (IBM-SPSS, IBM Inc), by a statistician that was not masked to research protocol.

The variables PD, CAL, GR, and Crest-BD were expressed in millimeters, the FMPS and FMBS were expressed in percentages, while the radiographic angles were reported in degrees. Means and standard deviations (SD) were calculated for each parameter. The assumption of normal distribution was evaluated for all parameters by means of Shapiro-Wilk test and parametric or not parametric tests were used accordingly. A Chi-Square test was used to compare gender and smoking habits between test and control procedures, while age and teeth location (i.e. mandible/maxillae) were evaluated using Mann-Whitney U

test. The inter-group and intra-group analysis of FMPS and FMBS was made using an unpaired and a paired t-test, respectively. An intra-group analysis for the variables PD, CAL, GR, BOP, C-BD, and defect angle was performed using the Wilcoxon test, while the inter-group evaluation was made by means of Mann-Whitney U test. Intra-group analysis of differences in number and percentages of sites with PD $\leq$ 4 mm was tested using lambda test, while the inter-group evaluation was evaluated by means of McNemar's test. To compare the frequency distribution of sites with residual PD and CAL gain between test and control procedures the lambda test was used. A *p*-value <0.05 was set to accept a statistical significance.

RESULTS

Patient accountability

A total of 70 patients were invited to participate in the study. After initial screening 20 patients not meeting the inclusion criteria were excluded, while 8 patients declined to participate to the study. Finally, a total of 42 patients with 42 intrabony defects were included in the present investigation. At 6 months 38 patients with 38 intrabony defects were available for the analysis. Four patients were lost to follow-up: in control group 2 patients were excluded during the follow-up due to poor level of oral hygiene, while in test group 2 patients declined to continue at 1 and 2 months, respectively. During the follow-up, no adverse events were recorded, and no teeth were lost.

Patient characteristics

The characteristics of the sample enrolled in the trial are described in Table 1. Fourteen females and 5 males (mean age 49.3±11.6 years) and 10 females and 9 males (mean age 50.8±10.8 years) with a diagnosis of generalized Stage III, Grade C periodontitis were allocated in test and control group, respectively. Nine patients were tobacco smokers (4 patients in test group and 5 in control group). Five intrabony defects in the mandible and 14 in the maxilla received the experimental procedure, while 8 intrabony defects in the mandible and 11 in the maxilla were treated by means of control procedure alone. No statistically significant differences were found between test and control group (p>0.05) (Table 1).

Full mouth plaque score (FMPS) and full mouth bleeding score (FMBS)

All patients showed a statistically significant improvement of FMPS and FMBS after 6 months (p<0.05). At 6 months, FMPS and FMBS decreased from 58.6±6.0% and 53.4±6.6% to 18.7±2.2% and 14.3±3.6% in patients of test group, while in the control group the FMPS and FMBS changed from 59.5±6.5% to 18.9±1.8% and from 55.8±6.6% to 14.7±2.5%. The intergroup comparison did not show statistically significant differences (p>0.05) (Table 2).

Changes in Probing depth (PD)

The primary outcome PD decreased statistically significantly at 3 and 6 months in each group (p<0.05). At baseline, the intrabony defects treated with experimental procedures showed a PD was 6.7±1.4 mm, while in the control group the PD was 6.8±0.8 mm. At 3 months, the PD was 3.3±1.0 mm and 5.2±0.7 mm in test and control group, respectively, while after 6 months PD of 4±0.8 mm and 4.2±0.8 mm was recorded for test and control procedures, respectively. No statistically significant differences between test and control

group were recorded at baseline and after 6 months (p>0.05), however a statistically significant difference was noted at 3 months (p<0.05) (Table 3).

Changes in clinical attachment level (CAL)

Statistically significant changes were noted between baseline, 3 and 6 months in both groups (p<0.05). In test group, CAL changed from 8.4±2.8 mm to 4.9±2.0 mm and to 5.5±1.9mm between baseline, 3 and 6 months, while the defects of control group showed a CAL change from 8.2±1.7 mm to 6.8±1.9 mm and to 6±2.4 mm. The intergroup comparison showed no statistically significant difference at baseline and after 6 months (p>0.05), however a statistically significant difference was noted at 3 months (p<0.05). No statistically significant differences (p>0.05) were noted between test and control procedures at baseline and at follow-up periods (Table 3).

Changes in gingival recession (GR)

At baseline, patients treated with test procedure reported a GR of 1.6±1.7 mm, while patients of control group showed a GR 1.4±1.5 mm. At 3 months follow-up the GR was 1.6±1.6 mm and 1.6±1.9 mm in test and control group, respectively. After 6 months a GR of 1.5±1.7 mm and 1.8±2.2 mm was assessed in each group (Table 3).

Number and percentage of sites with BOP-positive

The number and percentage of sites with BOP-positive at baseline,3-and 6-months follow-up are summarized in table 4. At baseline, BOP-positive sites were assessed at 12 defects (63.1%) of test group and at 11 defects (57.9%) of control group. After 3 months, the number and percentage of sites with BOP-positive was 2 (10.5%) and 5 (26.3%) in test and control group, respectively. At 6 months, 2 (10%) sites in test group and 5 (21%) in control group were BOP-positive. A statistically significant improvement was observed when the number and percentage of sites with BOP-positive were compared at baseline and after 3 months (p<0.05). Comparable results were observed evaluating the presence of sites with BOP-positive between baseline and 6 months (p<0.05). No statistically significant changes were recorded between 3 and 6 months (p>0.05) (Table 4).

Number and percentage of defect sites with “pocket closure”.

The number and percentage of sites displayed a PD $\leq$ 4 mm without BOP are illustrated in table 5. After 3 months, the number of sites with pocket closure was 16 (84.2%) and 2 (10.5%) in test and control group, while after 6 months in 15 (78.9%) test sites and 12 (63.1%) control sites with PD $\leq$ 4 mm was achieved. Statistically significant differences were observed between test and control group at 3 months (p<0.05), while at 6 months no statistically significant differences were recorded (p>0.05). The intragroup analysis demonstrated no statistically significant changes between 3 and 6 months in test group (p>0.05), while a statistically significant difference was observed in control group (p<0.05) (Table 5).

Frequency distribution of sites with residual PDs and CAL changes

Table 6 summarizes the frequency distribution of residual PDs with or without BOP-positive and CAL changes after 3 and 6 months. A statistically significant improvement in residual

PDs and CAL changes were obtained after 3 months when xHyA gel was used (p<0.05), while no statistically significant changes were noted at 6 months (p>0.05) (Table 6).

Radiographic outcomes

A statistically significant difference was noted between baseline and 6 months for both procedures when RDD values were compared (p<0.05). RDD was 2.7±0.8 mm and 1.2±1.1 mm in test group, while a mean of 2.8±0.8 mm and 1.9±1.1 mm was assessed in control group. After 6 months, a statistically significant difference was found comparing RDD values of intrabony defects treated with MINST and xHyA gel compared with MINST alone (p<0.05). At baseline, a RDA of 36±14.8 degrees and 44.7±12.9 degrees were assessed in test and control patients, respectively. At 6 months in test group RDA was 51.7±24.0 degrees and 48.4±19.8 degrees in the control group. The intragroup comparison showed a statistically significant difference (p<0.05) in the test group and no statistically significant difference in control group (p>0.05). At 6 months the intergroup analysis did not report statistically significant differences (p>0.05).

No statistically significant differences (p>0.05) were found when intergroup analysis was made. However, the intragroup comparison demonstrated a statistically significant change for patients of control group (p<0.05) (Table 7).

CONCLUSION

In conclusion, within the limitations of the present study, the results indicated an improvement in clinical and radiographic parameters of periodontal pockets associated with intrabony defects following MINST irrespective of adjunctive delivery of xHyA after 6 months. However, sites treated by means of MINST and application of xHyA showed better results compared with MINST alone after 3 months.

TAB.1 PATIENTS' CHARACTERISTICS

	Test group (N=19)	**Control group (N=19)**	***p*-value**
Gender (f/m)	14/5	10/9	0.179 (NS)
Mean Age (years)	49.3±11.6	50.8±10.8	0.452 (NS)
Smoking Habit (y/n)	4/15	5/14	0.703 (NS)
Infrabony defect's location (mdb/max)	5/14	8/11	0.418 (NS)

f=female, m=male; y= yes, n=no; mdb=mandible, max=maxilla

TAB.2 FMPS and FMBS at baseline and after 6-months follow-up

		Test group (N=19)	Control group (N=19)	*p*-value
FMPS (%)				
Baseline		58.6±6.0	59.5±6.5	0.625 (NS)
6 months		18.7±2.2	18.9±1.8	0.686 (NS)
	***p*-value**	<0.001 (S)	<0.001 (S)	
FMBS (%)				
Baseline		53.4±6.6	55.8±6.6	0.237 (NS)
6 months		14.3±3.6	14.7±2.5	0.642 (NS)
	***p*-value**	<0.001 (S)	<0.001 (S)	

FMPS= full mouth plaque score, FMBS=full mouth bleeding score

TAB.3 CHANGES IN PD, CAL, AND GR AT BASELINE, 3- AND 6-MONTHS FOLLOW-UP

Parameters	**Baseline**	**3 months**	**6 months**	**Δ BL-3m**	**Δ 3m-6m**	**Δ BL-6m**	***p*-value BL-3m**	***p*-value 3m-6m**	***p*-value BL-6m**
PD (mm)									
Test Group (N=19)	6.7±1.4	3.3±1.0	4±0.8	3.4±1.4	0.7±1.0	2.7±1.5	< 0.001 (S)	0.011 (S)	< 0.001 (S)
Control Group (N=19)	6.8±0.8	5.2±0.7	4.2±0.8	1.6±0.6	0.9±0.8	2.6±1.1	< 0.001 (S)	0.002 (S)	< 0.001 (S)
***p*-value**	0.258 (NS)	< 0.001 (S)	0.435 (NS)						
CAL (mm)									
Test Group (N=19)	8.4±2.8	4.9±2.0	5.5±1.9	3.4±1.8	0.6±0.9	2.8±2.1	< 0.001 (S)	0.017 (S)	< 0.001 (S)
Control Group (N=19)	8.2±1.7	6.8±1.9	6±2.4	1.3±0.9	0.5±1.1	1.9±1.6	< 0.001 (S)	0.034 (S)	< 0.001 (S)
***p*-value**	0.729(NS)	0.015 (S)	0.563 (NS)						
GR (mm)									
Test Group (N=19)	1.6±1.7	1.6±1.6	1.5±1.7	0.05±1.0	0.05±0.6	0.1±1.0	0.665 (NS)	0.705 (NS)	0.516 (NS)
Control Group (N=19)	1.4±1.5	1.6±1.9	1.8±2.2	0.3±0.6	0.4±0.7	07±1.1	0.238 (NS)	0.339 (NS)	0.119 (NS)
***p*-value**	0.795 (NS)	0.954 (NS)	0.795 (NS)						

PD= probing depth, CAL=clinical attachment level, GR= gingival recession
Δ BL-3m= difference baseline-3months, Δ 3m-6m= difference 3 months-6 months, Δ BL-6m= difference baseline-6 months

TAB.4 NUMBER AND PERCENTAGE OF SITES WITH BOP-POSITIVE AT BASELINE,3-AND 6-MONTHS FOLLOW-UP

Parameters	**Baseline**	**3 months**	**6 months**	***p*-value BL-3m**	***p*-value 3m-6m**	***p*-value BL-6m**
BOP-POSITIVE (N/%)						
Test Group (N=19)	12/63.1	2/10.5	2/10	0.002 (S)	0.999 (NS)	0.012 (S)
Control Group (N=19)	11/57.9	5/26.3	4/2	0.031 (S)	0.999 (NS)	0.016 (S)
***p*-value**	0.795 (NS)	0.418 (NS)	0.795 (NS)			

BOP= Bleeding on probing; BL= baseline

TAB.5 NUMBER AND PERCENTAGE OF SITE WITH PD ≤ 4mm (POCKET CLOSED) AT BASELINE AND AFTER 3 AND 6 MONTHS.

	Test group (N=19)	**Control group (N=19)**	***p*-value**
N/% of sites with PD ≤ 4mm			
3-months	16/84.2	2/10.5	< 0.001 (S)
6-months	15/78.9	12/63.1	0.360 (NS)
***p*-value**	0.999 (NS)	0.004 (S)	
N/% of sites with PD ≥ 5 mm			
3-months	3/15.8	17/89.5	< 0.001 (S)
6-months	4/21.05	7/36.8	0.360 (NS)
***p*-value**	0.999 (NS)	0.004 (S)	

PD=probing depth

TAB.6 FREQUENCY DISTRIBUTION (N/%) OF RESIDUAL PD AND CAL GAIN AT 3 AND 6-MONTHS

			Test group (N=19)					Control group (N=19)				*p*-value
			0-4mm	5mm	≥6mm			0-4mm	5mm	≥6mm		
Residual PD												
3-month												
With BOP-negative			15/78.9	2/10.5	0			2/10.5	9/47.4	3/15.8		< 0.001 (S)
With BOP-positive			1/5.3	1/5.3	0			0	4/ 21.1	1/5.3		
6-month												
With BOP-negative			13/68.4	2/10.5	1/5.3			10/52.6	4/ 21.1	1/5.3		0.311 (NS)
With BOP-positive			2/10.5	1/5.3	0			2/10.5	2/10.5	0		
CAL gain												
	0 to 1mm	**2mm**	**3mm**	**4mm**	**≥5mm**	**0 to 1mm**	**2mm**	**3mm**	**4mm**	**≥5mm**		
3-month	2/10.5%	1/5.3%	9/47.4%	4/21.1%	3/15.8%	8/42,1%	10/52.6%	0	1/5.3%	0		< 0.001 (S)
6-month	3/15.8%	2/26.3%	6/31.6%	3/15.8%	2/10.5%	6/31.6%	5/26.3%	4/21.1	2/10.5%	2/10.5%		0.442 (NS)

PD= probing depth, CAL=clinical attachment level

TAB.7 RADIOGRAPHIC DEFECT CHANGES AT BASELINE AND AFTER 6-MONTHS FOLLOW-UP

	TEST GROUP (N=19)	**CONTROL GROUP (N=19)**	**Δ**	***p*-value**
RDD (mm)				
Baseline	2.7±0.8	2.8±0.8	0.1±1.3	0.402 (NS)
6-months	1.2±1.1	1.9±1.1	0.7±1.4	0.040 (S)
Δ BL-6m	1.5±0.2	0.8±1.4		
***p*-value**	< 0.001 (S)	0.006 (S)		
RDA (degree)				
Baseline	36±14.8	44.7±12.9	8.7±19.2	0.610 (NS)
6-months	51.7±24.0	48.4±19.8	3.2±31.8	0.653 (NS)
Δ BL-6m	15.6±23.3	3.74±12.5		
***p*-value**	0.011 (S)	0.492 (NS)		

RDD= Radiographic defect depth measured from the alveolar bone crest to the most apical extension of the bone defect.

RDA= Radiographic defect angle defined as angle between the line connecting the CEJ of the tooth presenting the intrabony defect to the most apical point of the defect and the line connecting the most apical point of the defect and the point where the bone crest touched the neighboring tooth.

REFERENCES

1. Barbato, L., Selvaggi, F., Kalemaj, Z.,Buti, J.,Bendinelli, E., La Marca, M., Cairo, F.(2020). Clinical efficacy of minimally invasive surgery (MIS) and non-surgical (MINST) treatments of periodontal intrabony defects. A systematic review and network meta-analysis of RCT's. Clinical Oral Investigations, 24,1125-1135. doi: 10.1007/s00784-020-03229-0.

2. Belibasakis, G., N., Belstrom, D.,Eick, S., Gursoy, U.,K.,Johansson, A.,Kononen, E.(2023). Periodontal microbiology and microbial etiology of periodontal disease: Historical concepts and contemporary perspectives. Periodontoloy 2000,10.1111/prd.12473.

3. Claffey, N., Nylund, K., Kiger, R.,Garrett, S.,Egelberg, J.(1990). Diagnostic predictability of scores of plaque,bleeding,suppuration and probing depth for probing attachment loss.3 ½ years of observation following initial periodontal therapy. Journal of Clinical Periodontology,17,108-114. doi: 10.1111/j.1600-051x.1990.tb01071.x.

4. Eliezer, M., Imber, J.C., Sculean, A., Pandis, N.,Teich, S.(2019). Hyaluronic acid as adjunctive to non-surgical periodontal therapy: a systematic review and meta-analysis. Clinical Oral Investigations,23,3423-3435.doi:10.1007/s00784-01903012-w.

5. Lang, N.P., Salvi, G.E., Sculean, A.(2019). Nonsurgical therapy for teeth and implants-When and why? Periodontology 2000, 79,15-21. https://doi.org/10.1111./prd.12240.

6. Matuliene, G., Pjetursson, B.E.,Salvi, G.E.,Schmidlin, K.,Bragger, U.,Zwahlen, M.,Lang, N.P.(2008). Influence of residual pockets on progression of periodontitis and tooth loss: results after 11 years of maintenance. Journal of Clinical Periodontology, 35,685-695. doi: 10.1111/j.1600-051x.2008.01245.x.

7. Mendes, R.M.,Silva, G.A.,Lima, M.F.,Calliari, M.V.,Almeida, A.P.,Alves, J.B.,Ferreira, A.J.(2008). Sodium hyaluronate accelerates the healing process in tooth sockets of rats. Archives of Oral Biology,53,1155.1162.doi:10.1016/j.archorabio.2008.07.001.

8. Nibali, L.,Pometti, D., Chen, T.T.,Tu, Y.K.(2015). Minimally invasive non-surgical approach for the treatment of periodontal intrabony defects:a retrospective analysis. Journal of Clinical Periodontology,42,853-859. doi: 10.1111/jcpe.12443.

9. Nibali, L., Yeh, Y.C.,Pometti, D.,Tu, Y.K.(2018). Long term stability of intrabony defects treated with minimally invasive non-surgical therapy. Journal of Clinical Periodontology,45,1458-1464. doi:10.1111/jcpe.13021.

10. Nibali, L., Koidou, V.,Salomone, S.,Hamborg, T.,Allaker, R.,Ezra, R.,Zou, L.,Tsakos, G., Gkranias, N., Donos, N.(2019). Minimally invasive non-surgical vs surgical approach for periodontal intrabony defects:a ranodomised controlled trial. Trials.20,461. doi:10.1186/s13063-019-3544-8.

11. O'Leary, T.J.,Drake, R.B., Naylor, J.E. (1972). The plaque control record. Journal of Periodontology, 43, 38. doi:10.1902/1972.43.1.38.23.

12. Papapanou, P.N., Wennstrom, J.L. (1991). The angular bony defect as indicator of further alveolar bone loss. Journal of Clinical Periodontology,18,317-322.doi:10.1111/j.1600-051x.1991.tb00435.x

13. Rabbani, G.M.,Ash, M.M. Jr., Caffesse, R.G.(1981). The effectiveness of subgingival scaling and root planning in calculus removal. Journal of Periodontology, 52,110-123. doi:10.1902/jop.1981.52.3.119.

14. Rajan, P.,Baramappa, R.,Rao, N.M.,Pavalurim A.K., Indeevar, P.,Rahaman, S.M.U.(2014). Hyaluronic acid as an adjunct to scaling and root planing in chronic periodontitis. A randomized clinical trial. Journal of Clinical and Diagnostic Research,8,ZC11-ZC14. doi: 10.7860/JCDR/2014/8848.5237.

15. Riberio, F.V.,Casarin, R.C.V.,Palma, M.A.G.Junior., F.H.N.,Sallum, E.A.,Casati, M.Z.(2011). Clinical and patient-centered outcomes after minimally invasive non-surgical or surgical approaches for the treatment of intrabony defects: a randomized clinical trial. Journal of Periodontology,82,1256-1266.

16. Riberio, F.V., Mehta, J.J., Monteiro, M.F.,Moore, J.,Casati, M.Z., Nibali, L.(2023). Minimally invasiviness in nonsurgical periodontal therapy. Periodontology 2000 ,91,7-19. doi:10.1111/prd.12476.

17. Sanz, M.,Herrera, D.,Kebschull, M.,Chapple, I.,Jepsen, S.,Berglundh, T., Sculean, T., Tonettim M.S.(2020). On behalf of the EFP Workshop Participants and Methodological Consultants. Treatment of stage I-III periodontitis-The EFP S3 level clinical practice guideline. Journal of Clinical Periodontology,47,4-60. doi: 10.1111/jcpe.13290.

18. Steffensen, B., Webert, H.P. (1989). Relationship between the radiographic periodontal defect angle and healing after treatment. Journal of Periodontology, 60,248-254.doi:10.1902/jop.1989.60.5.248.

19. Suvan, J., Leira, Y.,Sancho, F.M.M.,Graziani, F.,Derks, J.,Tomasi, C.(2020). Subgingival instrumentation fro treatment of periodontitis. A systematic review. Journal of Clinical Periodontology,47,155-175. doi:10.1111/jcpe.13215.

20. Tonetti,M.S.,Greenwell,H.,Kornmann,K.S. (2018). Staging and grading of periodontitis:framework and proposal of a new classification and case definition. Journal of Clinical Periodontology,45,(Suppl 20),S149-S161. doi: 10.1111/jcpe.12945.