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Effect of Diode Laser Treatment and Nano-Desensitizing Agent on Degree of Tubular Occlusion "In Vitro Study"

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ABSTRACT

Background: Dentin Hypersensitivity is a common dental problem affecting a huge section of every population that doesn't have a permanent treatment yet. ***Aim:*** The purpose of this study is to compare the effect of Diode laser (940nm) and Nano-desensitizing agent on the degree of tubular occlusion compared to the conventional fluoride varnish for the treatment of dentin hypersensitivity. ***Materials and methods:*** Twenty dentin specimens were prepared from extracted human premolars. Dentin specimens will be randomly allocated in 4 groups (n=5) according to desensitizing agent used: D_1 (Diode Laser (940nm), D_2 (Nano-hydroxyapatite), D_3 (Diode Laser + Nano-hydroxyapatite) and D_4 (Fluoride). The specimens will be treated with EDTA for 2 mins to open dentinal tubules simulating Dentin Hypersensitivity. Each specimen will be evaluated at 3 different times: T_0 (before material application), T_1 (after material application) and T_2 (after acid attack) using Environmental Scanning Electron Microscope and Image Analysis software to detect degree of occlusion of dentinal tubules. ***Results:*** Group D_3 showed statistically significant tubular occlusion percentage compared to the other groups except group D_1. After acid attack group D_3 were the only group that showed non-statistically significant decrease in tubular occlusion percentage denoting the best resistance to acid attack, while other groups were drastically affected by the acid attack. ***Conclusion:*** Combining DL (940nm) and Nano-hydroxyapatite could be a successful treatment option for Dentin Hypersensitivity, due to its high degree of tubular occlusion effect and sustainability in the acidic environment.

***Keywords*:** Dentin Hypersensitivity, Tooth Sensitivity, Diode Lasers.

INTRODUCTION

Dentin, cervical or root hypersensitivity are all synonyms for the same condition. It occurs when there is an exaggerated response to non-noxious stimuli to the teeth. It is defined as "short sharp pain arising from exposed dentin in

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response to stimuli typically thermal, evaporative, tactile, osmotic or chemical and which cannot be related to any other form of dental defect or pathology."[1,2] It affects the cervical area of facial surfaces of teeth and it is commonly seen in premolars and canines.[3] Dentin Hypersensitivity (DH) is caused by loss of enamel directly or by gingival recession. Loss of enamel occurs through attrition, abrasion, erosion or even abfraction. In both situations dentinal tubules exposure is a must for occurrence of DH. Hydrodynamic theory suggested by Brannestorm in 1964 is claimed to be the most reasonable till now and it is based on the idea of fluid movement that occurs inside opened dentinal tubules as a response to different stimuli leading to activation and stimulation of a-delta fibers inducing pain.[2]

Fluorides were one of the first materials used to treat DH e.g. Stannous Fluoride and Sodium Fluoride (NaF). The mode of action of NaF is through the deposition of a protective layer of Calcium Fluoride. This protective layer acts as a barrier that blocks opened dentinal tubules and reduce hypersensitivity.[4,5,6] However, NaF provide temporary pain relief because it is affected by the acidic oral environment and it's easily removed by washing the tooth surface or by brushing.[4] Hence, longevity of NaF is questionable.[6] Recently Lasers are becoming of great use in dentistry. A crucial role of Lasers whether high or low power Lasers is their effect on DH. High power Lasers causes melting effect occluding the dentinal tubules due to the rise in temperature. However, high power Lasers must be used with caution because the rise in temperature may cause irreversible pulpal damage. With Low power Lasers no rise in temperature occurs and there is no risk of necrosis. Low power Lasers act by changing the neural transmission by controlling the amount of ATP generated thus decreasing pain response. Also, few alterations in dentinal tubules might occur. It was reported by a clinical trial conducted by Suri I et al.[7] 2016 that combining Lasers and desensitizing agents e.g. 5 % sodium fluoride varnish give more satisfactory results than any of the proposed treatments alone.[7-13] Many studies showed promising results when combining Lasers with other agents such as Fluoride. They claim it improves the tubular occlusion ability and enhance durability.[14,15]

In contemporary dentistry nanotechnology is of a vital importance. One of the main uses of nanotechnology (science of dwarf particles) is the fabrication of nanoparticles whether organic or inorganic to deal with dentin hypersensitivity.[16-24]

Hydroxyapatite (HAP) is the major constituent of human teeth and bone.

Inorganic Nano-modified materials such as Nano-hydroxyapatite (Nhap) crystal are effective in enamel remineralization through modifying the enamel surfaces and occluding dentinal tubules. This dentinal tubules occluding function makes Nhap crystals a potential candidate for use in treatment of DH. Also, Nhap crystals are claimed to decrease DH by penetrating inside dentinal tubules and sealing them in an easy and quick way due to their extremely small size.[16-24]

Some studies claims that Nhap has an effective remineralizing and desensitizing capacity that surpass the other commonly used desensitizing agents, while other studies shows that Nhap effectiveness is similar to other desensitizing agents.[25] Many studies showed promising results when combining Lasers with other agents such as Fluoride. They claim it improves the tubular occlusion ability and enhance durability.[14,15]

The aim of this study will compare the ability of Diode Laser 940nm (DL 940nm), and Nhap (alone or combined) to the conventional Fluoride treatment on reducing DH by measuring degree of dentinal tubules occlusion. Also, sustainability of the different treatment approaches will be tested by subjecting the materials to acid attack. Hence, determining the ability of the different treatment approaches to endure the acidic oral conditions.

MATERIALS AND METHODS

Materials

Materials used in the study are shown in Table (1).

Methodology

Specimen's preparation:

A total of 20 extracted human premolars were collected. Facial or lingual enamel was removed to expose superficial dentin using an isometric saw (Isomet4000) to ensure equal amount of enamel is removed for dentin discs preparation, Figures (1a and 1b). Two consecutive cuts were cut through the tooth in a mesio-distal direction with 1mm thickness between each other to produce a dentin disc of 1mm thickness, Figure (1c). Dimensions were ensured using a millimeter caliber, Figure (1d and 1e).

Grouping of samples:

Dentin specimens were randomly allocated in 4 groups (n=5) according to desensitizing agent used: D_1 (Diode Laser (940nm), D_2 (Nano-hydroxyapatite), D_3 (Diode Laser + Nano-hydroxyapatite) and D_4 (Fluoride).

All samples were placed in ultra-sonicator containing distilled water for removal of debris for 10 mins.[26] Each group was marked by painting the pulpal surface of

Table (1): Materials used in the study each.

Material	Trade name	Composition	Manufacturer	Batch number
Nano-hydroxyapatite (Nhap) (prepared)	NT-HA-NP	5ml Hydroxyapatite Nanoparticles in hydrogel (Carboxymethyl Cellulose)	Nano-Tech Egypt for Photo-Electronics	------------
Fluoride varnish	Biflourid 10 (Single Dose)	Ethyl acetate, Sodium Fluoride, Calcium Fluoride, Cellulose Ester and Eugenol	VOCO GmbH	1830324
EDTA gel 19%	MD-ChelCream EDTA cream	Ethylene diamine Tetra acetic Acid and Polyethylene glycol	META BIOMED	MCH1901041
Artificial saliva (prepared)	Artificial saliva	$CaCl_2$ (0.7m/M/L), $MgCl_2.6H_2O$ (0.2mM/L), KH_2PO_4 (4mM/L), KCl (30mM/L), NaN3 (0.3mM/L) and HEPES buffer (20mM/L). PH 7.4	Faculty of Pharmacy Cairo University	------------
Citric acid (prepared)	Citric acid	6% Citric acid (60 g of citric acid dissolved in 1000ml of distilled water)	Faculty of Pharmacy Cairo University	------------

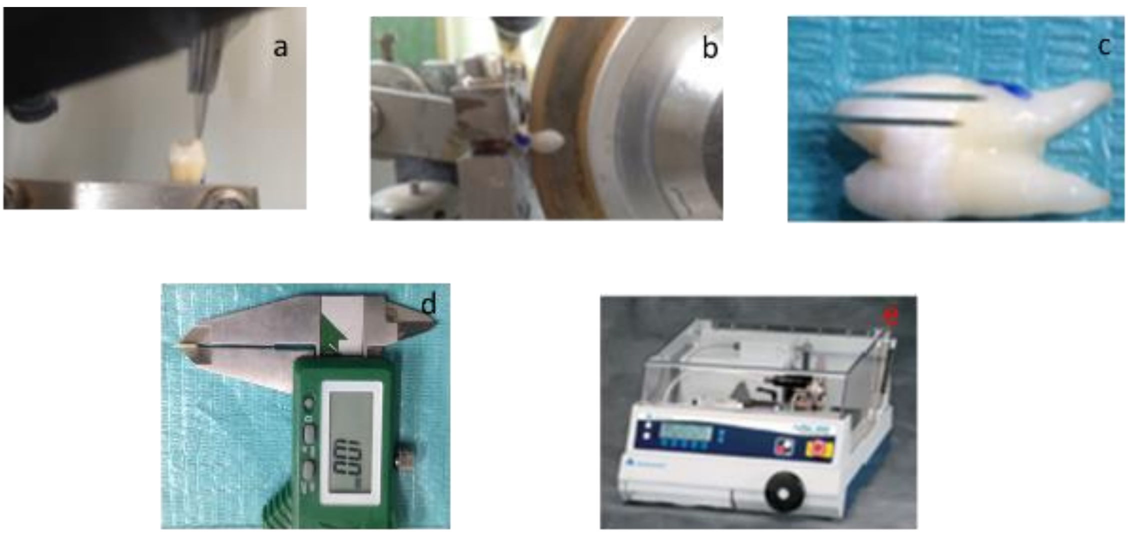

Figure (1): Specimen preparation. a) Teeth positioning, b) Sectioning of the specimens, c) Two consecutive longitudinal cuts, d) Resulted 1mm dentin discs measured by millimeter caliber, e) Isomet4000.

disc with a different color nail polish. Also, they were stored in artificial saliva at room temperature until use. The artificial saliva was changed every 24hours.[26]

Simulation of hypersensitive dentin:

The specimens were treated with EDTA for 2 mins to open dentinal tubules simulating Dentin Hypersensitivity.

Application of desensitizing treatments:

Each desensitizing treatment was applied according to manufacturer instructions.

DL (940nm) treatment (D_1):

DL (940nm) handle was hanged (for standardization of the distance from the dentin samples), on clamp and stand so that the tip was fixed at 5mm away from sample. The Distance was checked using Endodontics ruler. DL (940nm) was applied for 30 sec, power 1.5 W (50%duty cycle) repeated 3 times (total 90 sec) using E3 tip. During DL (940nm) application dentin disc samples were held using a tweezer at the required distance on the bench and moved in small circles as recommended by the manufacturer simulating clinical application. (According to direct contact with Biolase Company). Figures (2a, 2b and 2c)

Nhap desensitizing agent application (D_2):

One ml Nhap gel was applied using a graduated plastic syringe for 3 mins while rubbing using a micro-brush then removed gently using slightly moist cotton for each sample. According to manufacturer's instructions.

DL (940nm) and Nhap treatment combined (D_3):

One ml Nhap gel was applied using a graduated plastic syringe for 3 mins while rubbing using a micro-brush followed by DL (940nm) irradiation for 30 sec, power 1.5 W (50%duty cycle) repeated 3 times (total 90 sec) for each sample. The same methodology for Diode Laser application was used as mentioned previously in D_1 group.

Fluoride varnish application (D_4):

According to manufacturer's instructions Fluoride varnish single dose (Biflorid 10) was applied using micro-brush while rubbing, then it was left for 20 secs to be absorbed then air sprayed to dry for one min.

Acidic challenge:

Six percent citric acid was added to the surface using a micro-brush for 1 min while rubbing followed by washing with distilled water and storage in artificial saliva till evaluation time after 12 hours.[26]

Testing of the sample (Scanning using ESEM):

In each of the testing periods, samples were left for 15 mins in the air to dry before evaluation. All of the samples were evaluated using ESEM at 3000 X

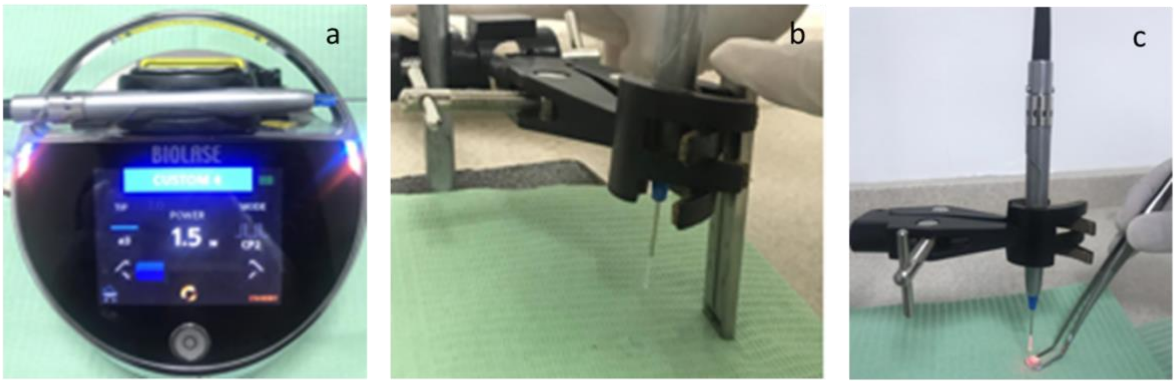

Figure (2): DL (940nm) treatment. a) DL (940nm) (EPIC X) by Biolase company, **b)** DL (940nm) handle hanged on clamp and stand and tip position calibrated using endodontic ruler, **c)** DL (940nm) application.

magnification for observation of degree tubular occlusion.[26,27]

All of the specimens were examined using ESEM at 3 different times, before application of the desensitizing agent (T_0 baseline), after application of the desensitizing treatment (T_1) and after acidic attack (T_2).

Image analysis:

The scanned images were evaluated using image analysis software SPSS Statistics 25 and image j53a to evaluate and calculate degree of dentinal tubules occlusion which is analyzed automatically using the software. The tubules occlusion was calculated as a percentage from the base line tubules. Figure (3)

Tubular occlusion percentage = T_0 – T_1/T_2 X 100

RESULTS

Statistical analysis:

Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). Dentinal tubules occlusion % data showed normal (parametric) distribution while opened dentinal tubules % data showed non-normal (non-parametric) distribution. Data were presented as mean and standard deviation (SD) values.

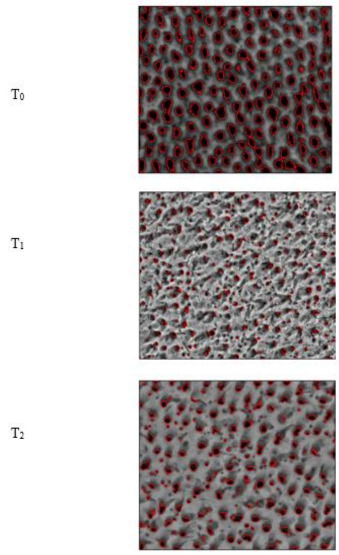

Figure (3): Representative sample of Image analysis (T_0, T_1, T_2).

For parametric data; repeated measures Analysis of Variance (ANOVA) was used to study the effect of desensitizing agent, time and their interaction on mean dentinal tubules occlusion %. Bonferroni's post-hoc test was used for pair-wise comparisons when ANOVA test is significant. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

ESEM photomicrographs showing representative samples of each test group in each testing period T0, T1 and T2 at 3000x magnification are represented in Figure (4).

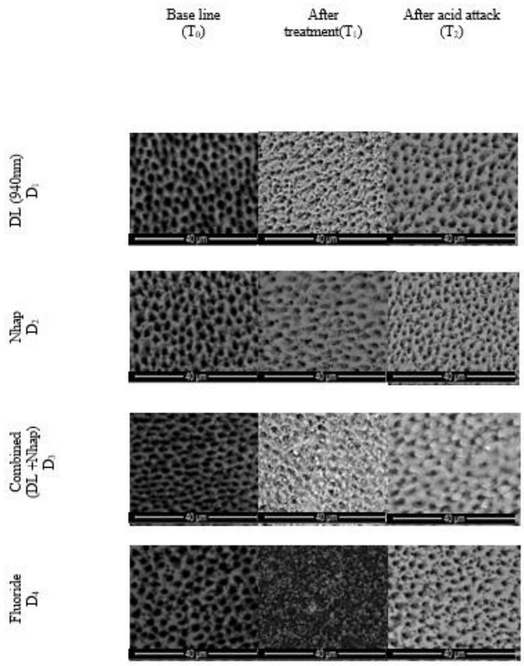

Figure (4): ESEM photomicrographs showing representative samples of each test group in each testing period at 3000x magnification.

Results Tables (2 to 4) and figures (5 to 7) represents the statistical analysis and test of significance of the dentinal tubules occlusion represented in percentage occlusion.

Effect of different interactions on dentinal tubules occlusion %

a) Comparison between desensitizing treatments:

After application (T1); there was a statistically significant difference between mean dentinal tubules occlusion % with different desensitizing agents (P-value <0.001, Effect size = 0.380).

Pair-wise comparisons between desensitizing agents revealed that DL (940nm) + Nhap showed the highest mean occlusion % with non-statistically significant difference from DL (940nm) but a statistically significantly higher values compared with Nhap and Fluoride. There was no statistically significant difference between DL (940nm), Nhap and Fluoride; all showed lower mean values, Table (2), Figure (5).

After acid attack (T2); there was a statistically significant difference between mean dentinal tubules occlusion % with different desensitizing agents (P-value <0.001, Effect size = 0.827).

Pair-wise comparisons between desensitizing agents revealed that DL (940nm) + Nhap showed the statistically significantly highest mean occlusion %. There was no statistically significant difference between DL (940nm), Nhap and Fluoride; all showed statistically

Table (2): The mean, standard deviation (SD) values and results of repeated measures ANOVA test for comparison between dentinal tubules occlusion % values with different interactions of variables .

Time	DL		Nhap		DL+ Nhap		Fluoride		P-value	Effect size (Partial eta squared)
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
After application	81.3^{AB}	12.3	75.5^{B}	9.9	88.5^{A}	3.8	71.1^{B}	9.3	<0.001*	0.380
After acid attack	49^{B}	10.2	50.3^{B}	10.3	83.5^{A}	3.9	48.2^{B}	2.3	<0.001*	0.827
P-value	<0.001*		<0.001*		0.375		0.001*			
Effect size (Partial eta squared)	0.686		0.569		0.049		0.524			

*: Significant at P ≤ 0.05, Different superscripts in the same row indicate statistically significant differences between desensitizing agents

Table (3). The mean, standard deviation (SD) values and results of repeated measures ANOVA test for comparison between dentinal tubules occlusion % with different desensitizing agents regardless of time.

DL		Nhap		DL + Nhap		Fluoride		P-value	Effect size (Partial eta squared)
Mean	SD	Mean	SD	Mean	SD	Mean	SD		
65.2^{B}	20.1	62.9^{B}	16.3	86^{A}	4.5	59.6^{B}	13.7	<0.001*	0.792

*: Significant at P ≤ 0.05, Different superscripts are statistically significantly different

Table (4). The mean, standard deviation (SD) values and results of repeated measures ANOVA test for comparison between dentinal tubules occlusion % at different times regardless of desensitizing agent.

After application		After acid attack		P-value	Effect size (Partial eta squared)
Mean	SD	Mean	SD		
79.1	10.9	57.8	16.8	<0.001*	0.792

*: Significant at P ≤ 0.05

significantly lower mean values, Table (2), Figure (5).

b) Comparison between times:

With DL (940nm), Nhap as well as Fluoride; there was a statistically significant decrease in mean dentinal tubules occlusion

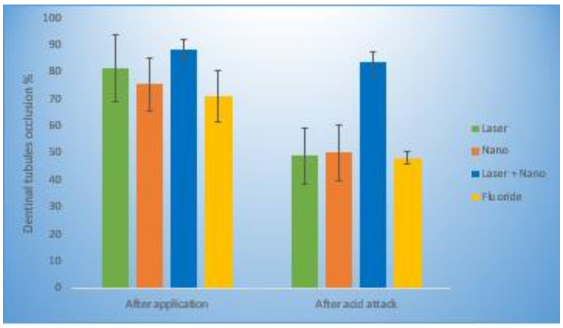

Figure (5): Bar chart representing mean and standard deviation values for dentinal tubules occlusion % of different interactions of variables.

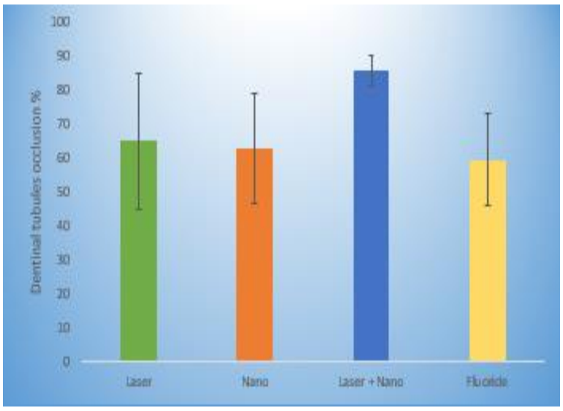

Figure (6): Bar chart representing mean and standard deviation values for dentinal tubules occlusion % with different desensitizing agents regardless of time.

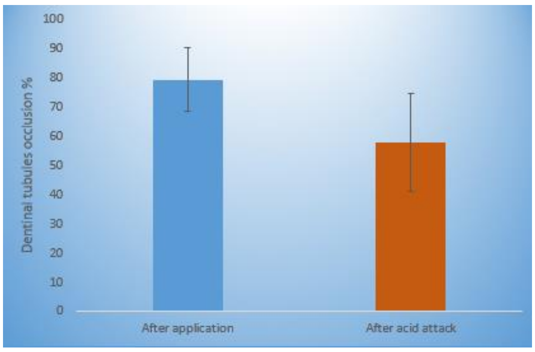

Figure (7): Bar chart representing mean and standard deviation values for dentinal tubules occlusion % at different times regardless of desensitizing agent.

% after acid attack (P-value <0.001, Effect size = 0.686), (P-value <0.001, Effect size = 0.569) and (P-value = 0.001, Effect size = 0.524), respectively, Table (2), Figure (5).

With DL (940nm) + Nhap; there was no statistically significant change in mean dentinal tubules occlusion % after acid attack (P-value = 0.375, Effect size = 0.049), Table (2), Figure (5).

Effect of desensitizing agent regardless of time

Regardless of time; there was a statistically significant difference between mean dentinal tubules occlusion % with different desensitizing agents (P-value <0.001, Effect size = 0.792).

Pair-wise comparisons between desensitizing agents revealed that DL (940nm) + Nhap showed the statistically significantly highest mean occlusion %. There was no statistically significant difference between DL (940nm), Nhap and Fluoride; all showed statistically significantly lower mean values, Table (3), Figure (6).

Effect of time regardless of desensitizing agent

Regardless of desensitizing agent; there was a statistically significant decrease in mean dentinal tubules occlusion % after acid attack (P-value <0.001, Effect size = 0.792), Table (4), Figure (7).

DISCUSSION

Till now there is no gold standard treatment for DH and no consensus on the use of specific combinations for treating that condition.[4,28] The current study investigated the effect of the recently advocated desensitizing approaches of DL (940nm) and Nhap desensitizing agent on the degree of tubular occlusion alone and combined. Also, detected the effect of acidic challenge to determine whether the desensitizing treatments will withstand the acidic oral environment or not. Thus, detecting their sustainability.

ESEM and image analysis were used for the qualitative and quantitative evaluation of degree of tubular occlusion before and after material application and after acidic challenge. ESEM was used because of its non-invasive approach (no need for staining) that ensures non altered samples also, because of its high resolution capacity. Thus it allows accurate tracing of the tubular changes throughout the study. Image analysis software was used to detect the exact width and number of dentinal tubules and percentage of tubular occlusion.

Effect of different desensitizing treatments on the tubular occlusion percentage:

The results of this study showed there was a statistically significant difference between mean dentinal tubules occlusion percentage with different desensitizing agents. Table (2). Regarding the effect of treatment on initial tubular occlusion, DL (940nm) combined with Nhap revealed the best followed by DL (940nm) alone, however, the difference between the two groups was not statistically significant. This shows that DL (940nm) and Nhap combination could be a winning strategy for management of DH. This result is in agreement with Al Maliky et al. (2014)[29] and Patil and Gaikwad (2020)[30] who found that combing Laser and Nhap gave the best occlusion percentage.[29,30] This effect was explained to be due to the melting effect of Lasers which leads to the bonding of Nhap to dentinal walls not just on the surface but up to 10-15mm penetration inside dentinal tubules.[30] The effect of combining DL with other materials such as Fluoride showed enhanced tubular occlusion percentage in in-vitro studies compared to the use of these materials alone.[15,31] This effect was explained to be due to the formation of crystal globules on the dentin surface when DL is combined with Fluoride. However, the other groups showed grainy amorphous appearance that is easily affected by the acid attack.[31] Also, many clinical studies proved the positive effect of combining Lasers to other materials on DH.[14,32] Femiano et al. (2013)[32] discovered that combining DL and Fluoride gave the best results. This was explained to be due to the effect of DL that allows deeper penetration of NaF. Also, the DL protein melting effect causes longer maintenance of the formed layer giving better results and longer term pain relief.[32]

In the current study, all groups showed tubular occlusion effect. However, there was no statistically significant difference between DL (940nm), Nhap and Fluoride groups as shown in Table (2) and Figure (8). This finding was in agreement with Jayram et al. (2020)[31] who found that there is no statistically significant difference between DL (940nm) group and Fluoride group.[31]

In the current study it was revealed that Nhap was not statistically different from DL (940nm) neither Fluoride. This result could be hypothesized to be due to the different modes of application of each material. Where the specimens were tested immediately after application of Nhap (for standardization) which did not allow enough crystal growth for effective dentinal tubules occlusion.

Effect of acid attack on the degree of tubular occlusion:

Regarding the effect of acid attack on the degree of tubular occlusion, it was shown that only the group that combined DL (940nm) and Nhap showed no statistically significant decrease in tubular occlusion denoting, its resistance the acid attack. However, all the other tested treatments showed drastic decrease in the degree of tubular occlusion. This result suggests that combing DL (940nm) and Nhap could be a sustainable treatment option for DH. This result is in agreement with Uslu and Donmez (2020)[28] who found that Laser application combined with other desensitizing agents such as Teethmate and Nhap gave the highest degree of tubular occlusion before and after acid attack. The better performance of combination groups was explained to be due to the melting effect of Lasers on dentin that allow better penetration of the materials. Hence, better tubular occlusion and better resistance to the acid attack.[28] Also, Uslu and Donmez (2020)[28] found that Nhap was drastically affected by the erosive cycle especially when used without Laser. They observed that Nhap cause narrowing the dentinal tubules due to its small size. However, it doesn't sustain the acid attack leaving the dentinal tubules opened again after erosive cycle exposure. Thus, advising the avoidance of acidic beverages in case of the use of Nhap treatment.[28] Also. Jayram et al. (2020)[31] mentioned that combining Lasers and Fluoride gels enhance the resistance to the acidic challenges.[31]

Moreover, Cunha et al. (2017)[26] reported that the use of Laser combinations with other desensitizing agents performs better in opposing the re-opening of the dentinal tubules in case of the exposure to acidic attack. This effect was attributed to be due to the structural changes that Laser causes in dentin which allow the fusion of the material within the dentinal tubules. But, when the desensitizing agents where used alone the pastes only created a layer that was easily removed when subjected to any stimulus such as acid.[26] Also, El Kassas (2016)[33] found that Nhap desensitizing agents were affected by the acidic challenges and that it needs time to give its best performance concerning tubular occlusion, revealing its decreased sustainability.[33]

Femiano et al. (2013)[32] conducted an RCT proving that combination treatment of DL (808nm) and NaF proved successful in DH pain management immediately, after one month and after 6 months. The effectiveness of the combination was explained by the action of the DL(808nm) that allow better penetration of NaF inside dentinal tubules which allows precipitation of Calcium Fluoride deeply inside dentinal tubules. This effect combined with the melting effect and protein coagulation of DL (808nm) leading to better tubular occlusion and long term sustainability (up to 6 months). Comparing the effect of NaF alone to combination treatment, NaF alone only causes precipitation of Calcium Fluoride mechanically without adhesion leading to its rapid loss in the saliva. Hence, its short term effectiveness.[32]

Considering the effect of acid attack on the DL (940nm) group, it could be hypothesized to be due to that the melting and coagulation effect only caused partial tubular occlusion that was not enough to sustain the acidic attack. This shows that DL (940nm) is more effective in the management of DH when used in combination with Nhap. However, if DL (940nm) is used alone, it will provide only short term relief of DH symptoms because of its liability to be affected by the acids in the oral environment.

According to the results of this study, the null hypothesis in which there is no difference between DL (940nm), Nhap desensitizing agent and Fluoride on the degree of tubular occlusion was partially rejected, since there was a statistically significant difference between mean dentinal tubules occlusion percentage with different desensitizing agents. The effect of combination treatment (DL940nm+Nhap) showed statistically significant tubular occlusion percentage than other groups of treatment before and after acid attack. Also, there was no significant difference between other groups before and after acid attack, all revealed almost the same effect.

CONCLUSIONS

Under the circumstances of the current study, the following conclusions could be derived:

1. Combining DL (940nm) and Nhap could be a successful treatment option for Dentin Hypersensitivity, due to its high degree of tubular occlusion effect.

2. All treatment modalities gave a considerable degree of tubular occlusion which varies according to its mode of action.

3. Combination protocol (DL940nm+Nhap) proved to be the most sustainable treatment for Dentin Hypersensitivity, due to its resistance to the acid attack. Hence, could be used as long term treatment for DH.

4. The other treatment modalities such as DL (940nm), Nhap and Fluoride could be considered as short term treatment modalities since they were affected drastically by the acidic attack.

CLINICAL RECOMMENDATIONS

1. It is recommended to use the combination of DL (940nm) + Nhap mode of treatment for the long term management of DH, especially in people with bad oral hygiene who have more acidic oral environment since they are less liable to be affected by acid attack.

2. Other treatment modalities such as DL (940nm), Nhap and Flouride could be considered as a short term mode of treatment for DH and if they are used for a long term, repeated application and follow up is advised.

3. Consumption of highly acidic food such as citrus fruits and acidic beverages, should be avoided during the course of treatment of DH, since all types of treatment modalities are affected to some degree by the acidic oral environment.

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