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EFFECT OF DIFFERENT OVER-THE-COUNTER TOOTHPASTES ON ENAMEL REMINERALIZATION: A DOUBLE BLINDED RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Objective: The aim of the study was to compare between over-the-counter toothpastes (Novamin & Floride) and (Sodium Floride) in remineralization of enamel.

Materials and methods: Fifty-five patients were randomly divided into two groups (n=28 per group) according to the type of toothpaste. Scoring was done by taking photographs at the beginning of the study and at each follow-up visit. Data was statistically analyzed, and the significance level was set at P-value <0.05.

Results: Within Group (A), most patients with Decalcification Index (DI) score of {0} and 55.56% with score of {1} showed high brushing frequency. All patients with (ICDAS) score {0} and 70 % with (ICDAS) score of {1} had high brushing frequency. Within Group (B), most patients with (DI) score of {0} showed high brushing frequency, and all patients with (ICDAS) score of {0} had high brushing frequency. A statistically significant negative correlation was detected between (ICDAS) score of group (A) and brushing frequency. and logistic regression analysis revealed a significant result. A non-significant negative correlation was detected between (ICDAS) score of group (B) and brushing frequency, also between (DI) score of group (A) and brushing frequency, and finally between (DI) score of group (B) and brushing frequency.

Conclusions: No difference in remineralization of White spot lesions (WSLs) for both toothpastes, and that high brushing frequency (2 times/ day) was important to achieve promising and effective remineralization for WSLs.

KEYWORDS: Dental caries, Enamel demineralization, Remineralization, White spot lesions, Bioactive glass, Novamin toothpaste.

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INTRODUCTION

Dental caries remains a significant global health concern across both industrialised and developing societies. It is a multifactorial, contagious bacterial infection resulting from the interaction of cariogenic bacteria, fermentable carbohydrates, a susceptible tooth, the host, and time **(Kazeminia et al., 2020; Abbass et al., 2019; Nyvad and Takahashi, 2020; Ribeiro and Paster, 2023).** Caries progresses through a dynamic cycle of demineralisation and remineralisation, rather than a one-way breakdown of tooth minerals. Remineralisation naturally restores ionic minerals to the hydroxyapatite (HAP) lattice in enamel when conditions, such as near-neutral pH, allow calcium and phosphate ions from saliva and plaque fluid to be redeposited, forming larger, more acid-resistant HAP crystals **(Noaman et al., 2020; Alsamolly, 2021).**

White spot lesions (WSLs) are early indicators of enamel demineralisation, appearing as milky white opacities due to changes in tooth optics. These lesions are initially reversible; however, if left unmanaged, increased porosity leads to irreversible cavitation **(Khijmatgar et al., 2020; Sadıkoğlu, 2020).** The primary goal in caries control is to enhance natural remineralisation and prevent lesion progression. A variety of therapeutic agents have been developed and studied for their remineralising effects, many showing predictable clinical success **(Arifa, 2019; Abosamra et al., 2022).**

Fluoride remains the cornerstone of remineralisation therapy, especially for non-cavitated lesions. High-concentration fluoride formulations such as varnishes, gels, and mouthwashes are widely used to prevent lesion progression and promote remineralisation **(González-Cabezas and Fernández, 2018; Ratnakar, 2020).** Public health fluoridation efforts have contributed significantly to declining caries rates worldwide. However, despite its strong evidence base, fluoride's effectiveness appears to be plateauing at the population level. Moreover, individual variability in response to fluoride has prompted research into alternative or adjunctive therapies **(González-Cabezas and Fernández, 2018).**

Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) emerged as one such fluoride alternative, offering a stable delivery of calcium and phosphate to promote remineralisation **(González-Cabezas and Fernández, 2018).** Later, bioactive glass-containing toothpastes such as NovaMin were developed. NovaMin acts both by facilitating apatite formation on demineralised enamel and dentin and by exerting antimicrobial effects **(Abbasoglu, 2019; Mollabashi et al., 2022).** Some studies have found NovaMin to be comparable to fluoride and CPP-ACP in remineralisation potential.

Nevertheless, most of the research supporting NovaMin's efficacy has been conducted in vitro, and there is a paucity of robust clinical data. This limits the ability to draw definitive conclusions about its effectiveness in real-world settings. Comprehensive, well-structured clinical trials are necessary to validate NovaMin's potential as a mainstream remineralisation agent **(Khijmatgar et al., 2020).**

The present study aims to clinically compare the remineralisation effectiveness of newer over-the-counter toothpastes containing NovaMin with traditional fluoride-based toothpastes. Specifically, it investigates whether Calcium Sodium Phosphosilicate (NovaMin) toothpaste is superior to Sodium Fluoride toothpaste in remineralising demineralised enamel. The null hypothesis posits that there is no significant difference in the remineralisation efficacy between the two types of toothpaste, particularly in reducing dentinal hypersensitivity and enhancing enamel repair in adult patients with demineralised enamel.

SUBJECTS AND METHODS

MATERIALS

Two toothpastes were used, *Sensodyne repair and protect* which is a toothpaste with Novamin technology that contains 5% NovaMin, and *Sensodyne Daily Care* which is a Sodium fluoride toothpaste that contains 5% potassium nitrate. The materials' names, descriptions, compositions, and manufacture are presented in Table (1).

METHODS

Study settings:

The protocol of the current study was registered on (*WWW. clinicaltrail.gov)* under the title "Effect of different over-the-counter toothpastes on enamel remineralization: A double blinded randomized clinical trial" with an identifier NCT03774498 that was released on the 12th of December 2018. All procedures performed in the study, involving human participants were in accordance with the ethical standards of research ethics committee of Faculty of Dentistry, Cairo University (Ref.18 – 6 - 20). The Evidence-Based Committee revised and approved the protocol on the 4th of June 2018. The Approval of the Board of Operative Dentistry Department was obtained on the 26th of June 2018. The randomized control clinical study was conducted in main clinic of Conservative Dentistry Department, Faculty of Dentistry, Cairo University.

Trial design:

The current study was a randomized clinical trial (RCT) where Randomization was generated using

Table (1): Comparison between intervention and control group toothpastes.

Points of comparison	Sensodyne repair and protect (Intervention)	Sensodyne Daily Care Toothpaste (control)
composition	• Calcium sodium phosphosilicate (Novamin) 5% w/w. • sodium fluoride. • Aroma. • Carbomer. • Cocamidopropyl betaine. • Glycerin. • Hydrated silica. • Peg-8. • Sodium methyl cocoyl taurate. • Sodium saccharin. • Titanium dioxide.	• Aqua. • Sorbitol. • Hydrated Silica. • Glycerine. • Potassium Nitrate. • Cocamidopropyl Betaine. • Aroma. • Xanthan Gum. • Titanium Dioxide. • Sodium Fluoride. • Sodium Saccharin. • Sodium Hydroxide. • Sucralose. • Limonene.
Manufacturer	Sensodyne is owned by Haleon and is marketed under the name Shumitect in Japan	Sensodyne is owned by Haleon and is marketed under the name Shumitect in Japan
ppm	1450 ppm fluoride	1450 ppm fluoride
W/W ratio	0.315%	0.3152%

computerized random number generator (*www.randomization.com*). The allocation ratio was 1:1.

Sample size calculation:

The aim of this study was to compare different over-the-counter toothpaste products in remineralization potential through the effect on hypersensitivity, to be able to know which of the toothpastes had the best effect in reducing hypersensitivity and thus can had a remineralization potential. Based on a previous study by **Hoffman, et al., 2015** the difference in DI between the 2 groups was 0.24±0.3. Using power 80% and 5% significance level we had to study 26 cases in each group. This number could be increased to a sample size of 30 cases to compensate for losses during follow-up (25% more than the calculated). Sample size calculation was achieved using PS: Power and Sample Size Calculation Software Version 3.1.2 (Vanderbilt University, Nashville, Tennessee, USA).

Eligibility Criteria:

Inclusion criteria of participants:

- Patients having at least two permanent tooth surfaces having decalcified lesions (buccal/facial aspects of incisors, canines or pre-molars) with score of 1 regarding the Decalcification index (DI) and scores of 1or 2 regarding the (ICDAS).
- Subjects with orthodontic appliances.
- Systemically healthy subjects of both genders, between the ages of 18 to 45 years, who were well versed with the use of toothbrush and dentifrice for oral hygiene maintenance, will be considered for the study.

Exclusion criteria of participants:

- Presently on desensitizing treatment.
- Subjects with bridge work that may interfere with evaluation.
- Medical histories that may compromise study protocol including psychiatric and pharmaco-therapeutic problems.
- Allergies of any kind or to toothpastes' contents.
- Systemic conditions which are etiologic/predisposing to dentinal hypersensitivity (Enamel and dentine genetic abnormalities) or any other pathology.
- Eating disorders.
- Pregnancy or breast feeding.

Allocation of participants:

Sequence generation and allocation concealment

Simple randomization was done according to a check list including the number of participants divided into two groups denoted with letter (A) for the intervention group, and (B) for the control group. Randomization was generated using computerized random number generator (*www.randomization.com*). The number of patients in each group was 30 (26 in each group & this number increased to 30 to compensate for losses during follow-up).

Allocation of patients in each group was done by putting the patients' numbers that were created by computerized randomization in an opaque sealed envelope to hide any method of identification for which patient was assigned to which group.

Blinding:

Both dentist and patient were blinded. This was done by painting the brand names on the tubes with the same color by a third person to avoid bias, and that third person had a table with him that showed the actual distribution of patients for each group. The participants were blinded to intervention/control assessment methods.

Recruitment:

Patients were recruited from outpatient's clinic in Conservative Dentistry Department seeking dental

care from which eligible patients were recruited to fulfill the eligible criteria according to participant time until the target population was achieved. The patients were subjected to full screening, examination and diagnosis using dental charts.

Clinical procedures:

All participants who fulfil eligibility criteria and who give consent for participation were randomized into two groups. A participant dentist other than the researcher performed the allocation sequence and assigned the participants to toothpaste in sequentially numbered opaque envelops after these toothpastes have been painted for blinding. Patients were selected according to the inclusion criteria, then they were sent to the periodontology department to undergo proper scaling and to be able to reach the best results.

Since tooth brushing is generally considered as a key self-care behavior necessary for maintaining good oral health, and since tooth brushing twice-daily is widely recommended as beneficial by Centers for Disease Control (CDC) for prevention of dental caries as it provides both biofilm removal and a regular application of fluoride according to **Melo et al., 2021** and **Kumar et al., 2016**. So, Patients were given a tooth brushing checklist that they should fill twice daily after each brushing procedure where the first time was in the morning and the other was before bedtime according to the World Dental Federation known as FDI that developed an educational program called Brush Day & Night (BDN) which was designed to establish the habit of brushing day and night with fluoride toothpaste **(Melo et al., 2021).**

The tooth brushing procedure was explained in detail to the participants as follows:

Participants were given the tubes of toothpaste and a toothbrush with a colored mark at 2 cm length of the bristle surface and the brushing technique was summarized in four steps:

1. 2 cm of the toothpaste is to be squeezed over the wet toothbrush bristles.
2. The upper and lower teeth are to be brushed for 2 min by modified bass technique where a video was demonstrated to the patient and applied in the clinic, and patients were told not to spit out more than necessary during brushing.
3. After brushing, the remaining toothpaste foam and saliva "slurry" are to be swished around the dentition with active movements of the cheeks, lips and tongue, forcing the slurry in between the teeth for about half a minute before spitting it out.
4. No post-brushing water rinsing is to be carried out and no eating/drinking for a minimum of 2 hours after brushing.

This procedure was repeated twice daily for 8 weeks and follow up was done in 2nd, 4th, 6th and 8th week. Also, a WhatsApp group was made including all participants reminding them of the timing on daily basis and notifying them about the importance of brushing teeth.

During each follow up visit, the researcher was handled the 2 week- checklist from each patient and captured proper frontal view photo using check retractor at a distance of 30 cm. Then the researcher was able to write down the results of the follow-up visit in his own results checklist in addition to the score readings according to both the DI and the ICDAS. The same step was repeated every two weeks until the end of the whole 8 weeks where a collective results table was created with the patients' numbers.

If any allergic reaction to any of the toothpaste ingredients showed up, the use of the toothbrushing procedure was discontinued.

Every patient was given a check list to tick in front of every tooth brushing procedure done (Two spaces for each day). The check list was designed

for 2 weeks on each page. The patient brought that checklist every follow-up visit. The researcher checked that list at the beginning of every follow-up visit and counted any missing brushing timings. Commitment to the assigned toothpaste is a must and never switch to another type during the period of the study.

During the study, two patients from group (A) were removed as one did not show from second and the other did not show after the fourth week. As for group (B), three patients were lost after the second and the third weeks.

Assessment, scoring & Data management

Assessment

All data were entered electronically where patients' files were stored in numerical order in a secure place (locked cabinets). Access to the study data was restricted. Data entry was carried out by the researcher and revised by the co-supervisor. All data were stored on computer and were encrypted using a password. This was done to allow accurate data entry through revision and protect data from being incorrectly used. The data was entered and stored on a personal computer. Double data entry was saved on an external hard disc to prevent loss of data. Results were entered on the word table and excel sheet on computer according to the serial number given for each patient. The researcher informed the participant that the whole procedure would take a short time, and it would be painless, and explained the result and how it will differ in his/her oral hygiene. Participants were withdrawn if they were "off study" and the outcome data cannot be obtained for them.

The outcome to be measured was Enamel remineralization and the outcome measuring tools were the Decalcification index (DI) and the International Caries Detection and Assessment System (ICDAS)

A) Decalcification index (DI) which is Modified version of the white spot lesions (WSL) index developed by Hoffman et al. ,2015. The modified decalcification index scores individual teeth as follows:

- (0): No white spot lesion present,
- (1): Visible white spots without surface interruption (mild decalcification),
- (2): Visible white spot lesion having a roughened surface but not requiring restoration (moderate),
- (3): Visible white spot lesion with surface interruption (severe decalcification),
- (4): Cavitation.

B) International Caries Detection and Assessment System (ICDAS) Gugnani et al.,2011.:

- (0): Sound tooth surface: No evidence of caries after 5 sec air drying,
- (1): First visual change in enamel: Opacity or discoloration (white or brown) is visible at the entrance to the pit or fissure seen after prolonged air drying,
- (2): Distinct visual change in enamel visible when wet, lesion must be visible when dry,
- (3): Localized enamel breakdown (without clinical visual signs of dentinal involvement) seen when wet and after prolonged drying,
- (4): Underlying dark shadow from dentine,
- (5): Distinct cavity with visible dentine,
- (6): Extensive (more than half the surface) distinct cavity with visible dentine.

Scoring: Scoring was done by taking photographs at the beginning of the study and at each follow-up visit with the same setting each time (Frontal view using a check retractor at distance of 30 cm) to serve as documentation, then these data were translated into scores in the results table._Photographs were taken by an iphone 13 ProMax camera that had a

Pro 12MP camera system with Telephoto (*f*/2.8 aperture), Wide(*f*/1.5 aperture), and Ultra-Wide (*f*/1.8 aperture and 120° field of view) cameras. The primary requirement for the examination of remineralization is clean and dry teeth. Drying of the tooth surface was the key for detecting non-cavitated lesions because water usually clogs the pores in the carious teeth and the similar refractive index of tooth and water obscures the detection of early white spot lesions.

Outcome assessment:

A ball-ended explorer was used to remove any remaining plaque and debris, and to check surface contour, or minor cavitation. The teeth were cleaned with a prophylaxis cup before clinical examination. No sharp explorer was used as it might damage the enamel surface covering the early carious lesions. A checklist was made for each patient to mark in every brushing procedure, and the researcher checked that list and wrote down the results in his checklist.

Statistical analysis:

Data was analyzed using IBM SPSS advanced statistics (Statistical Package for Social Sciences), version 24 (SPSS Inc., Chicago, IL). Numerical data was described as mean and standard deviation or median and range. Categorical data was described as numbers and percentages. Data was explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test. Comparisons between two groups for normally distributed numeric variables were done using the Student's t-test while for non-normally distributed numeric variables were done by Mann-Whitney test. Comparisons between categorical variables were performed using the chi square test. A p-value less than or equal to 0.05 was considered statistically significant. All tests were two tailed.

RESULTS

Patients' demographics and frequency of males and females with DI and ICDAS scores:

A total of 55 patients participated in the study, 28 were allocated to group (A) and 27 were allocated in group (B). Group (A) included 17(60.71%) females and 11(39.29%) males. While group (B) included 17(62.96%) females and 10(37.04%) males.

Regarding DI score at start, within group (A) 3(75.00%) females and 1(25.00%) male had score of 0, while 14(58.33%) females and 10(41.67%) males had score of 1. Within group (B) 3(60.00%) females and 2(40.00%) males had score of 0, while 14(63.64%) females and 8(36.36%) males had score of 1. While regarding final DI score, within group (A) 11(57.89%) females and 8(42.11%) males had score of 0 and 6(66.67%) females and 3(33.33%) males had score of 1. Within group (B), 13(65.00%) females and 7(35.00%) males had score of 0. On the other hand, 4(57.14%) females and 3(42.86%) males had score of 1 as shown in **Table (2).**

Regarding ICDAS score at start, within group (A) 3(75.00%) females and 1(25.00%) male had score of 1 and 14(58.33%) females and 10(41.67%) males had score of 2. As for group (B) 3(60.00%) females and 2(40.00%) males had score of 1 and 14(63.64%) females and 8(36.36%) males had score of 2. As per final score, within group (A) 1(20.00%) female and 4(80.00%) males had score of 0, 15(75.00%) females and 5(25.00%) males had score of 1, and 1(33.33%) female and 2(66.67%) males had score of 2. Within group (B) 3(50.00%) females and 3(50.00%) males had score of 0, 11(64.71%) females and 6(35.29%) males had score of 1and 3(75.00%) females, and 1(25.00%) male had score of 2 as shown in **Table (2)**

TABLE (2): Patients demographics and frequency of males and females with DI score ICDAS scores.

Parameter	Categories			Sex N(%)	
				Females	Males
DI Score	**Group A**	**Start**	**Score 0**	3(75.00%)	1(25.00%)
			Score 1	14(58.33%)	10(41.67%)
			Score 2	0	0
	Group B	**Start**	**Score 0**	3(60.00%)	2(40.00%)
			Score 1	14(63.64%)	8(36.36%)
			Score 2	0	0
DI Score	**Group A**	**Final**	**Score 0**	11(57.89%)	8(42.11%)
			Score 1	6(66.67%)	3(33.33%)
			Score 2	0	0
	Group B	**Final**	**Score 0**	13(65.00%)	7(35.00%)
			Score 1	4(57.14%)	3(42.86%)
			Score 2	0	0
ICDAS score	**Group A**	**Start**	**Score 0**	0	0
			Score 1	3(75.00%)	1(25.00%)
			Score 2	14(58.33%)	10(41.67%)
	Group B	**Start**	**Score 0**	0	0
			Score 1	3(60.00%)	2(40.00%)
			Score 2	14(63.64%)	8(36.36%)
ICDAS score	**Group A**	**Final**	**Score 0**	1(20.00%)	4(80.00%)
			Score 1	15(75.00%)	5(25.00%)
			Score 2	1(33.33%)	2(66.67%)
	Group B	**Final**	**Score 0**	3(50.00%)	3(50.00%)
			Score 1	11(64.71%)	6(35.29%)
			Score 2	3(75.00%)	1(25.00%)

Comparison between DI score at start and final time points for each Group:

Regarding Group (A) at the beginning of the study, 4 (14.29%) patients recorded DI score 0, while the majority 24 (85.71%) recorded score 1. When it came to the final scores, they showed that while the majority 19 (67.86%) recorded score 0 and 9 (32.14%) showed the score of 1. Therefore, the difference between final DI score and start DI score for Group (A) was statistically significant (P=0.001) as shown in **Table (3).**

Similarly, regarding Group (B), at the beginning of the study, most of the patients 22 (81.48%) showed DI score 1, while 5 (18.52%) showed score 0. As for the final point, the majority 20 (74.07%) recorded score 0, and 7 (25.93%) recorded score 1. Therefore, the difference between final DI score and start DI score for Group (B) was statistically significant (P=0.001) as shown in **Table (3).**

Comparison between ICDAS score at start and final time points for each Group:

Regarding the ICDAS score, for Group (A) at the beginning of our research, most patients 24 (85.71%) showed an ICDAS score of 2, and 4 (14.29%) showed the score of 1. But at the final point, the majority of patients 20 (71.43%) recorded score of 1, and 5 (17.86%) recorded score of 0, and 3 (10.71%) recorded score 2. Therefore, the difference between final ICDAS score and start ICDAS score for Group (A) was considered statistically significant (P=0.001) as shown in **Table (3).**

Regarding Group (B) at start of the research, most patients 22 (81.48%) recorded score of 2, and 5 (18.52%) recorded score of 1. But at the final time point, most of the patients 17 (62.96%) recorded score of 1, 6 (22.22%) recorded score of 0, and 4 (14.81%) recorded score of 2. Therefore, the difference between final and start ICDAS score for Group (B) was statistically significant (P=0.001) as shown in **Table (3).**

Comparison between Group (A) and Group (B) at starting and final time points for DI Score and ICDAS score:

Mann–Whitney U test revealed that there is no significant difference that exists between Group (A) and Group (B) at start or at final DI score. Similarly, there was also no significant difference between Group (A) and Group (B) at start or at final ICDAS score as shown in **Table (4).**

Correlation between brushing frequency and DI and ICDAS scores:

Within Group (A), the majority of patients 14 (73.68%) with DI score of 0 showed high brushing frequency, while 5 (26.32%) showed low brushing frequency. Also, 5(55.56%) with DI score 1 showed high brushing frequency, while 4 (44.44%) showed

TABLE (3) Descriptive statistics and comparison between each Group at start and final time points (Wilcoxon ranked sign test).

Parameter	Categories		Score (%)			Wilcoxon ranked sign test
			0	1	2	p-value
DI Score	**Group A**	**Starting**	4 (14.29%)	24 (85.71%)	0	0.001*
		Final	19 (67.86%)	9 (32.14%)	0	
	Group B	**Starting**	5 (18.52%)	22 (81.48%)	0	0.001*
		Final	20 (74.07%)	7 (25.93%)	0	
ICDAS score	**Group A**	**Starting**	0	4 (14.29%)	24 (85.71%)	0.000*
		Final	5 (17.86%)	20 (71.43%)	3 (10.71%)	
	Group B	**Starting**	0	5 (18.52%)	22 (81.48%)	0.000*
		Final	6 (22.22%)	17 (62.96%)	4 (14.81%)	

Significance level P<0.05, *significant.

TABLE (4) Comparison between Group A and Group B at starting and final time points for DI Score and ICDAS score (Mann–Whitney U test).

Parameter	Categories		Mann–Whitney U test
			p-value
DI Score	**Starting**	**Group A**	0.684
		Group B	
	Final	**Group A**	0.623
		Group B	
ICDAS score	**Starting**	**Group A**	0.684
		Group B	
	Final	**Group A**	0.976
		Group B	

Significance level P<0.05, *significant.

low brushing frequency. Additionally, 5(100%) of patients with ICDAS score 0, and 14(70 %) of patients with ICDAS score 1 had high brushing frequency while 6 (30%) of patients with ICDAS score 1 and 3 (100%) of patients with ICDAS score 2 had low brushing frequency as shown in **Table (5) and Figure (1).**

Similarly, within Group (B) the majority of patients 15 (75%) with DI score 0 showed high brushing frequency, while 5 (25%) showed low brushing frequency. Also, 5 (71.43%) of patients with DI score 1 had high brushing frequency while 2 (28.57%) had low brushing frequency. 6(100%) of patients with ICDAS score 0, 12(70.59%) of patients with ICDAS score 1 and 2(50%) of patients with ICDAS score 2 had high brushing frequency while 5(29.41%) of patients with ICDAS score 1 and 2 (50%) of patients with ICDAS score 2 had low brushing frequency as shown in (Table 6) and (Figure 8). A statistically significant negative correlation was detected between ICDAS score of group (A) and brushing frequency, and logistic regression analysis revealed a significant result. A non-significant negative correlation was detected between ICDAS score of group (B) and brushing frequency also between DI score of group (A) and brushing frequency and DI score of group (B) and brushing frequency as shown in **Table (5) and Figure (1).**

Some cases photographs for Group (A) and Group (B):

The progress that occurred in a successful case in the intervention group (A) is shown in **table (6)**, while **table (7)** shows a successful case for the control group (B).

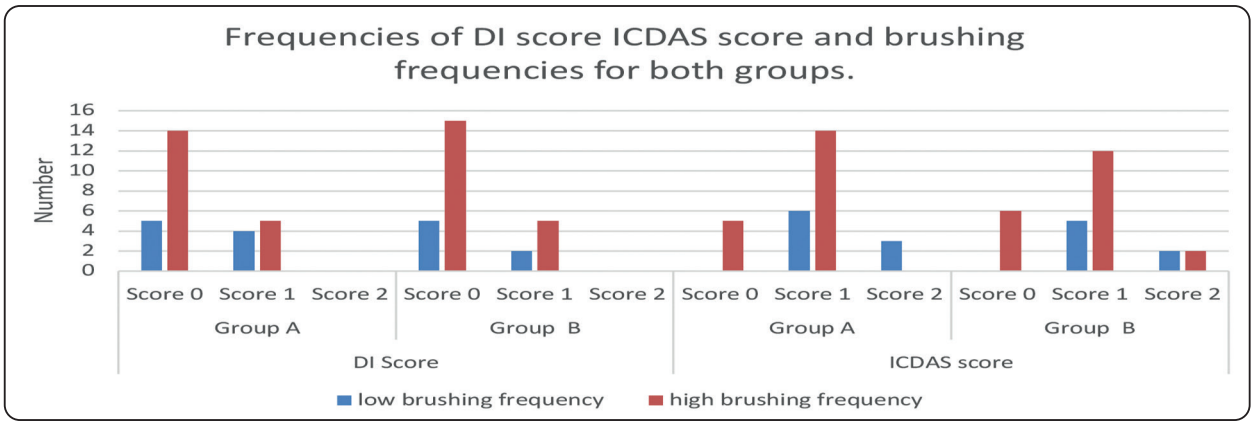

Fig. (1) Bar chart showing Frequencies of DI score ICDAS score and brushing frequencies for both groups.

TABLE (5) Frequencies and correlation between DI score ICDAS score and brushing frequencies for both Groups.

Parameter	Categories		Brushing frequency N(%)		Spearman's rank correlation		Logistic regression
			Less than 2 times per day	2 or more times per day	rho	P-value	P-value
DI Score	**Group (A)**	**Score 0**	5 (26.32%)	14 (73.68%)	-0.181	0.356	0.356
		Score 1	4 (44.44%)	5 (55.56%)			
		Score 2	0	0			
	Group (B)	**Score 0**	5 (25%)	15 (75%)	-0.036	0.860	0.860
		Score 1	2 (28.57%)	5 (71.43%)			
		Score 2	0	0			
ICDAS score	**Group (A)**	**Score 0**	0	5 (100%)	-0.519	0.005*	0.004*
		Score 1	6 (30%)	14 (70 %)			
		Score 2	3 (100%)	0			
	Group (B)	**Score 0**	0	6 (100%)	-0.354	0.070	0.071
		Score 1	5 (29.41%)	12 (70.59%)			
		Score 2	2 (50%)	2 (50%)			

TABLE (6) The progress of a successful case in the intervention group (A)

TABLE (7) Case for the control group (B).

DISCUSSION

In fact, clinical trials are thought to be among the most trustworthy ways to determine the effectiveness of dental materials since they offer vital information about the clinical performance of these materials, which is necessary for dentists to make well-informed judgements. Randomized controlled trials (RCTs) are at the highest point of the evidence pyramid in the hierarchy of evidence. Their placement is indicative of their high internal validity, which means that they are made to reduce bias and offer solid proof of the efficacy of the treatments or materials under examination **(Bédécarrats et al. 2020, Refaat et al., 2020; Fedyk et al., 2022).**

Randomized controlled trials (RCTs) offer trustworthy information on the clinical effectiveness and results of dental materials because they adhere to strict procedures and guidelines. This data is essential for treatment protocols, regulatory clearances, and educating dentists about the safest and most efficient materials to employ in clinical settings. As such, they are essential instruments for improving dental care and guaranteeing patient security and treatment effectiveness **(Ordinola-Zapata et al., 2022).**

White spot lesions (WSLs), which are softer than unbroken enamel and whiter when dried, are the clinical representation of first carious lesions. It is thought to be difficult to treat WSLs with conventional techniques. Therefore, using remineralization chemicals on WSLs may stop cavities from forming and maintain the integrity of the enamel. One of the side effects of orthodontic treatment is the development of white spot lesions (WSLs), which are mostly caused by inadequate maintenance of oral hygiene. Furthermore, bonding bonds impair natural dental self-cleaning processes and impede traditional oral care, which results in the buildup of plaque and a decreased Potential of Hydrogen (PH) **(Shihabi et al., 2021; Mollabashi et al., 2022).**

Caries demineralization-related subsurface enamel porosity is known as white spot lesions (WSLs). They appear on the tooth's surface as milky white opacities that extend from the gingival region to the bracket. These are the first visible signs of enamel caries. The primary goal of orthodontic therapy is often an aesthetically pleasant smile, which may not be attained due to such lesions **(Mollabashi et al., 2022).**

Research on enamel remineralization has been ongoing for a long time. Remineralization, a non-invasive therapy for early caries lesions, has been proposed as "the major advance in the clinical management of the disease." Researchers and

doctors are becoming more interested in these conservative approaches for WSLs that include remineralization therapy **(Shihabi et al., 2021; Mollabashi et al., 2022).**

Fluorides, the first substance to be recommended for WSL, are thought to be the gold standard for remineralization since they prevent demineralization by generating fluorapatite crystals (FAP). Several non-invasive techniques have also been developed. When it comes to acid attack resistance, these crystals outperform hydroxyapatite crystals. Moreover, fluoride promotes the development of new FAP and suppresses the action of carious bacteria that produce acid. Fluoride may be harmful in high doses, and its use should be restricted since even small amounts beyond therapeutic limits can cause fluorosis. Lately, scientists have been searching for a substitute substance that can have positive remineralization benefits without carrying the risk of fluoride toxicity **(Mollabashi et al., 2022).**

Other remineralizing agents have also been suggested. One such agent is NovaMin, a synthetic, extremely biocompatible substance that was first created as a bone-regenerative and sensitivity-reducing agent. It is casein phosphopeptide-amorphous calcium phosphate **(Manoharan et al., 2018; Mollabashi et al., 2022).**

NovaMin is a remineralization ingredient that was recently added to toothpaste. Bioactive glass (BAG) is a multi-component inorganic product that contains silicon, calcium, sodium, phosphorus, and other elements. It is regarded as a significant breakthrough in remineralization technology. The sodium ions from the NovaMin particles begin to quickly exchange with the hydrogen in the tooth structure when they are exposed to the aqueous environment of the oral cavity, releasing calcium and phosphate ions. Because of the quick pH rise brought on by this ion release, calcium and phosphate from NovaMin and saliva precipitate onto the tooth surface, covering it in a coating of calcium phosphate that forms a hydroxycarbonate apatite layer (HCA) on the tooth structure **(Hoffman et al., 2015; Elmancy, Abd El Aziz, and Awad,2022).**

Furthermore, NovaMin's temporary pH rise can aid in preventing demineralization. Because of its structural and chemical similarities to naturally occurring biological apatite, HCA might be used in toothpaste in place of fluoride thanks to NovaMin. Additionally, it has been suggested that fluoride and NovaMin work well together in remineralization processes because of NovaMin's capacity to provide calcium and phosphorus ions, which are necessary for the synthesis of fluorapatite **(Mollabashi et al., 2022).**

In order to determine which over-the-counter toothpaste had a better remineralisation potential on demineralised enamel, a randomised clinical trial (RCT) was carried out to compare the remineralisation potential of recent over-the-counter toothpaste (Novamin & Floride) and regular over-the-counter toothpaste (Sodium Floride).This is due to the fact that all research on the remineralisation capability of over-the-counter toothpastes for WSLs covered surface roughness and changes in enamel microhardness, but none examined the rate of remineralisation in relation to application frequency and duration. Furthermore, because the majority of research on that topic was done in vitro rather than on actual patients, it did not incorporate organic components like mouth bacteria and plaque **(Dhanya et al., 2021; Hsu et al., 2021).**

Two groups were allocated, with Group (A) serving as the intervention group and using Sensodyne repair and protect toothpaste, which contained bioactive glass as an active ingredient under the brand name NovaMin because research has shown that Novamin can reduce sensitivity in teeth and repair small cavitations. Additionally, group (B) used Sensodyne Daily Care as the control group. Because toothpaste is inexpensive and easy

to use, it is the standard of excellence material for remineralisation. Furthermore, since using fluoride toothpaste to brush is the best non-professional way to prevent dental decay **(Hsu et al., 2021; Fernandes et al; 2022).**

The patients were selected based on the presence of a minimum of two permanent tooth surfaces with decalcified lesions normally or following the removal of orthodontic appliances. This is because WSLs are the first macroscopic indication of enamel caries and pose a common but difficult problem for orthodontists because of increased plaque retention, which increases the microbial load and produces acid, which lowers pH and increases porosity of the enamel, allowing microorganisms to penetrate to the subsurface layer where remineralization is inhibited. **(Hoffman et al., 2015; Bangi et al., 2020).**

Both genders of systemically healthy participants were taken into consideration for the study since comprehensive patient medical histories may assist minimize difficulties associated with systemic disorders and will guarantee the best possible treatment outcomes **(Oktay et al., 2019; Akl et al., 2021).**

In order to avoid wasting time or money, the sample size was calculated to create a research sample that was big enough to be representative of the target population and to give adequate power to detect a statistically significant difference **(Andrade, 2020; Daniël Lakens, 2022).**

The study was carried out at Cairo University's Faculty of Dentistry because it is one of the top educational institutions in the domains of quality control and curriculum development, and because a large number of patients visit out-patients' dental clinics in quest of appropriate care at no cost **(Zaki and Morsy,2023).**

To guarantee the conduct of excellent research in accordance with global ethical norms, ethical approval was carried out. To maintain the research's voluntary character and provide participants with the option to accept or decline participation, informed consent was sought **(Arellano, Alcubilla, and Leguízamo, 2023).**

Participants were assigned using simple randomization as it preserves the total randomness of assigning a subject to a specific group, preventing bias in both performance and selection aspects. Because maintaining the entire randomization and allocation procedure without the assistance of computer software becomes challenging, randomization was produced using a computerized random number generator. Additionally, computer software makes it possible to modify many aspects of the random assignment sequence and generate qualifying lists for group trials that occur simultaneously. Double blinding was used in the study because blinding is a crucial methodological component of clinical trials that helps to maximize the credibility of the research findings and is meant to prevent bias **(Moustgaard et al, 2020).**

Initially, in-vitro investigations were carried out with the goal of comparing the possible remineralization effects of topical NovaMin and sodium fluoride gel on caries-like lesions in permanent teeth. In 2012, a pH cycling was applied to sixty healthy human teeth that had recently been removed. Specimens were split into two treatment groups at random, with the intervention group receiving NovaMin-containing toothpaste and the control group receiving toothpaste containing 1.1% basic sodium fluoride. The study revealed that, in comparison to toothpaste containing fluoride, NovaMin dentifrice appears to have a larger effect on the remineralization of carious-like lesions and a superior rise in microhardness outcomes **(Vahid et al., 2012).**

In different research, the remineralization capacity of CPP-ACP, Novamin, and fluoride-containing "Sensodyne Repair and Protect" dental products were compared. The findings indicated

that Novamin had more microhardness but that both Novamin and fluoride had the same impact on remineralization. However, even remineralization outcomes for both fluoride and novamin were seen in other investigations (**Asgartooran et al., 2023).**

Several in-vitro studies have been conducted to assess the ability of re-mineralizing agents to re-mineralize tooth enamel in a laboratory setting. We conducted that in-vivo study to demonstrate and validate better outcomes in reality because clinical mimics the oral environment and highlights the significance and advantages of patient-centered outcomes **(Bangi et al., 2020).**

Sensodyne repair and protect, the intervention group, demonstrated a substantial difference in remineralization potential between the study's start and ending points. The control group also shown a significant difference, which improved the DI and ICDAS scores. This was similar to Hofman et al. (2015) findings. This might be due to the fact that surface roughness was not taken into consideration when scoring by DI, which was based only on size and form. It could also be because images may not be as clinically accurate **(Robertson et al., 2011).**

These findings ran contradictory to those of Robertson et al. (2011), who reported that Novamin reduced WSLs while demonstrating decreases in DI scores and ICDAS of 53.3% and 44.8%, respectively. However, standard fluoride toothpaste showed increases in DI and ICDAS scores of 91.1% and 43.1%, respectively, with more WSLs. This could be because standard toothpaste's high fluoride concentrations cause the surface layer to remineralization, while fluorapatite inhibits the remineralization of subsurface layers, leading to an increase in DI and ICDAS score readings. While white spot lesions may have improved more than those in the control group due to the reduced fluoride levels in Novamin toothpaste interacting with salivary calcium and phosphorus **(Grohe and Mittler,2021).**

The remineralization potential in group (A) improved, which was consistent with findings from studies by **Narayana et al. (2014), Rajan et al. (2015), Dhanya et al. (2021)** that found that Novamin outperforms fluoride in remineralization because it increases calcium concentration and contains bioactive glass particles that can lower the longevity of planktonic bacterial cultures of Streptococcus mutans, Fusobacterium nucleatum, Actinomyces naeslundi, and Streptococcus sanguis. These findings are related to the increased pH of the oral cavity that causes caries **(Dhanya et al., 2021).**

Results showed that there was statistically significant improvement in WSLs for group (A) in the ICDAS scores which was in line with the findings of **Salah et al. (2022)** where the Novamin group shown improvement in ICDAS scores with a 32.2% decrease in the demineralized area. This may be explained by the discovery that NovaMin is just as successful as fluoride in enhancing the remineralization outcomes. However, NovaMin may be a more advantageous new alternative material for enamel remineralization than fluorides due to its fewer harmful effects. **(Hsu et al., 2021).**

The findings showed no statistically significant difference between Group (A) and Group (B) at either the beginning or the end of the DI score. This was similar to **Bangi et al. (2020),** where newly commercially available products demonstrated a regression of WSL size and shape. However, similar to fluoride materials, this could be because daily consumption of acidic foods with lower pH levels can damage tooth surfaces and negate saliva's natural buffering effect, which can lead to regression in the impact of Novamin. Additionally, the DI scoring may be somewhat subjective **(Khijmatgar et al., 2020).**

Given the importance of maintaining one's oral health, brushing one's teeth is one of the most basic self-care practices that one may see in a person. In order to assess the relationship between dental

caries and brushing frequency, a study was carried out demonstrating that 76.1% of the participants brushed once a day, indicating a low brushing frequency, and 23.9% of the participants brushed twice a day, indicating a high brushing frequency. It was determined that those who did not brush as frequently as they should have had higher caries scores **(Jain, 2021).**

A negative correlation between the initial and final DI scores and the ICDAS scores was seen in our study, suggesting that enhanced remineralization capability for WSLs is also a result of increased tooth brushing frequency (twice daily). These findings were consistent with those of **Kumar, Tadakamadla and Johnson (2016)** and this is likely due to the participants' excellent preparation and knowledge prior to the study's start, which maximized the reliability of the findings **(Jain, 2021).**

These findings ran counter to those of **Brusius, Alves and Maltz (2023**) who found that brushing more frequently is necessary to slow the advancement of dental caries in adolescence. This could be because the third brushing session in that study proved to be advantageous, particularly for adolescents who are at high risk for developing dental caries. However, other studies found no correlation between brushing frequency and dental caries, indicating that there is no proof that increasing brushing frequency improves the quality of biofilm control. Brushing once a day should be enough to prevent caries because dental biofilm needs two days to produce enough acid to cause demineralization of the enamel **(Brusius, Alves, and Maltz ,2023).**

We can conclude from all of the earlier findings, justifications, and conclusions that there was no difference between the toothpastes used in the control and intervention groups, and that there was a strong correlation between toothbrushing frequency and the remineralization results. These findings can help us determine whether more research with a wider range of variables is necessary.

The remineralization potential for WSLs in two different over-the-counter toothpaste standard sodium fluoride toothpaste and the new bio glass Novamin toothpaste—was compared in that study. The findings indicated that brushing frequency affected the rate of remineralization progress and that both products had the same effect, with no toothpaste outperforming the other. Nevertheless, we should also take into account a few limitations, such as the fact that laser fluorescence and quantitative light-induced fluorescence were not used to evaluate WSLs, which would have offered an even better assessment technique. However, because of budget limitations, using this technology in our experiment was not possible **(Bangi et al., 2020).**

Furthermore, patient compliance is difficult to control even with measures taken to reduce the impact of this confounding factor, such as closely monitoring the toothpaste tubes provided at every follow-up appointment and providing patients with pamphlets and images to improve their understanding of the brushing process **(Salah, Kehela, and Afifi, 2023).**

Lastly, the evaluation was conducted using images, which may not be as clinically precise and may introduce bias. As a result, it is advised to employ additional helpful aids to obtain clinical results that are more accurate **(Robertson et al., 2011).**

Some recommendations can be made in light of the limits discovered, such as extending the study's duration to three or six months in order to potentially improve the process of remineralization **(Dhanya et al., 2021).**

Additionally, it would be crucial to include information on the food consumed during the trial in order to track the frequency of acidic intake that might affect the outcomes and the rate at which remineralization proceeds **(Bangi et al., 2020).**

Furthermore, in order to prevent performance bias, self-administered home applications must be combined with standardized in-office applications **(Salah, Kehela, and Afifi, 2023).**

Lastly, because of our findings, Novamin toothpaste has the benefit of no longer having the fluoride toxicity downside, which makes it a better toothpaste option for younger age groups than regular sodium fluoride toothpaste since toothpaste swallowing is boosted **(Shihabi et al., 2021).**

Limitations:

1. Budget limitations that prohibited using technologies such as laser fluorescence for better assessment for the white spot lesions.
2. Difficult patient compliance although patients were provided with pamphlets and images to improve their understanding of the brushing.
3. Evaluation was conducted using images, which may not be as clinically precise and may introduce bias.

CONCLUSIONS:

Under the limitations of the current investigation, the following can be concluded:

1. No difference in remineralization potential of WSLs for both Novamin and Sodium fluoride toothpastes,
2. High brushing frequency (2 times/ day) is important to achieve promising and effective remineralization for WSLs.

Clinical relevance:

It was found that recent over-the-counter toothpaste (Novamin & Floride) has a role in remineralization on early white spot lesions depending on the commitment with the proper frequency of toothbrushing to achieve that remineralization potential.

RECOMMENDATIONS

1. Increase the duration of investigations to reach 3 or 6 months because this might improve the progress of remineralization for enamel caries.
2. Add details about the food intake during the investigations to avoid acidic food that can impair the remineralization progress.
3. Combine some in-office toothbrushing sessions along with self-administered home brushing

Conflict of interest:

No conflict of interest.

Funding:

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Compliance with Ethical Standards:

The protocol of the current study was registered on clinical trials with a unique identification number (I.D.: NCT03774498). Ethical approval was obtained before the start of the study. The study was approved by the Research Ethics Committee (CREC), Faculty of Oral and Dental Medicine with ethical approval number (Ref.18 – 6 - 20). The Evidence-Based Committee revised the protocol, and The Board of Operative Dentistry Department was also approved.

Informed consent:

An informed consent with an easy Arabic language was signed by the recruited participants.

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