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ORIGINAL RESEARCH

Remineralizing Effect of Topical NovaMin and Nano-hydroxyapatite on Caries-like Lesions in Primary Teeth

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ABSTRACT

Introduction: NovaMin is a synthetic mineral compound composed of calcium, sodium, phosphorus, and silica. It releases crystalline hydroxyl-carbonate apatite (HCA), which structurally resembles the minerals naturally found in the teeth. Nano-hydroxyapatite (NHA) is a biocompatible compound with high affinity for tooth enamel. NHA particles morphologically resemble dental enamel apatite crystals. Considering the efficacy of remineralizing agents and the importance of conservative preventive measures, this study aimed to compare the remineralizing effects of NovaMin and NHA on caries-like lesions in primary teeth.

Materials and methods: This *in vitro* experimental study was conducted on 30 sound human primary anterior teeth with no cracks or fractures. The surface microhardness (SMH) of each tooth was measured at baseline using a Vickers microhardness tester. The teeth were then subjected to remineralization/demineralization cycles, and artificial caries lesions were created in them. The SMH of each tooth was measured again and the teeth were then randomly treated with toothpastes containing NovaMin or 10% NHA powder for 2 minutes daily for a period of 5 days. The SMH of each was again measured afterward. Data were statistically analyzed using independent t-tests and Mann–Whitney U tests.

Results: The mean SMH was found to be higher in the teeth treated with NovaMin toothpaste (422.67 kgf/mm^2) than in the teeth treated with NHA (384.2 kgf/mm^2); However, this difference was not statistically significant.

Conclusion: Both NHA and NovaMin were effective for remineralization of caries-like lesions of primary teeth and no significant difference was detected in their efficacy.

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INTRODUCTION

With the introduction of noninvasive cariostatic measures, noncavitated carious lesions that maximally extend into the dentinoenamel junction may be stopped or even repaired. Bioactive materials produced from dairy products can promote enamel and dentin remineralization under cariogenic conditions by releasing special remineralizing agents.[1] This conservative approach to the treatment of tooth caries has led to a significant number of research projects focusing on the development of remineralizing agents to cease the progression of initial caries.

NovaMin is a synthetic mineral compound composed of calcium, sodium, phosphorus, and silica that can effectively enhance remineralization. It adheres to the tooth surface and continuously deposits crystalline hydroxyl-carbonate apatite (HCA). Microscopic particles of NovaMin release millions of mineral ions upon exposure to humidity, resulting in the formation of a firm hydroxyapatite (HA) layer on the surface of the enamel and dentin. This capability not only repairs initial carious lesions, but also eliminates tooth hypersensitivity.[2] In a wet environment, hydrogen cations are exchanged with sodium ions in the particles, allowing the calcium and phosphate ions present in this material to be released. These reactions occur within seconds. Release of calcium and phosphate ions continues as long as the material is in a humid environment. Due to the release of sodium, the local pH temporarily increases. As a result of the transient

rise in pH, the calcium and phosphate ions released from NovaMin along with the calcium and phosphate ions present in the saliva form a calcium phosphate layer on the tooth surface. By the continuous deposition of calcium and phosphorus, this layer converts to HCA, which structurally and chemically resembles biological apatite. A previous study evaluated the efficacy of NovaMin for the remineralization of caries-like lesions and found that toothpastes containing NovaMin had greater efficacy than fluoridated toothpastes for the remineralization of caries-like lesions in permanent teeth.[2]

Hydroxyapatite is the mineral crystalline form of calcium and phosphorus found in the enamel, dentin, cementum, and bone. It is widely used in biology, medicine, and dentistry due to its optimal characteristics, such as similarity to the mineral structure of hard tissues, biocompatibility, and low solubility.[3] It has remineralizing effects when applied to tooth enamel. Nano-hydroxyapatite (NHA), due to its higher surface/volume ratio, is more effective than large HA particles. With the recent advances in nanotechnology, the size of particles has decreased and some modifications were made in their shape, yielding highly bioactive calcium phosphate compounds that may have higher potential for penetration into the porosities of the demineralized area as remineralizing agents.[4,5]

Some previous studies evaluated the effect of NHA solution on erosive enamel lesions of human permanent teeth and reported that NHA was capable of repairing these lesions.[6,7] Also, it has been demonstrated that NHA toothpastes and mouthwashes can remineralize initial enamel caries.[8,9]

Considering the significance and superiority of preventive measures over invasive procedures for treatment of initial caries and the existing concerns regarding the use of fluoride due to its potential side effects, attempts have been made to use synthetic remineralizing agents as an alternative to fluoride. Thus, owing to the remineralizing properties of NHA and NovaMin and the significance of preventive and conservative treatments, this study aimed to assess and compare the remineralizing effects of NHA and NovaMin on artificially created carious lesions in primary anterior teeth.

MATERIALS AND METHODS

This *in vitro* experimental study was conducted on 30 primary anterior teeth with sound enamel and no cracks, fractures, or hypoplastic defects. Sample size calculation and method of sampling were in accord with a study conducted by Cerruti et al.[15] Statistical analysis was performed using two-sample t-test with $\alpha = \beta = 0.05$ in Minitab software. After cleaning and disinfection, the teeth were mounted and their enamel surfaces were ground using an abrasive paper (Fig. 1).

The baseline surface microhardness (SMH) of the teeth was measured using a Vickers microhardness tester (Shimadzu, M-g5037, Japan) by applying 25 gm load for 5 seconds. The teeth were then immersed for 1 hour in demineralizing solution composed of 1.4 mM calcium from $Ca(NO_3)_2$, 0.9 mM phosphorus from KH_2PO_4, 0.1 M acetate buffer from acetic acid with a pH of 4.5, and 0.03-ppm fluoride with a pH of 5.0 from Nave.[2] Next, the specimens were immersed in remineralizing solution composed of 1.5 mM calcium from $Ca(NO_3)_2$, 0.9 mM phosphorus from KH_2PO_4, 0.1 M Tris buffer (hydroxymethyl ammonium ethane) with a pH of 6.5 to 7.6 and 0.05 ppm fluoride with a pH of 7.0 for 22 hours in order to artificially create carious lesions in the teeth.[2] The teeth were then subjected to three rounds of demineralization/remineralization cycles as described earlier, and after the development of artificial caries, SMH testing was performed again. The SMH was measured twice using the same microhardness tester machine under similar conditions. Subsequently, the teeth were immersed in artificial saliva (2 g/L methyl-p-hydroxybenzoate, 10 g/L sodium

Fig. 1: Primary mounted teeth

Table 1: Comparison of the efficacy of NovaMin and NHA for remineralization of caries-like lesions in primary anterior teeth

Surface micro hardness	*Group*	*Number*	*Average*	*Standard deviation*	*Difference of average*	*p-value 1*	*p-value 2*
Initial	Novamin	15	422.67	65.64	38.47	0.08	0.06
	Nanohydroxy apatite	15	384.2	50.821			
Secondary	Novamin	15	330.73	70.06	40.73	0.08	0.08
	Nanohydroxy apatite	15	290.0	51.61			
Tertiary	Novamin	15	369.67	74.43	13.6	0.57	0.35
	Nanohydroxy apatite	15	356.07	55.49			

carboxymethyl cellulose, 0.675 g/L KCl, 0.059 g/L $MgCl_2$ $6H_2O$, 0.166 g/L $CaCl_2$ $2H_2O$, 0.804 g/L K_2HPO_4, and 0.32 6g/L KH_2PO_4; the pH of the solution was adjusted to 6.75) to be coated with a thin layer of saliva in order to simulate clinical oral conditions prior to the application of remineralizing agents.[2]

NovaMin and NHA were prepared in the form of solutions. Of the 30 primary teeth, 15 were immersed in toothpaste solution containing NovaMin and 15 in toothpaste solution containing NHA. The teeth in each group were immersed in these solutions for 2 minutes daily during each treatment cycle. Throughout the remainder of this period, the teeth were stored in artificial saliva with the same composition described earlier. This process was continued for 5 days. The SMH values were measured again following completion of the described treatment protocols using the same Vickers microhardness tester with conditions as described before.

An independent t-test and Mann–Whitney U test were used to assess the differences between the mean SMH values. Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20.0.

RESULTS

The SMH was found to be higher in the teeth treated with NovaMin toothpaste (422.67 kgf/mm^2) than in the teeth treated with NHA (384.2 kgf/mm^2). However, this difference was not statistically significant ($p = 0.57$) (Table 1).

DISCUSSION

NovaMin is a synthetic mineral compound composed of calcium, sodium, phosphorus, and silica. It releases crystalline HCA with a structure resembling the human tooth mineral. Nanohydroxyapatite is a biocompatible compound with a high affinity to tooth enamel. Hydroxyapatite nanoparticles highly resemble natural enamel HA crystals. The current study was the first to compare the efficacy of NovaMin and NHA for remineralization of caries-like lesions in primary teeth. The results showed that the SMH values were higher in the teeth treated with NovaMin than in the teeth treated with NHA, although this difference was not statistically significant.

The process of enamel demineralization depends on the pH and calcium, phosphate, and fluoride contents of teeth. These factors determine the level of mineral saturation.[10] Thus, a subsaturation condition can result in the dissolution of HA crystals in the tooth and diffusion of calcium and phosphate ions toward the enamel surface. A hypersaturation of these ions on the enamel surface can lead to redeposition of HA crystals, known as remineralization, and consequently to the formation of an intact superficial layer on the enamel surface. An increased SMH indicates remineralization, and a decreased SMH is indicative of demineralization.[11]

The role of calcium and phosphate ions in the process of demineralization/remineralization has been well recognized. The organic content of saliva also plays an important role in this regard. In the current study, the artificial saliva was prepared using both organic and mineral compounds in order to simulate the clinical setting as much as possible. The specimens were immersed in this solution prior to exposure to the toothpaste solutions being studied. By doing so, we allowed calcium sodium phosphosilicate to gradually replace hydrogen ions.[10] As a result, a thick layer composed of calcium and phosphate was formed on the tooth surfaces and, at the same time, the increased pH of the environment prevented the process of demineralization.[2,12] Thus, taking these measures into account, we expect that these results may generalize to the clinical setting to a large extent.

Following immersion in an aqueous environment, NovaMin releases ions into its surroundings. Sodium ions present in the formulation of calcium sodium phosphosilicate bioactive glass are replaced with hydrogen ions and, thus, the pH increases. Subsequently, calcium and phosphate ions deposit and form a superficial layer saturated with calcium phosphate on the tooth surface.[10] This ionic reservoir can inhibit the process of demineralization and enhance remineralization by protecting the enamel against cariogenic conditions.[10] Following the immersion of calcium sodium phosphosilicate in the saliva or body fluid analogs, Na^+ ions are exchanged with hydrogen cations (H^+ or H_3O^+) within a minute.[13-15] Such quick exchange of ions leads to the release of calcium (Ca^{2+}) and phosphate (PO_4^{3-}) from the particles. Subsequently, a local transient rise in the pH results in the release of

calcium and phosphate ions present in the particles and saliva, and the formation of an amorphous layer of calcium phosphate ($CaO\text{-}P_2O_5$) on the tooth surfaces as well as within the demineralized dentin. Simultaneously, with the continuation of these reactions and the deposition of Ca-P compounds, this layer crystallizes inside the HA, forming a structure that chemically and structurally resembles biological apatite.[13,14] The interaction between the residual calcium sodium phosphosilicate and the HA layer leads to remineralization and physical occlusion of dentinal tubules. Calcium sodium phosphosilicate also induces chemical reactions to enhance the formation of HA. This may prevent demineralization of tooth structure and enhance remineralization of a hybrid layer inside the lesions at the resin–dentin interface when used in bonding processes.

Tschoppe et al[16] in 2011 evaluated the effects of a toothpaste containing NHA on enamel and dentin remineralization and showed that NHA toothpaste had greater efficacy for enamel and dentin remineralization than amine fluoride toothpaste. Moreover, Haghgoo et al[19] evaluated the effects of toothpastes containing various concentrations of NHA on the remineralization of initial caries and reported that NHA toothpastes successfully remineralized these lesions. Their findings are in line with the results of the current study. Huang et al[3] in 2009 reported that NHA had the potential to remineralize initial enamel lesions. The remineralizing effect of NHA on demineralized enamel and dentin has also been confirmed in several other studies.[7,10,17,18] The HA nanoparticles penetrate into the porosities and act like a scaffold. They uptake calcium and phosphate ions from the remineralizing solution and lodge them into the superficial enamel. By doing so, they fill the gaps in between the enamel calcium crystals, yielding a uniform crystalline enamel structure.[3]

According to the results of a study by Golpaygani et al[2] in 2012, the SMH of tooth enamel increased following treatment with fluoride and a toothpaste containing NovaMin. In their study, the efficacy of NovaMin was significantly higher than that of the toothpaste containing 1.1% fluoride; these results are in accord with our findings. Moreover, Alauddin et al[19] in 2005 revealed that NovaMin-containing toothpaste caused greater remineralization than fluoride. Burwell and Litkowski[20] in 2007 also demonstrated that NovaMin toothpaste alone and in combination with fluoride caused greater remineralization of caries-like lesions in bovine teeth compared with fluoridated toothpastes without NovaMin. Our results also confirm their findings, although our study was conducted on human teeth.

The results of the current study demonstrate that both NovaMin and NHA increased the SMH and enhanced the remineralization of teeth. Moreover, although there are some concerns regarding the formation of hypoplastic spots following overuse or swallowing of fluoridated toothpastes, no adverse side effects have been reported for NovaMin or NHA.[21] Thus, it appears that NovaMin and NHA are suitable for prevention of caries in both children and adults.

One possible limitation of the current study is that although we tried our best to simulate the formulation of natural saliva, some differences always exist between natural and artificial saliva and, thus, generalization to the clinical setting must be done with caution. Another limitation of this study was the scarcity of materials being studied in the Iranian dental market.

CONCLUSION

Based on these results, both NHA and NovaMin toothpastes are effective for remineralization of caries-like lesions of primary teeth and the efficacy of NovaMin is slightly higher than that of NHA for this purpose.

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