Comparative Evaluation of Effect of Nano-hydroxyapatite and 8% Arginine Containing Toothpastes in Managing Dentin Hypersensitivity: Double Blind Randomized Clinical Trial

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ABSTRACT

Purpose: This double blind randomized clinical trial was conducted with the purpose of evaluating the effects of Nano-hydroxyapatite toothpaste as compared to 8% Arginine containing toothpaste in the management of Dentin hypersensitivity (DH).

Method and materials: Patients (30 in each group) suffering from DH and eliciting a VAS score higher than 2 in air blast and tactile test were randomly allocated (block randomization) into either a group 1 (arginine toothpaste) or group 2 (nHA toothpaste). The primary outcome evaluated was the reduction of DH as measured by the electrical stimulus reading on the digital pulp tester. Current required for eliciting a VAS score of 2 was recorded before application of dentifrice. 1 cm of toothpaste was then expressed on the tooth surface for two minutes in each group and rinsed off. The electrical stimulus required to elicit a VAS score of 2 was recorded after 5 minutes, 1 week and 4 weeks.

Results: The desensitizing paste containing arginine provided a statistically significant reduction in DH and so did the paste containing nHA. Mean increase in amperage value (reduction in DH) was higher for nHA based than the arginine containing dentifrice. This difference was not statistically significant showing that both toothpastes are equally effective.

Conclusions: The findings of the present study encourage the use of Nano-hydroxyapatite and arginine containing dentifrice as an effective desensitizing agent providing relief from symptoms 5 minutes after application and after 1 and 4 weeks.

KEYWORDS

arginine; Dentin hypersensitivity; Nano-hydroxyapatite

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INTRODUCTION

Dentin hypersensitivity (DH) is a common problem in clinical practice and is defined as a short, sharp pain arising from exposed dentin as a result of various stimuli, such as heat, cold, chemical or osmotic, that cannot be ascribed to any other form of dental defect or pathology (1). The condition has a predilection for individuals in their third and fourth decades of life, canines and premolars are usually affected. Brannstrom's hydrodynamic theory is the most accepted explanation for this condition (2, 3). An increase in life expectancy of the population has resulted in a concomitant rise in the prevalence of DH. The disorder can impede adequate maintenance of oral hygiene, thereby contributing to accumulation of dental plaque, caries, gingivitis and periodontal disease (4). DH hence needs to be addressed in order to provide patients with better oral comfort and quality of life.

To date, no gold standard exists for the treatment of DH. The primary approaches used in its management are tubular occlusion and nerve desensitization. The symptoms often reappear because of toothbrush abrasion, acid challenges in the mouth or degradation of the coating material. There is a need to develop desensitizing agents that provide instant and sustained relief from DH symptoms and is economically viable.

Kleinberg et al. (5) in 2002 demonstrated a saliva-based dentifrice containing arginine, bicarbonate and calcium carbonate to form a solid plug, sealing the patent dentinal tubules and limiting fluid movement. The dentifrice provided a statistically significant reduction in DH immediately after a single professional application, which sustained over a period of 28 days (5).

Hydroxyapatite (HA) is the major inorganic constituent of mineralized biological tissues. Orsini et al. (6) reported nHA containing dentifrice to significantly reduce DH after 4 and 8 weeks, supporting its utility in clinical practice.

No study has yet been published comparing the effect of arginine and nHA containing dentifrices. This double blind randomized clinical trial was carried out to identify the more clinically effective dentifrice in the management of DH – immediately, at 1st week and 4th week of use. The null hypothesis generated was that there is no difference in clinical efficacy of nHA toothpaste as compared to arginine containing toothpaste in the management of DH.

MATERIALS AND METHODS

A double blind randomized clinical trial was carried out over a period of 12 months following approval from the Institutional Ethics Committee [IEC/C/72/2013/DCT/dated 09-12-13] and Clinical Trials Registry of India (CTRI). The reference population was patients suffering from DH. Patients reporting to outpatient section of the Department of Conservative Dentistry and Endodontics constituted the source population. The study population was selected from the source population based on the inclusion criteria described by Holland (7). Only those subjects who were willing to provide informed consent were included in the study.

COMPOSITION OF THE TOOTHPASTES

1. Colgate Sensitive Pro-Relief toothpaste contains 8% arginine bicarbonate, calcium carbonate, sorbitol, sodium lauryl sulphate, flavor, sodium silicate, sodium carboxymethyl cellulose, sodium monofluorophosphate, sodium bicarbonate, titanium dioxide, potassium acesulfame, xanthan gum, sucralose, in aqueous base
2. Acclaim toothpaste contains 1% Nano-hydroxyapatite, sorbitol, glycerin, silica, purified water, cocamido propyl betaine, hydroxy ethyl cellulose, titanium di-oxide, flavoring agents, sodium saccharin.

SAMPLE SIZE CALCULATION

A minimum sample size of 15 in each group was calculated using data from previous studies (6, 8).

The minimal relevant difference (MIREDIF) used in these calculations were 0.595.

Power of our inter group comparison results calculated is 99%.

To increase the power of the study and to compensate for possible dropouts during the study period, it was decided to include more patients (30 in each group).

SAMPLE SELECTION AND INTERVENTION

Subjects were randomly allotted to group 1 or group 2 with an allocation ratio of 1 : 1. Blocks of random numbers were assigned using computer generated tables. To ensure that the principal investigator and the study subjects were not involved in the allotment of treatment arms, random numbers were generated and allocated by a clinician not involved in the study. Blinding was achieved by wrapping the two dentifrices under study.

Eligibility for recruitment into the study was assessed at the screening visit. A single tooth was evaluated in a subject. In individuals with multiple cervical abrasions, a single tooth was randomly chosen. The tooth to be tested was isolated using cotton rolls. To identify a tooth with DH, two stimulus tests were performed with an interval of 5 minutes between the tests (9).

1. Tactile test: An explorer was gently run across the affected tooth surface (Fig. 1A).

2. Air blast test: A blast of air from a three-way dental syringe for one second (Fig. 1B).

The subjects were asked to score the elicited pain based on the VAS (Fig. 2) and those indicating a score greater than 2 were included in the trial. 95 patients were assessed for eligibility and 60 patients were selected for this study into two groups.

Group I: 30 patients assigned to use dentifrice containing arginine.

Group II: 30 patients assigned to use dentifrice containing nHA.

The electrode of the digital electric pulp tester was placed on the selected tooth (Fig. 1C) and the current required for eliciting a VAS score of 2 was recorded before application of dentifrice. The electrical pulp tester was applied to the abraded area of the tooth in all patients. Digitest II (PARKELL, Inc., New York) was the pulp test-

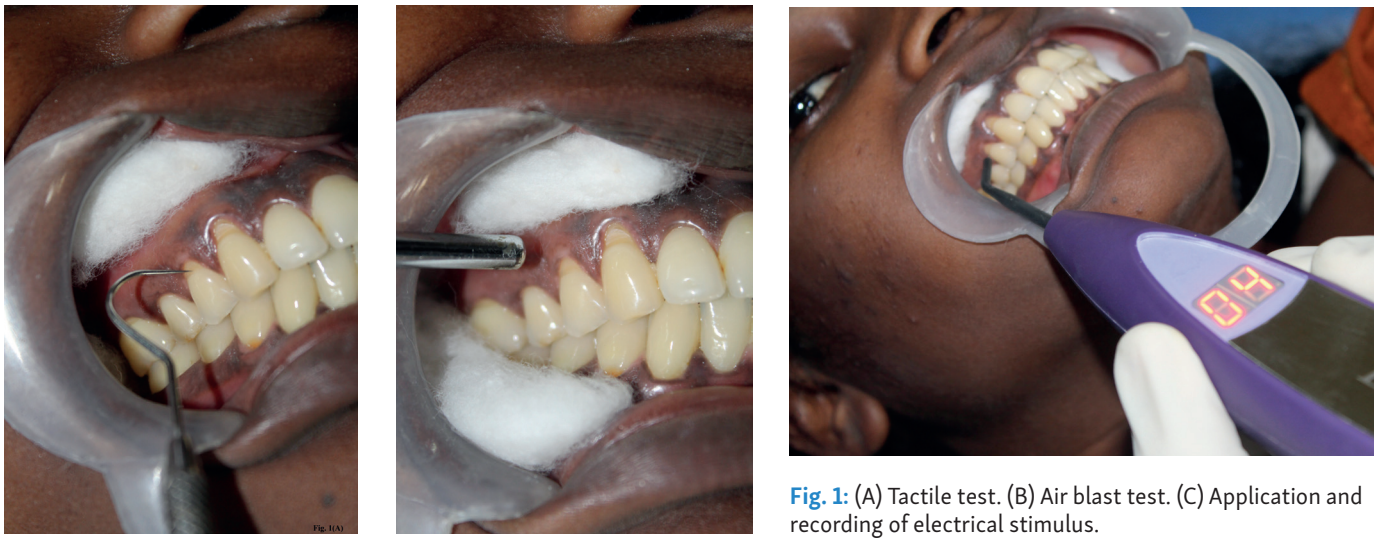

Fig. 1: (A) Tactile test. (B) Air blast test. (C) Application and recording of electrical stimulus.

er used. One cm of toothpaste was then expressed on the tooth surface for two minutes in each group and rinsed off. The electrical stimulus required to elicit a VAS score of 2 was recorded after 5 minutes to assess the immediate relief from DH.

To assess the effectiveness at the 1st and 4th week, the patients were provided with dentifrices to be used at home regularly for 4 weeks and no other oral hygiene measures were to be used during this period. The patients were instructed to apply 1cm of toothpaste directly on the sensitive site of the selected tooth using a soft brush for 1 minute followed by brushing for 2 minutes twice a day. They were given proper oral hygiene instructions including tooth brushing techniques. At the end of 1st and 4th week, electrical stimulus measurements to elicit a VAS score of 2 were made.

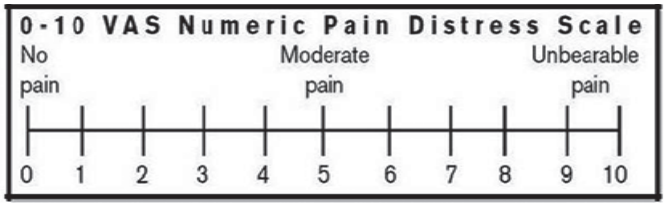

Fig. 2: Visual Analog Scale (VAS).

PRIMARY OUTCOME

The primary outcome was the electrical stimulus reading as provided by the digital pulp tester.

STATISTICAL ANALYSIS

Data was entered using Microsoft Excel and analyzed using SPSS (Statistical Package for Social Sciences) version 22.0. Shapiro-Wilk test was used to assess normality of the data. Descriptive statistics (mean & standard deviation) were calculated and the baseline characteristics were compared using Pearson's chi-squared test for qualitative and independent t-test for quantitative variables. To compare the effectiveness of dentifrices at different time intervals, independent t-test was used for inter group comparison and repeated measures analysis of variance (ANOVA) for within group comparison.

RESULTS

The present randomized clinical trial investigated the efficacy of two commercially available toothpastes in reducing DH. The improvement in DH was assessed clinically by measuring the change in amperage values over time using an electrical stimulus test. The CONSORT flowchart depicting the progress of subjects through the various stages of this trial is shown in Fig. 3. All the enrolled (n = 60) subjects completed the study. No adverse effects on the oral soft or hard tissues were observed by the examiner or reported by the participants.

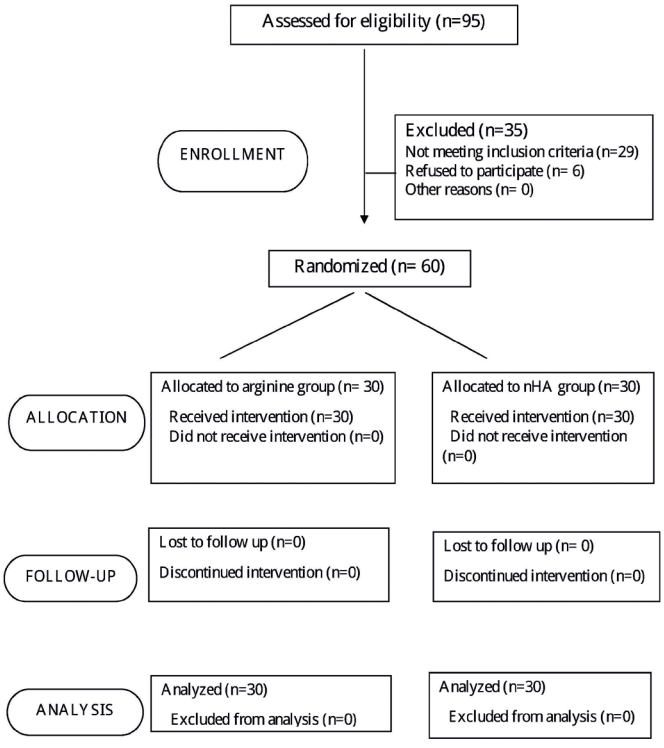

Fig. 3: Consort Flowchart.

Tab. 1: Comparison of baseline characteristics.

	arginine group	nHA group	P value
Chronological age	42.17 ± 7.344	42.33 ± 7.581	0.931[a]
Baseline amperage	6.27 ± 1.530	6.23 ± 1.251	0.927[a]
Gender distribution (males/females)	12/18	13/17	0.793[b]

a) Significance in t-test
b) Pearson chi-square significance

Tab. 2: Descriptive statistics of amperage values.

Group	Amperage reading at	Mean	SD
Arginine group	Baseline	6.27	1.53
	After 5 minutes	8.23	1.68
	After 1 week	9.87	1.48
	After 4 weeks	11.27	1.41
nHA group	Baseline	6.23	1.25
	After 5 minutes	8.27	1.34
	After 1 week	9.93	1.17
	After 4 weeks	11.53	1.33

Tab. 3: Statistical analysis of within group comparison.

Repeated measures ANOVA					
Group		**Paired differences**			
		Mean	**Confidence interval**		**Sig**
			Lower bound	**Upper bound**	
Arginine group	Amperage after 5 min-amperage baseline	1.97	1.65	2.29	.000
	Amperage after 1 week-amperage after 5min	1.63	1.29	1.98	.000
	Amperage after 4 week- amperage 1 week	1.40	1.08	1.72	.000
nHA group	Amperage after 5 min-amperage baseline	2.03	1.82	2.25	.000
	Amperage after 1 week-amperage after 5min	1.67	1.33	2.01	.000
	Amperage after 4 week- amperage 1 week	1.60	1.25	1.95	.000

Tab. 4: Statistical analysis for intergroup comparison.

Electrical stimulus reading	**Arginine group**		**nHA group**		
	Mean	SD	Mean	SD	Significance (independent t-test)
Amperage after 5min-Baseline amperage	1.97	.615	2.03	.414	.624
Amperage after 1week-Baseline amperage	3.60	.932	3.70	.794	.656
Amperage after 4week-Baseline amperage	5.00	1.017	5.30	1.022	.259

BASELINE CHARACTERISTICS (TABLE 1)

Descriptive statistics (mean and standard deviation) of the baseline variables were calculated. The gender distribution in the two groups were analyzed using Pearson chi-squared test which showed no significant difference (P = 0.793).

Independent t-test was done to assess the difference in mean age between the groups and was found to be not statistically significant (P = 0.931). The values were compared using independent t-test. No statistical difference was observed between the two groups (P = 0.927). Thus, the baseline variables of the two groups were comparable in all the characteristics.

WITHIN GROUP COMPARISON (TABLE 2, TABLE 3)

To test the significance of this difference in amperage readings, repeated measures analysis of variance (ANOVA) was used. The significance level was set at 0.05 and Bonferroni correction was applied to eliminate the error factor associated with multiple comparisons. Statistical analysis of intragroup comparison showed that the mean difference was highly statistically significant (P = 0.000) in both groups (Table 3).

INTERGROUP COMPARISON (TABLE 4)

The mean change in amperage values from baseline at 5 minutes, 1 week and 4 weeks between two groups were analyzed

using student t-test. Since there was no statistically significant difference between the two toothpastes at any of the time intervals, the null hypothesis stands accepted.

DISCUSSION

DH is one of the most common painful conditions of vital teeth associated with exposed dentin that affects approximately 33% of the population and is of multifactorial etiology (10). Two treatment modalities are currently utilized to manage this condition. The first is based on the occlusion of patent exposed dentinal tubules, causing alteration of fluid flow and reducing hydraulic conductance (11). The other option is the blocking of pulpal nerve response with ions which reduce intra-dental nerve excitability by depolarization, which interrupts the transmission of pain stimuli (12).

DH is primarily treated with tubular occlusion procedures using cavity varnishes, bonding agents and restorative resins. Although laser therapy has gained some popularity, it has disadvantages like complexity of use and high cost (13). Toothpastes have the benefit of low cost, ease of use and at-home application (14).

Advances in dentifrice technology have focused on creating dentifrices which works by tubular occlusion. One such toothpaste based on Pro-Argin technologyTM has been developed utilizing the physiological action of the amino acid, arginine (5). Another recently available formula is based on nanotechnology, which delivers hydroxyapatite nanocrystals, thereby causing tubular occlusion (6). There have been a number of studies supporting the superiority of arginine and nHA containing dentifrices over the popular desensitizing toothpastes (6, 15). No studies have been reported to date comparing the effect of arginine and nHA containing dentifrices and hence the rationale for the study.

The present randomized clinical trial investigated the effect of two commercially available toothpastes – containing 8% arginine and 1% nHA in reducing DH. As the aim of this study was to compare the reduction in dentin hypersensitivity between the two toothpastes, control group with placebo was not included in the study. Tooth sensitivity was measured using an electrical stimulus which provided an objective assessment of reduction in DH. The methodology consisted of a progressive elevation of the magnitude of the electrical stimulus until a sense of prepain rather than pain was felt. Electric pulp tester was used to utilize the advantage of an objective assessment of DH. Amperage readings were recorded before treatment and at three time points following dentifrice application – at 5 min, 1 week and 4 weeks of treatment. Oral self-care was standardized since brushing technique and frequency has significantly high correlation with hypersensitivity (16). The patients were instructed to brush twice daily for 4 weeks using only the particular dentifrice provided and a soft toothbrush.

There was a progressive increase in amperage values from the preceding appointment at each time intervals tested in both the groups as shown in Table 2. This indicated that both arginine and nHA dentifrices were effective in the reduction of DH, which in turn can be attributed to an increasing degree of tubular occlusion at successive appointments.

Within group comparison of amperage, readings showed statistically significant difference within both the groups (P = 0.000). The progressive increase in amperage values over time is suggestive of a cumulative effect of the toothpastes tested in the reduction of DH. The results showed that both toothpastes provided instant and lasting relief from DH. An interesting finding of our study was a reduction in the difference in amperage values between successive appointments as shown in Table 3. It can be suggested that the highest amount of relief from hypersensitivity is obtained in the immediate phase of dentifrice application.

Furthermore, the nHA group showed consistently higher reduction in DH at each of the time intervals as shown in Table 3. This could be due to the superior remineralization potential of nHA which has been clinically proven. This difference in reduction of DH was however not found to be significant statistically.

In the present study, 79% reduction in DH was obtained by electrical stimulus assessment at 4 weeks with arginine containing dentifrice and was comparable with the results obtained by Kleinberg et al. (5). Docimo et al (17) has reported a reduction of 11–38% only, which is not comparable to the present study. Thomas Schiff et al. (18) as well as Ayad et al. (8) obtained much higher reduction in DH as compared to the 79% reduction in DH in our study. This variability may be due to difference in the stimulus tests applied.

The combination of arginine and calcium carbonate acts by forming a plug that occludes the dentinal tubules. The positively charged arginine is attracted to the negatively charged dentin surface, where it promotes adhesion of calcium carbonate to the dentin surface and deep into the tubules. The association of the arginine and calcium carbonate in situ provides an alkaline environment which encourages endogenous calcium and phosphate ions to deposit and occlude the dentinal tubules (19).

The promising results of nHA toothpaste obtained in our study were substantiated by the studies done by Shetty et al. (20), Michele Vano (14) and Gopinath et al. (21). Using a double-blind, randomized design, Orsini et al. (6) compared a dentifrice containing nHA with potassium nitrate/fluoride dentifrice. In the present study, 85% reduction in DH was obtained by electrical stimulus assessment at 4 weeks which was greater than the findings of Orsini et al. (6). This variability can be attributed to the difference in the methodology followed.

The desensitizing effect of nHA crystals is due to the closure of dentinal tubules with plugs of HA within a few minutes and regeneration of a mineralized layer in a few hours (22, 23, 24). Roveri et al. (23) described deposition of HA on the enamel or dentin surfaces filling the pits and scratches thereby sealing the exposed dentinal tubules. Another reason for the reduced DH experienced by the subjects using the nHA dentifrice could be due to the lower abrasion value in relative dentin abrasivity (RDA) of about 23 compared to dentifrices containing silica (RDA 37.5) (25, 26).

Our study findings confirm the clinical effectiveness of both arginine and nHA containing toothpastes as desensitizing agents. The results are in accordance with several studies using different assessment tools.

However, this study is not without drawbacks. The difference in the readings in the EPT may not necessarily represent remineralization of dentinal tubules alone. A positioning gig would have been ideal to allow accurate reproduction of the site of application of the probe. We have to also acknowledge the inherent difference in response to noxious stimuli between individuals. This might have influenced the results. In addition, as with any prospective clinical trial of this nature, the possibility of Hawthorne effect could have also biased the participants of this study.

CONCLUSIONS

It appears from this study that both nHA based and arginine based tooth pastes are useful in the management of dentin hypersensitivity. Future studies with larger sample size preferably with patient centered quality of life based outcome measurements should be conducted in testing the efficacy of products used to treat dentin hypersensitivity.

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