

An In-Vivo Comparative Study of the Efficacy of Propolis, Nano-Hydroxyapatite and Potassium Nitrate Containing Desensitizing Agents.

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ABSTRACT

Dentin hypersensitivity is an oft encountered dental complaint, the management of which has evolved incredibly but remains an enigma. Nano-hydroxyapatite (n-HAp) is considered one of the most biocompatible and bioactive materials, and has gained wide acceptance in medicine and dentistry in recent years. An increasing number of reports have shown that nano-hydroxyapatite has the potential to remineralize artificial carious lesions following addition to toothpastes, mouthwashes, etc. Recently, occlusion of exposed dentinal tubules by nano-hydroxyapatite, helping to reduce hypersensitivity, has been reported. Propolis, a natural, non-toxic resin produced by honey bees has also been reported to partially obliterate dentinal tubules and can be a good modality of treatment for hypersensitivity. Hence, the aim of this clinical trial is to compare the efficacy of propolis and nanohydroxyapatite dentifrice with benchmark potassium nitrate in controlling dentin hypersensitivity. Forty five patients with a complain of dentin hypersensitivity were recruited. Baseline examination was conducted using tactile and cold stimuli. Patients were randomly divided into three groups.(n=15)

Grp I: Potassium nitrate desensitizing agent

Grp II: Nanohydroxyapatite desensitizing agent

Grp III: Propolis containing agent

A visual analog scale was used to evaluate participants' pain at baseline, one week, and four weeks after the usage of the dentifrices. According to paired t test, all the three desensitizing agents had a significant reduction in the dentin hypersensitivity ($p < 0.01$). According to one way ANOVA, the sensitivity scores were significantly lower in the group II in comparison with group I ($p = 0.03$). However the difference between group I and group III, as well as group II and group III were not significant i.e. $p = 0.63$, $p = 0.21$ respectively. Within the limitations of the study, it can be concluded that nanohydroxyapatite and propolis are a potential treatment modality for dentin hypersensitivity.

Clinical significance: Nano-hydroxyapatite and propolis have proved to be a biocompatible and natural alternative for the treatment of dentin hypersensitivity, respectively.

INTRODUCTION

Dentinal hypersensitivity, or cervical dentinal sensitivity, is an oft encountered and significant clinical problem. It is defined as pain arising from exposed dentine typically in response to thermal, chemical, tactile or osmotic stimuli ^[1].

Dentine exposure may occur via several means of enamel denudation such as attrition, abrasion or erosion. In some individuals the cementum and enamel do not meet and result in dentine exposure as a result of a developmental anomaly [2]. Also, the role of dental plaque in dentin hypersensitivity is unclear.³ In general, it appears that dentinal hypersensitivity is rarely a result of just one of the above factors, but rather a combination of more than one factor.

Dentinal hypersensitivity appears to be a common problem in the age group of 20 -40 years with various reports indicating an incidence of between 4 to 74 per cent of the population [2].

Management of dentin hypersensitivity can be challenging for the dental professional because of the difficulty related to measuring the pain response since the response varies from patient to patient. A plethora of treatment modalities have been prescribed which include invasive therapies like gingival surgery, application of resins, or a pulpectomy [4] and lasers [5].

Non-invasive treatment options are topical agents and dentifrices that contain a desensitizing active ingredient. These are considered to be the simplest, cost-effective, and efficacious first line of treatment for most patients.

According to the literature, the most widely available desensitizing toothpaste ingredient is potassium nitrate.⁶A number of studies have reported the efficacy of potassium nitrate for managing dentinal hypersensitivity. While the Hodosh study was the first to report that potassium nitrate was a “superior desensitizer” this study was not well controlled and it was not until the studies of Tarbet *et al.* that good evidence for the efficacy of potassium nitrate in managing dentinal hypersensitivity was demonstrated. These controlled studies demonstrated that potassium nitrate at a concentration of 5% in a low abrasive toothpaste was able to desensitize dentine for up to four weeks compared to a control paste [7,8].

The mechanism of action of potassium nitrate is the reduction in the dentinal sensory nerve activity due to the depolarizing activity of the K⁺ions which are the active component [7].

Nano-hydroxyapatite (n-HAp) is considered one of the most biocompatible and bioactive materials, and has gained wide acceptance in medicine and dentistry in recent years.⁹ An increasing number of reports have shown that nano-hydroxyapatite has the potential to remineralize artificial carious lesions following addition to toothpastes, mouthwashes, etc [9,10,11,12].

Recently, occlusion of exposed dentinal tubules by nano-hydroxyapatite, and by nano-hydroxyapatite/protein complexes, helping to reduce hypersensitivity, has also been reported [13], although insufficient data is available in literature regarding the desensitizing efficacy of nanohydroxyapatite.

Propolis, also known as bee glue and bee propolis, is a natural non-toxic resin produced by honey bees. It possesses a variety of biological and pharmacologic activities, attracting the interest of an increasing number of researchers [14].

It is a potent antimicrobial, antioxidant, and anti-inflammatory agent. The main chemical elements present in propolis are flavonoids, phenolics, and various aromatic compounds. Flavonoids are well known plant compounds that have antioxidant, antibacterial, antifungal, antiviral, and anti-inflammatory properties [15].

A different research has shown that propolis can control the dental caries, accelerate and facilitate the healing of oral tissue, reduce the pulp inflammation, with no major side effects [16].

Recently it has been reported that propolis showed capacity of partially obliterating the dentin tubules and can be a good option in the treatment of patients with dentin sensitivity [17].

The lack of scientific data comparing these three desensitizing agents, have prompted the need for a study to eliminate the doubts clinically and in literature and evaluate the desensitizing efficacy of potassium nitrate, nano hydroxyapatite and propolis in this clinical trial.

MATERIALS AND METHODS

Patients for the study were recruited from the regular pool of patients visiting the Department Of Conservative Dentistry And Endodontics, Bapuji Dental College and Hospital, Davangere. The study and informed consent forms were approved by the Ethics Committee of the college. Oral and written informed consents were obtained from all participants.

A detailed medical and dental history was recorded by to rule out certain participants. Patients were considered suitable for the study if they had sensitive teeth showing abrasion, erosion or recession with exposure of cervical dentin in atleast two teeth.

Teeth with evidence of pulpitis, carious lesions, defective restorations, cracked enamel, active periodontal disease, active cervical caries or deep abrasions requiring Class V fillings, or had any fractured or endodontically treated teeth or teeth with large restorations, on daily doses of medications or any factor that could be responsible for sensitivity complaints, were also excluded. Other exclusion criteria were professional desensitizing therapy during the previous 3 months, periodontal surgery in the past 3 months, immunocompromised patients; neither pregnant nor lactating women were recruited.

Baseline Screening

A total of 45 patients were chosen and randomly divided into three groups. (Table 1) Dentin hypersensitivity was assessed by a tactile and cold air stimulus. The subject's response was considered as a baseline measurement, according to the visual analogue scale of pain (VAS). Each patient was asked to rate the perception of discomfort after the application of air by a dental syringe, 2 mm away from and perpendicular to the tested surface for 3 seconds and on probing with a sharp dental explorer. Neighboring teeth were isolated during testing using the operator's fingers and cotton rolls.

Table 1: Groups, desensitizing agents and compositions

| Group | Product And Manufacturer | Composition |
|------------------------------|--|-----------------------|
| GRP I Potassium Nitrate | Sensodent -K (Indico Remedies Ltd, Mumbai, India) | 5% potassium nitrate |
| GRP II Nanohydroxyapatite | Acclaim (Group Pharmaceuticals Limited , Malur , India) | 1% Nanohydroxyapatite |
| GRP III Propolis | Custom made toothpaste | 10% Propolis |

Pain Measurement

The measurement of pain was done using the VISUAL ANALOGUE SCALE. The VAS scale consists of a horizontal line, 100 mm long, anchored at the left end by the descriptor "no pain" and at the other end by "unbearable pain." The patients were asked to rate their pain according to the scale in order to mark the severity of their hypersensitivity. The distance of this point in millimeters from the left end of the scale was recorded and used as the VAS score. Patients were accepted entry into the study with a VAS score ≥ 40 mm [18].

The desensitizing agents were prescribed and the instructions to use the pastes were given to the patients (Table 1). All the patients were given the VAS forms and contacted by telephone at each interval to remind them to complete and return the forms. The patients were then evaluated for a period of two intervals ie 1 week and 4 weeks.

RESULTS

Table 2: Mean values of the sensitivity score and p values of one way ANOVA and Post hoc Tukeys test

| Groups | No. | Base line | 1 Week | 4 Weeks |
|--|-------|---------------|---------------|------------------|
| Sensodent K | 14 | 7.1 \pm 1.4 | 5.3 \pm 1.2 | 2.7 \pm 1.4 |
| Nanohydroxyapatite | 14 | 7.5 \pm 0.9 | 5.0 \pm 0.7 | 1.6 \pm 0.8 |
| Propolis | 14 | 7.3 \pm 0.8 | 5.6 \pm 0.9 | 2.3 \pm 1.0 |
| ANOVA * | F | 0.54 | 1.34 | 3.60 |
| | P | 0.59, ns | 0.27, ns | 0.04, Sig |
| Difference between groups (P values)** | 1 - 2 | 0.56, ns | 0.74, ns | 0.03, Sig |
| | 1 - 3 | 0.83, ns | 0.64, ns | 0.63, ns |
| | 2 - 3 | 0.89, ns | 0.24, ns | 0.21, ns |

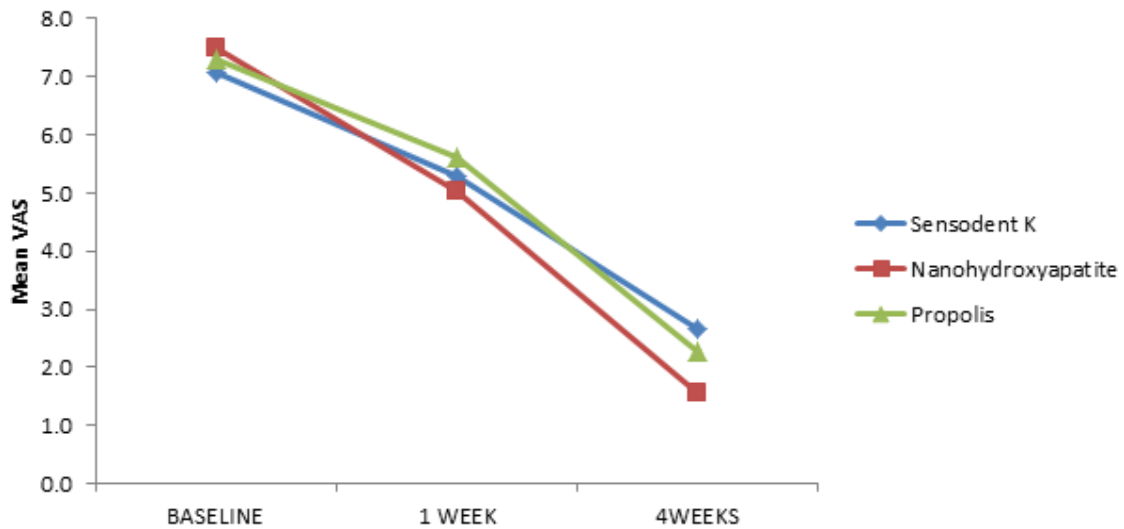
* One way ANOVA

** Post hoc Tukey's Test

According to paired t test, all the three desensitizing agents had a significant reduction in the dentin hypersensitivity ($p < 0.01$). According to ANOVA, the sensitivity scores were significantly lower in the nanohydroxyapatite paste group in comparison with potassium nitrate desensitizing agent ($p = 0.03$). However the

difference between group I and group III, as well as group II and group III were not significant i.e. $p=0.63$, $p=0.21$ respectively.(Table 2) The overall reduction through the evaluation period is shown below.(Graph 1)

Graph 1: Reduction in the mean VAS scores at 1 and 4 weeks.



DISCUSSION

The results of this clinical study showed that all desensitizing agents relatively alleviated DH in response to both tactile and air stimulation within the four-week evaluation period.

Many treatment modalities and agents have been used to treat DH; however, the efficacy of most of them has varied and not been well established. The subjective nature of DH pain makes objective evaluation difficult. In this study, it was found that all of the agents tested were effective in reducing DH, as indicated by VAS scores with large SDs, which reflect the subjective nature of pain perception and the variability of responses over time. Such variability in pain response made it difficult to detect significant differences among groups.

The use of a control group in studies investigating DH can be problematic. A negative control, in which no treatment or placebo treatment is received, is an alternative; however, researchers have argued that the use of a negative control is unethical [19].

Nevertheless, most guidelines recommend that a negative control be included in clinical trials that are conducted to investigate DH [20].

In this study a benchmark control has been used ie potassium nitrate desensitizing agent, which is a well-accepted treatment protocol with sufficient literature support.

Ideally, the evaluation period in the study should have been longer than four weeks; however, it was anticipated that the participants would not be compliant after four weeks.

As the goal of the study was to determine which agents would eliminate the participant's acute complaints of DH rapidly and effectively, we decided to conduct a short-term (four-week) study. It is important, however, that studies be carried out to determine which agents provide long-term relief from DH.

To determine the participants' sensitivity levels in the study the subjective feedback to both tactile and air stimuli was translated into objective data using VAS, which is the most appropriate method used to diagnose pain levels.

To assess pain, we used more than one stimulus as recommended by Holland and colleagues [20].

Their recommendation arose from the fact that different stimuli can elicit different pain sensations. All dental lesions are investigated by using a probe tip as a tactile stimulus, which causes the inward movement of the dentinal fluid owing to the compression of the dentin. Thus, mechanoreceptors causing the painful sensation are activated [21].

Air stimulus decreases the temperature at the dentin surface, causes a rapid outward fluid flow from opened dentin tubules, which stimulates the painful sensation [22].

For these reasons, a standard dental explorer was used as a tactile stimulus and blasts of air as an evaporative stimulus.

To relieve DH, various therapeutic models and agents are recommended, which makes it challenging for practitioners when they are selecting the appropriate therapy for patients. Practitioners can choose between two treatment options: sealing and occluding the dentin tubules, thereby blocking the hydrodynamic mechanism; and blocking neural transmission at the pulp level.

Therefore, the effectiveness of three different desensitizing toothpastes were evaluated, each of which have been reported to be effective in use for the management of dentin hypersensitivity.

Nanoparticle HA- containing toothpastes were first introduced and tested in Japan in the 1980s (e.g. Apadent, Apagard, and others by Sangi Co., Ltd., Tokyo). Since then there have been several studies, including field trials, to test their efficacy in caries prevention, leading to their approval as anticaries agents by the Japanese Government in 1993 [12]. However insufficient data is available in literature regarding the desensitizing efficacy of nano-hydroxyapatite. This study is the first clinical trial comparing the desensitizing potential of nanohydroxyapatite.

In this study, nano-hydroxyapatite toothpaste (ACCLAIM, Group Pharmaceuticals Limited, Malur, India) was used which consists of 1% nanohydroxyapatite crystals. The sensitivity scores significantly decreased in this group when compared to the benchmark potassium nitrate. This can be attributed to the occlusion of the dentinal tubules by the nano-hydroxyapatite crystals and the formation of a protective biomimetic layer which is resistant to acid attack.

Mahmoud et al evaluated the effect of propolis on patients with dentin hypersensitivity. Twenty six patients were evaluated over a period of 4 weeks and pain assessment was done using a modified questionnaire and a numerical scale 0-10. The results between the base line findings and after four weeks were statistically significant. He reported that propolis had a significant effect on dentinal hypersensitivity during the study period and eighty five percent of the subjects were found highly satisfied. However he concluded that further research is needed with double blind clinical trial on a large sample size [23].

In this study, propolis was efficient in reducing the hypersensitivity scores ($p= 0.01$). This can be attributed to the obliteration of the dentinal tubules by propolis.¹⁷

CONCLUSION

Within the limitations of the study, it can be concluded that nanohydroxyapatite and propolis are a potential treatment modality for dentin hypersensitivity.

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