CLINICAL EVALUATION OF IN VIVO EFFECTS OF ORALLY ADMINISTERED CARBAMIDE PEROXIDE BLEACHING AGENT DISPENSED IN TABLET FORM

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Site of Study:	Salt Lake City, UT
Type of Study:	Dental office clinical patient evaluations using characteristic dental measurements
Study date:	October, November 1996
Study Report Date:	December 15, 1996
Study Purposes:	Clinical and scientific study to assess the oral effects of powder pressed tablets containing the active ingredient carbamide peroxide with details on tooth whitening, periodontal health and plaque inhibition.

Abstract:

Carbamide peroxide or urea hydrogen peroxide, CO(NH2)2H202, is a white crystalline powder which has been shown to bleach vital discolored teeth. The purpose of this study was to evaluate the lightening effect of a neutral 10% carbamide peroxide-bleaching tablet administered orally in a dissolving tablet form in vivo. Additionally, evaluations were made regarding periodontal health particularly in posterior regions of the mouth. The effects orally of the biochemical changes were evaluated when introducing carbamide peroxide bleaching tablets. Patient's perceptions of intrinsic cleanliness and subjective comments were recorded to measure acceptability of this route of administration. Taste perceptions, ease of use, convenience and likelihood of continued use were all evaluated. Patient's perceptions of teeth lightening and also objective shade guide measurements using the Vita shade guide system typical for the dental profession were measured and recorded.

Background:

Over the years, different methods have been used to remove intrinsic or extrinsic stains from enamel tooth surfaces.[1,2,3,4] Some of these methods have included applications with concentrated hydrogen peroxide solution (30-35% hydrogen peroxide) and controlled heat, or etching surfaces with phosphoric acid followed by the use of a concentrated hydrogen peroxide solution. These methods were applied professionally by dentists to patients in a clinical environment. In addition, abrasive materials and instruments have also been used to remove surface stain.[2,5] Tooth discoloration can be caused by fluorosis, tetracycline staining, trauma, shade changes as the enamel thins, dentinal darkening and enamel rod absorption of extrinsic stain. Yellowing due to aging is the most common kind of staining. Extrinsic staining due to stain producing food and drinks has also been shown to contribute to the discoloration.

In the past, professional treatment for these discolorations has included crowns, composite resin veneering, porcelain laminate veneers, vital bleaching, and enamel microabrasion. Of all these treatments vital bleaching

[1] Goldstein RE: Bleaching teeth: new materials-new role. *JADA* 115 (Special Issue):44-52,1987.
[2] Strassler H: Update on tooth whitening systems. *J Esthet Dent* 2:156-158,1990.
[3] Levin RP: Home whitening, *Esthet Dent Update* 1:10-12, 1990.
[4] Goldstein CE, *etal*: Bleaching vital teeth: State of the art, *Quintessence Int* 20: 729-736, 1989.
[5] Croll TP, Cavanaugh RR: Enamel color modification by controlled hydrochloric acid-pumice abrasion. I: Technique and examples. *Quintessence Int* 17:81-87, 1986.

is the most conservative. All of these procedures are performed by licensed dentists.

However, patients have become increasingly concerned and better informed about the clinical procedures that relate to aesthetic dentistry, including these extensive and irreversible restorative procedures which would include tooth reduction for the fabrication of crowns and some veneering techniques. These alternate techniques have proven to be expensive as well as irreversible in regards to the reduction of healthy tooth structure to attain the desired cosmetic results. A more conservative approach with less cost has been desired as dentists often evaluate patients with teeth that are normal and vital but are discolored.

Newer techniques for vital bleaching administered by dentists have been advocated to eliminate staining. These newer formulated materials contain the active ingredient carbamide peroxide. These techniques include the fabrication of bleaching trays that conform to the shape of the upper and lower dental arches and the administration of "bleaching gel" given to the patient to take home. A series of bleaching sessions where the gel is placed in the bleaching trays and then placed in the mouth is then performed at home under the direction of the dentist. The carbamide peroxide gel has shown to be successful in lightening teeth in this administration.[6]

It has been reported that at-home bleaching of vital teeth, a technique in which a bleaching agent is applied daily has gained acceptance by many practicing dentists. According to a 1980 use-survey, 66 percent of 9,846 dentists have used such at-home bleaching techniques, and 79 percent of those have recognized the technique's usefulness and overall clinical success.[7]

With the increasing acceptance of bleaching by the dental profession and the history of studies[8] supporting the safety of the active ingredient, carbamide peroxide, it is expedient that a convenient application used continually of the active ingredient be introduced. This study focuses on powder pressed tablet administration of the active ingredient. Tablet administration is a novel and convenient approach to a non-dentist

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[6] Tooth Whitening with At-Home Bleaching Agents: An Update. Strassler H., Weiner

[7] Christensen G, Christensen R: Home-Use bleaching survey, *Clinical Res Assoc Newsletter* 15:2, 1991.

[8] Dr. John Williams, "Topical Therapy of Infections of the Mouth and Pharynx" *Medical Times,* Vol 91, No.4, April 1963.

administered application, which provides the benefits of tooth whitening as well as enhancing periodontal health.

Biochemistry of active ingredient acids are formed in dental plaque subsequent to eating or drinking fermentable carbohydrates such as sugar in foods, beverages, snacks, desserts, sweets, confectionery, etc. Sugars, especially white refined sugar (sucrose), are known to initiate and promote dental canes especially when consumed frequently between meals. It is generally acknowledged that acids formed in dental plaque from sugars (hexoses, pentoses, aldoses, ketoses) will demineralize the tooth surface and produce cavities. Acid formation in plaque occurs within a few minutes after the consumption of sugar-containing foods or sweets. Data have been presented showing 100 times increase in plaque acidity within five minutes after exposure to sugar-containing foods or sweets.[9]

Alkaline compounds, such as sodium carbonate, sodium bicarbonate, ammonium phosphates and similar compounds have been suggested to neutralize plaque acids in order to inhibit the cariogenic potential of dietary fermentable carbohydrates. The soapy taste of alkaline buffers has hindered their general acceptance; in addition their acid neutralizing power fades rapidly because of immediate dilution of saliva.

The active ingredient of the tablet, carbamide peroxide, is decomposed by saliva, salivary lactoperoxidases and bacterial ureases. When introduced into the oral cavity carbamide peroxide immediately starts to release oxygen from the hydrogen peroxide (H202). The low molecular weight of peroxide allows it to travel freely through enamel and dentin. Staining may be due to disturbances in both organic and inorganic tooth formation. The oxygen attaches to the inorganic (stain) material on the teeth. The oxidation of the organic (protein) double bond in the enamel, and outer layers of dentin, may break the stain into smaller molecules. Stains are described as macromolecular aliphatic chains located in interprismatic spaces and cracks. Oxygen bubbling enhances physical removal of the stain. The extended exposure of the cleansing release of the oxygen from the tablets provides a continuous source of fresh oxygen to break down the staining macromolecules. This breakdown produces the desired cleansing and "whitening" effect.

Simultaneously, urea is released into mixed saliva. It diffuses freely on the oral mucosa and penetrates into clusters of microorganisms (or plaque) on the teeth. In the bacterial dental plaque, urea is transformed by the enzyme

[9] Imfeld, Th.: Proceedings of the ERGOB Conference on Health and Sugar Substitutes, Geneva, 1978 S. Karger, Basel p. 218.

urease into ammonia and carbonic acid. Ammonia, a colorless gas, is dissolved in plaque fluid and renders resting plaque highly alkaline, helping to reverse the increase in acidity from the intake of carbohydrates mentioned previously. In other words, plaque acidified by previous intake of fermentable carbohydrates such as sucrose containing foods or snacks will, due to the dissolved ammonia, shift its acidity toward neutrality. This reduction of acidity reduces the rate of tooth surface demineralization and thus the cariogenic potential of the consumed fermentable carbohydrate results in reduction of dental decay.[10] Additionally, the neutral shift is responsible for the reduction of gingivitis and breakdown of the soft tissues surrounding the teeth. The oxygen freed by the action of salivary lactoperoxidase also has an anti-plaque and anti-cavity effect.[11,12]

Eighteen patients that desired an aesthetic color change to either their maxillary or mandibular anterior teeth and premolars were selected for this study. The discoloration conditions that were included for vital tooth bleaching included mild fluorosis, yellowing of the teeth due to aging, discoloration due to tobacco use, extrinsic staining due to coffee and tea consumption and genetically discolored teeth.

Each patient was evaluated for availability to complete the study and compliance with the study requirements. Additionally, each was given an oral cancer examination and a hard and soft tissue examination. Patients who had active periodontitis with gingival pocket depths of 5mm or more were excluded, as well as those who demonstrated unfilled cavities needing extensive routine dental treatment. Patients who demonstrated excessive heavy calculus buildup were also excluded from the study.

Patient selection also included a random selection of age, gender, at-home oral hygiene care and random use of stain producing foods and drinks. Patients were instructed not to change any at their oral habits or diet during the course of the study.

Each patient received a dental prophylaxis to remove supragingival and subgingival calculus and had their teeth polished with a fluoride containing prophylaxis paste (medium grit NuPro, Johnson and Johnson).

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[10] Konig, K...G., Marthaler, T.M., Muhlemann, H.R.: Dtsch, Zahn, Mujnd. u. Kieferhik 29:99, 1958.
[11] Gangarosa, L.P., Ross, M.M.: *Pharmacology of Oxygenating Agents*, Vol. 5, Pharmacology, Toxicology and Therapeutics Groups International Association for Dental Research, Washington, D.C., March 1978.
[12] Brown, E.A., Cruickshank, G. A.,: J. Dent Res. 26: 83 1947.

Patients included in the study could have the presence of thermal tooth sensitivity, gingivitis, existing clinically acceptable restorations, malocclusion, tooth mobility and gingival recession. A health history was taken to rule out any known allergies to peroxide containing compounds.

Each patient was supplied with 60 650mg tablets containing 10% neutralized pH balanced carbamide peroxide by weight in each tablet. Instructions were given to the patient to place the tablet in their mouth and move the tablet around like sucking on a mint until the tablet dissolved. Emphasis of placing the tablet in the labial vestibule between the teeth and labial mucosa was given. Patients were instructed not to swallow or chew the tablets but to let them dissolve slowly in their mouth. Patients were instructed to use 3.5 tablets per day until their supply of 60 tablets was consumed. The patients were instructed to discontinue use in the event of irritation or inflammation. Patients were also instructed to call the office if they had questions or needed to be evaluated. Pre-operative photographs using a Dental-Eye II camera were taken.

Gingival bleeding points spontaneous on probing were evaluated. Ten of the eighteen patients had bleeding on probing between first and second maxillary and mandibular molars. Slight to moderate gingivitis was noted on all of the patients in the study which would be incident to needing a routine six month prophylaxis.

Results

All of the patients returned after the consumption of the 60 tablets. The rate of consumption of the tablets varied from two to three per day, to five or six per day. Final evaluation was made three to four weeks after the study began. After the treatment regiment period, color shade changes were noted by shade lab comparison using the Vita shade guide, and color photograph comparison. Color photograph comparison did not represent accuracy in pre-operative and post-operative shades in all cases. Final shade determination was made using the Vita shade guide.

For the 18 patients in this study there was an average of 1.8 shade change difference, the range being from .5 to 2.5. It should be noted that shade changes were measured within the same hue range as depicted on the shade guide. For example, from an A3 to an Al, the shade change is 2. Recent literature has shown examples of a rearrangement of the shade guide that intermixes the hue colors A, B, C and D. In this case the shade ranges would be from 4 to 12 with the average change being 8.

All patients showed a decrease in inflammation in gingival tissues both anterior and posterior. Nine of the ten patients with gingival bleeding points when probed on initial examination had no bleeding on final examination. All patients indicated that the product was easy and convenient to use. All patients said that they used the tablets in place of breath mints and that the tablets made their mouths feel fresher. All eighteen patients felt the taste was acceptable. Two patients requested other flavors than the mint flavoring. Seventeen of the eighteen patients were satisfied with the results overall. Seventeen of the eighteen patients represented that they saw that their teeth were whiter and that their breath felt fresher. One patient experienced 'irritation to the gums" and took one half as many tablets the next day with no irritation.

Conclusions

1. A pH balanced carbamide peroxide bleaching tablet taken as directed showed measurable lightening of teeth in all cases. The average shade changes were 1.8 using conventional dental shade measurements and 8 using non-conventional measurements.

2. Tablets containing the active ingredient were more convenient than gel application with trays or other routes of administration used in the past.

3. Flavoring of the tablets was deemed acceptable by all participants of the study. One patient requested different flavoring.

4. Gingival inflammation visible upon pre- and post-operative examination had decreased, which is consistent with previous studies. Gingival bleeding points upon probing had been eliminated on those participants who had bleeding at the outset.

5. The best method for assessing shade change was using the comparative shade guide method familiar to dental office procedures. Photographs were not as accurate in all cases in evaluating shade change due to the reflective enamel surface and the type of flash used for clinical photographs.

6. Based upon this data, this method of tooth whitening is a conservative and convenient treatment for tooth discoloration. It may also be concluded that there is a decrease in gingival inflammation, a decrease in gingival pocket bleeding and an overall enhancement of oral health due to the decrease in acidity from the active ingredient in the tablets.