Nightguard vital bleaching: how safe is it?

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The conservative technique for bleaching vital teeth using a nightguard and a 10% carbamide peroxide solution has captured the esthetic interests of the dental profession. The purpose of this article is to assess the safety of the products used in this bleaching technique based on results from past related research and current research. Ten percent carbamide peroxide solutions used in numerous studies have demonstrated tissue-healing properties as well as a propensity for the reduction of plaque and gingivitis. None of these clinical studies revealed any untoward or detrimental side effects, and all demonstrated beneficial effects. Although some concern exists regarding the potentiating effects of peroxide solutions in the presence of known carcinogens, concerns of toxicity or damage to hard and soft tissues appear unfounded. The majority of current and past research and literature indicates that the current use of a 10% carbamide peroxide solution in the method advocated for bleaching vital teeth is apparently safe when administered properly under the supervision of a dentist. (Quintessence Int *1991;22:515–523.*)

Introduction

Tooth bleaching has been reported in the literature as an esthetic treatment option as early as 1898.[1] Conventional bleaching of vital teeth utilizing heat and a strong chemical oxidizing agent has been performed since 1937.[2] Since that time, numerous modifications and improvements in vital tooth bleaching techniques have been reported.[3-15] However, virtually all of these clinical bleaching alternatives involve acid etching of enamel, strong and potentially caustic chemical bleaching agents, and heat. The application of heat is intended to potentiate the oxidizing effects of the bleaching agent and usually is applied directly with a heating element or indirectly with an intense light source.[11,12] Although the merits and efficacy of these conventional vital bleaching techniques are well doc-

umented, the procedures involved typically require multiple patients visits and extended chairtime. Furthermore, conventional bleaching is not without potential risks. Thermal burns, acid burns, or significant soft tissue damage from bleaching agents can result if proper precautions are not heeded. Many studies have addressed the potential for pulpal damage from excessive elevation in temperature,[16-18] as well as the short-term duration of the bleaching effects,[19] the effects of the chemicals on enzymes found in the pulp,[20,21] and the alteration of the surface of the enamel with conventional bleaching techniques.[22,23]

Recently, interest in vital tooth bleaching has experienced a resurgence after publication of an article describing a simplified, at-home bleaching method, "nightguard vital bleaching."[24] The basic clinical technique involves the use of a soft, plastic, nightguard-styled prosthesis filled with a commercially available 10% carbamide peroxide solution (Proxigel, Reed & Carnrick) to bleach vital teeth. A typical example of the effectiveness of this bleaching process is shown in Fig 1. Since the introduction of this treatment option, many new bleaching materials have been introduced and much new knowledge has been gained.[25-27] The purpose of this article is to provide an update on the most current information available regarding the safety of nightguard vital bleaching.

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Fig 1 Typical results of nightguard vital bleaching technique. The maxillary arch originally matched the mandibular teeth and the shade tab.

Materials overview

Although the initial report on nightguard vital bleaching introduced 10% *carbamide* peroxide as a bleaching agent, currently there are two classes of peroxides being used for nightguard vital bleaching: hydrogen peroxide and carbamide peroxide (synonyms: urea peroxide, hydrogen peroxide carbamide, or perhydrolurea[28]). Hydrogen peroxide has been used in dentistry for more than 75 years in a 30% to 35% concentration for in-office bleaching techniques. These in-office techniques typically involve use of a heavy rubber dam, acid etching of the enamel, and heat or light to potentiate the bleaching action of the hydrogen peroxide applied topically to the tooth.

The original and still predominant type of material used for nightguard vital bleaching is carbamide peroxide. Historically, 10% carbamide peroxide preparations have been used for intraoral treatment of minor oral inflammations, such as canker sores, denture irritations, and post–dental procedure irritations. Carbamide peroxide is applied directly to the tissue sites four or more times a day and allowed to remain in situ for 2 to 5 minutes before the patient expectorates. In the current bleaching application, a closely adapted nightguard-styled prosthesis keeps the carbamide peroxide preparation in contact with the teeth.

Carbamide peroxide solutions are very unstable and immediately disassociate into their constituent parts on contact with tissue or saliva.[29] The 10% to 15% carbamide peroxide solutions disassociate into 3% to 5% hydrogen peroxide and approximately 7% to 10%

urea.[29] The hydrogen peroxide further degrades into oxygen and water, while the urea degrades into ammonia and carbon dioxide.[30] The 10% to 15% carbamide peroxide preparation is, along with 1.5% and 3% hydrogen peroxide, classified as an "oral antiseptic" by a US Food and Drug Administration (FDA) monograph of 1988.[31] In this monograph, these concentrations of carbamide peroxide and hydrogen peroxide are classified in "Category I," which is "generally recognized as safe and effective, and not misbranded." Consideration of the carbamide peroxides by the FDA began with the call-for-data *Federal Register* of 1973 and includes the same classification (safe and effective) as the tentative final monograph of July 26, 1983, for "OTC oral mucosal injury drug products" and the final ruling of July 18, 1986, by the same title.[31] According to the FDA guidelines under which this class of "oral antiseptics" were originally accepted, all are safely handled by the body when used in the manner described.

A better understanding of the composition and actions of the various carbamide peroxide materials available for bleaching teeth may be gained by examining the now-expired patent of one of these over-the-counter materials. Proxigel was introduced as an oral antiseptic, primarily competing with the long-standing, successful oral antiseptic, Gly-Oxide (Marion Merell Dow, Inc). The composition of Proxigel, as listed on the package, is (active ingredient) 10% carbamide peroxide and (inactive ingredients) Carbomer 940, glycerin, flavors, phenacetin, phosphoric acid, and Trolamine. The term inactive means that the company is not making any claims to the FDA about the action of those ingredients. The composition of Gly-Oxide, as listed on the package, is 10% carbamide peroxide, citric acid, glycerin, flavor, propylene glycol, sodium stannate, water, and other ingredients.

The ingredients in Proxigel, by patent, are urea peroxide, 11.00 wt%; carboxypolymethylene polymer (Carbopol 940, BF Goodrich Co), 0.60 wt%; phenacetin, 0.05 wt%; mixed flavor, 0.05 wt%; triethanolamine (Trolamine), 0.40 wt%; and anhydrous glycerol, 87.90 wt%. As stated in the patent, Proxigel may be described as follows: "The purpose of this product (Proxigel) is to sustain the release of nascent oxygen (obtained by use of carboxypolymethylene polymer, Carbopol, to *thicken the material, improve tissue adherence, and prolong release of oxygen)* as compared to the release of oxygen of a urea peroxide in glycerol"[32] (Gly-Oxide–like material). According to the patent data, Proxigel required almost 3 to 4 times as

much time to release 94% of the oxygen as the urea peroxide in glycerol solution (Gly-Oxide–like material), which occurred mostly in the first 30 minutes. This change to a thicker, more adhesive, slower oxygen-releasing material by the addition of Carbopol was designed to enhance the antiseptic action of the material in its original use.

In light of this distinction, virtually all the present carbamide peroxide bleaching agents may be divided generically into two classes based on the presence or absence of Carbopol. The ingredients of the various commercially available solutions have been listed previously.[33] Based on this information, the solutions appear to fall into two classes, according to this compositional difference:

1. Ten percent carbamide peroxide solutions with Carbopol (slow oxygen-releasing):
   Proxigel
   Dentl-brite (Cura Pharamceutical)
   Rembrandt (Den-Mat Corp)
   Ultra-lite (Ultra Lite, Inc)
   Opalescence (Ultradent Products, Inc)
2. Ten percent carbamide peroxide solutions without Carbopol (fast oxygen-releasing):
   Gly-Oxide
   White & Brite (Omni International)
   Denta-Lite (Challenge Products)
3. Fifteen percent carbamide peroxide solution:
   Nu-Smile (M & M Innovations)—originally made without Carbopol, but later solutions contain Carbopol

The solutions containing Carbopol are slow oxygen-releasing solutions, while those without Carbopol are fast oxygen-releasing solutions. The rate of oxygen release of the solution affects the frequency of its replacement during bleaching treatment. The fast oxygen-releasing solutions appear to release a maximal amount of oxygen in less than 1 hour, while the slow oxygen-releasing solutions require 2 to 3 hours for total oxygen release.[32] Also, the thixotropic nature of the Carbopol results in better retention of the slow-releasing solutions in the nightguard, with the result that less bleaching solution is required for treatment (approximately 1 to 2 oz per arch). Because Carbopol retards the rate of oxygen release, it also reduces the effervescence of carbamide peroxide bleaching materials. Our initial clinical experience indicated that a more effective result was obtained with the Carbopol-containing material than with the regular carbamide

peroxide, when the solutions were used at night only. This would suggest that either the ability of the solution to remain in the guard longer or the slower release of oxygen over time improves the efficacy of the technique.

In addition to the two classes of 10% carbamide peroxide bleaching agent, carbamide peroxide solutions are also available in a 15% concentration (Nu-Smile). The higher percentage of carbamide peroxide (the maximal concentration approved for oral antiseptics in the FDA monograph[31] citing the 1979 report) is intended to result in the availability of a greater amount of hydrogen peroxide for the bleaching process. According to the inventor of this product, the original formulation did not contain Carbopol; however, the latest version is reported to contain Carbopol (Maddry G: Personal communication). There are also even higher concentrations of carbamide peroxide (35%) advocated for in-office bleaching techniques (Quickstart). These should be used with a rubber dam or a tissue-protecting guard to prevent burns of the soft tissue. Thirty-five percent carbamide peroxide is effectively 10% hydrogen peroxide. Hence, these in-office solutions are not as caustic as the conventional 30% hydrogen peroxide solution originally used for in-office bleaching. Differences in bleaching efficacy among the various carbamide peroxide solutions are not fully known.

Recently, concentrations of *hydrogen* peroxide solutions less than the original 30% to 35% solutions have been advocated for use in at-home techniques, both with the nightguard delivery system and without it. Currently, most of these hydrogen peroxide solutions are in a gel form, and range from 1% to 10% in concentration according to manufacturer's information:

One percent to 10% hydrogen peroxide solutions (at-home use):
   Peroxyl (1.5% gel solution) (Colgate-Hoyt Laboratories)
   Brite Smile (1% to 10% solution) (BriteSmile Systems, Inc)
   Natural White (6% gel solution) (Aesthete Laboratories)

Thirty percent to 35% concentrations of hydrogen peroxide, similar to conventional bleaching preparations, are also now available in a gel form (Starbrite). These gels are intended for conventional in-office bleaching procedures (with a rubber dam), but are

much easier to administer and control than are the original fluid preparations. They are advocated for use without heat or prior acid etching of the enamel. No determination has been made to date regarding their efficacy compared to conventional 35% hydrogen peroxide solutions used with heat or light and with or without etching of the enamel. Examples of these higher concentrations are as follows:

Thirty-five percent hydrogen peroxide solutions (in-office use):
  Superoxol (35% watery solution) (Union Broach Co)
  Starbrite (35% gel solution) (Starbrite Laboratories)
  Accel (35% solution) (BriteSmile Systems, Inc)
  Denta-Lite Plus (25% solution) (Challenge Products)

Mechanism of action

It has long been determined that peroxide solutions flow freely through enamel and dentin.[34-39] This free movement is due to the relatively low molecular weight of the peroxide molecule (30 g/mol).[35] The mechanism of action of the bleaching agent, hydrogen peroxide, is hypothesized to be oxidation of pigments in the tooth.[39,40] This process is different from the action of preparations or materials such as hydrochloric acid, which decalcifies the superficial 15% of the enamel surface[40] and is used to remove stains physically.[40,41]

Carbamide peroxide ultimately breaks down into water, oxygen, and urea. It has been shown that urea also moves freely through both enamel and dentin.[42] Urea also has a low molecular weight (64 g/mol),[35] and has been studied as a mouthrinse because of its effects on bacteria, plaque, and pH.[43] Studies at the University of North Carolina have shown that a carbamide peroxide bleaching solution will bleach laterally under covered surfaces, potentially making bleaching effective even under existing esthetic restorations.[44] The freely diffusible nature of the low–molecular weight peroxide and urea ions through enamel and dentin may account for the transient pulpal sensitivity occasionally experienced by some patients. However, knowledge of how easily these materials pass through tooth structure reduces the concern for pretreatment replacement of potentially leaking restorations or treatment of exposed root surfaces.

Effects on teeth

The most common side effect encountered during nightguard vital bleaching is mild sensitivity of the teeth to temperature changes. This thermal sensitivity is most frequently experienced in the first hour after removal of the loaded nightguard or during the early treatment stages.[24] This sensitivity is usually transient and appears to be dose related. It is now attributed to the freely diffusible nature of the material,[44] rather than to the pH of the solution.

Studies have demonstrated cellular changes in enzymes in the pulp from the use of 35% hydrogen peroxide with conventional in-office bleaching techniques and in laboratory tests.[20,21] However, no clinical significance has been attributed to these changes. Pulpal histology has not been assessed to date regarding materials used for nightguard vital bleaching techniques. Although long-term effects of carbamide peroxide treatments on the pulp are unknown, more than 75 years of conventional, in-office bleaching using a much more concentrated (35%) hydrogen peroxide solution with heat or light has not resulted in pulpal necrosis except when the tooth was overheated or traumatized.[11-13,16,17] This long-standing observation appears to support the current clinical observation that controlled nightguard vital bleaching with considerably milder carbamide peroxide preparations is safe to the pulp.

Initial concerns regarding the nightguard vital bleaching technique and different bleaching products involved the composition and pH of the solutions. Although not all products have been tested, the over-the-counter 10% carbamide peroxide materials (Proxigel and Gly-Oxide) contain trace amounts of both phosphoric and citric acids. These mild acids are reportedly present in minute amounts to help stabilize and preserve the materials. Initial concerns existed regarding the potential of these materials to etch enamel. However, this phenomenon has not been observed clinically or in laboratory tests.[44,45] More recent studies conducted at the University of North Carolina have shown no indication of either etching or significant change in surface morphology of enamel when evaluated under a scanning electron microscope at magnifications of $\times 100$, $\times 200$, $\times 1000$, and $\times 4000$ after a 6-week treatment with various bleaching agents. These included the 10% carbamide peroxide preparations, Proxigel (pH 5.3), Gly-Oxide (pH 7.2), and White & Brite (pH 6.6), as well as a hydrogen peroxide–containing material, Peroxyl (pH 4.6).[46,47] Also,

clinical observations through 75 years of bleaching with 35% hydrogen peroxide solutions have never revealed any detrimental effect on enamel surface texture.[11-13,15] Initial data from research in progress at the University of North Carolina indicate that subsurface enamel hardness does not appear significantly to be affected either.

Concern regarding the bleaching solutions with a lower pH was based on reports that the demineralization process of enamel begins when the pH falls below the "critical" pH of 5.2 to 5.8.[48-50] The pH necessary to demineralize the root surface also has been reported as different from that necessary to demineralize enamel; root surfaces require only a pH of 6.0 to 6.8.[51,52] However, no evidence of this process has been noted to date in any clinical trials or laboratory tests.[27,44,45] One explanation for this finding may lie in the breakdown products of the urea from the carbamide peroxide. The ammonia and carbon dioxide released on degradation of the urea appear to have the effect of elevating the pH.[30] Stephan[30] reported that the application of urea raises the pH of plaque material, even in the presence of carbohydrates, to as high as 9.0. Saliva normally contains a small amount of urea (0.02%), but not enough to inhibit the carious process. When applied to teeth, concentrations of urea higher than 1% not only furnish a sufficient amount of ammonium carbonate to neutralize the acidic effects of carbohydrates, but also markedly inhibit the production of acid by plaque.[30] Urea also inhibits the fermentation of carbohydrates and formation of lactic acid in plaque.[30,53] A 2-minute application of either a 1% solution or a 10% solution of urea has been shown to elevate the pH above the initial pH for 40 and 90 minutes, respectively, with no drop in pH below the initial pH during that time.[30] The immediate degradation of carbamide peroxide solutions on exposure to oral fluids with a concomitant rise in pH from the urea breakdown into ammonia and carbon dioxide appears to make the actual measured pH of the nascent solution clinically inconsequential.

Another factor related to the absence of enamel etching observed clinically may be the patient's oral condition. It has been shown that a fluoride concentration of 2 ppm at pH 4.5 is sufficient to effectively inhibit demineralization,[54] and that lesser concentrations partially inhibit the demineralization process as well. Hence any amount of fluoride present in the tooth will lessen the potential for demineralization. Therefore, the absence of perceptible damage to the enamel appears to be related to the fact that (1) the pH of the bleaching solution rises rapidly upon exposure to oral fluids and is related to the concentration of the urea that is present, and (2) demineralization is inhibited by the fluoride concentration in the tooth.

The only remaining concern relative to effects on the enamel concerns the bond strength of subsequently placed composite resin restorative materials. Titley et al[22] reported a decrease in bond strengths of composite resin to enamel of teeth bleached with 35% hydrogen peroxide. However, this phenomenon has only been recently investigated regarding nightguard vital bleaching techniques or solutions. Preliminary data at the University of Texas have indicated an initial decrease in bond strengths of composite resin to etched enamel immediately after nightguard bleaching. However, the bond strengths approach normal after 7 days. This initial reduction is attributed to the residual oxygen in the bleached tooth surface, which inhibits the polymerization of the composite resin.[55] Further studies should be forthcoming.

Effects on restorative materials

No significant color changes in composite resins, crowns, or other esthetic restorative materials have been noted to date as a result of nightguard vital bleaching other than those purely related to the removal of extrinsic stains. If restorations of this type are present in esthetically critical areas, they may need replacement for reasons of color matching following successful bleaching of the teeth. Superficial extrinsic stains on or around existing composite resin restorations may be removed to some degree. However, the actual intrinsic color of the composite resin does not appear to be appreciably altered by any of the bleaching solutions. Because these solutions travel laterally through enamel and dentin, bleaching portions of the tooth covered by existing composite resin or porcelain restorations may give the clinical impression that the material has lightened. However, this effect is primarily a result of superficial cleansing of the restoration and a lightening of the underlying tooth structure, not an intrinsic color change of the restorative material itself.[27] Another recent report substantiates the claim that there is no noticeable effect on either surface texture or color of restorative materials such as porcelain, composite resin, amalgam, or gold.[45]

Effects on soft tissue

Although soft tissue problems are infrequently en-

countered, the most common ill effect noted by patients is a minor ulceration or irritation of gingiva or mucosa during the initial course of treatment.[24] This infrequent occurrence has been described by patients as mild and transient. Often, the only treatment needed is a reduction in the time of exposure to the bleaching medium.[27] If the tissue irritation continues because of an apparent inflammatory response to one of the preparation's components, treatment should be discontinued and other alternatives pursued. Most irritations appear to involve the nightguard itself and are rarely due to chemical irritation. Cessation of treatment for 1 or 2 days, along with minor adjustments of the nightguard, usually alleviates the problem.

There have been no clinical reports of other significant tissue problems, odors, or particularly bad tastes associated with the procedure. Earlier reports indicated possibilities of a sore throat.[56] However, according to the originator of one of the products, this phenomenon was later found to be related to some materials containing a cinnamon flavoring, to which a small percentage of the female population was allergic (Archambault G: Personal communication). Most of these problems resolved following a change in formulation by the manufacturer.

Almost routinely, patients report having a fresh taste in their mouth following removal of the nightguard, and a "squeaky clean" texture to their teeth. This supports the observation cited in earlier works on the beneficial effects of urea as a plaque-reducing mouthwash.[30,57] Initial concerns regarding the occurrence of black hairy tongue,[56,58] reported to be associated with hydrogen peroxide rinses, have not materialized regarding the bleaching agents used for nightguard vital bleaching. However, for those few patients who may experience soft tissue irritation because of chemical sensitivity, the ability to continue treatment is compromised, and dosage (exposure time) should be reduced or treatment suspended.

Biologic concerns

The remaining area being evaluated for safety considerations is biologic concerns. These concerns must be compared to those for other commonly used dental materials, such as eugenol, periodontal dressings, denture resins, composite resins, cements etc. Studies now completed at Austin College have clearly demonstrated that the cytotoxicity of 10% carbamide peroxide (Proxigel and Gly-Oxide) on mouse fibroblasts (L929) is in the same range as that for IRM, zinc phosphate

cement, Tempbond temporary cement, Plax, Scope, Cepacol, and Crest toothpaste — all of which are used on a routine basis in dentistry today, typically without reported problems.[59]

Concern also has been expressed regarding the potential for soft tissue changes as described in a study by Weitzman et al.[60] However, in this study, the peroxide evaluated was either 3% hydrogen peroxide with DMBA, a known carcinogen associated with smoking, or 30% hydrogen peroxide (Superoxol) with and without DMBA. The assumption was that these chemicals would be used for the life of the patient on a regular basis. All the solutions with DMBA developed carcinomas in hamsters, while the 30% hydrogen peroxide solutions alone did not. Three percent hydrogen peroxide alone was not tested. According to the author,[56] these data cannot be extrapolated to include carbamide peroxide solutions used in the bleaching technique, because of (1) the different composition and percentage of the carbamide peroxide from the hydrogen peroxide that was tested, (2) the short treatment period of the bleaching treatment compared to a lifetime of use, and (3) the limited tissue contact of the carbamide peroxide as compared to a frequently administered rinse. However, it is prudent to encourage persons undergoing active bleaching treatment to refrain from smoking, both for the staining potential as well as the carcinogenic potential of DMBA in the mouth.[61] Other studies relating carcinogenesis with chemicals in the peroxide group have been concerned more with the other derivatives of the peroxides, such as benzoyl and lauroyl peroxides,[62] than with the hydrogen or carbamide peroxide itself.

Systemic effects

Early studies on the use of 10% carbamide peroxide solutions in anhydrous glycerine focused on its use as an oral antiseptic and irrigant. Numerous studies have shown the beneficial effects of carbamide peroxide in plaque reduction and wound healing, with no reported side effects.[63–71] Other articles have reviewed the safety of 10% carbamide peroxide in these various studies.[29,72] Dickstein[63] evaluated 10% carbamide peroxide as an agent in the treatment of thrush in 25 newborn infants. Ten drops of 10% carbamide peroxide were placed directly onto the tongue 10 minutes after each feeding. Treatment success averaged 4 days for resolution of the infection (range of 2 to 7 days) compared to 2 to 8 weeks healing time required when there was no intervention. Carbamide peroxide was

considered safe and effective in this treatment of infants.

Zinner et al[64] studied 64 patients (aged 15 to 55 years) with tuberculosis. Subjects were instructed to rub the 10% carbamide peroxide on the gingiva for 2 minutes, three times daily, for 1 month. This treatment resulted in a significant reduction in gingivitis, and no untoward side effects were reported. Twenty-two patients, aged 5 to 40 years, who had cerebral palsy were treated in a similar manner for 2 months with a similar result.[64] No deleterious side effects were observed in either portion of the study, and benefits resulted in both.

In another study by Zinner et al,[65] 94 patients, aged 19 to 54, applied 10% carbamide peroxide four times a day in a continuous line to the maxillary and mandibular gingiva adjacent to the teeth. Patients swished the solution in the mouth for 1 minute, then expectorated the excess. Patients were instructed to refrain from eating or drinking for 20 minutes following administration of the solution. After 20 days, a significant reduction in gingivitis was noted, and no side effects were observed in any of the test subjects.

Fogel and Magill[66] evaluated 33 orthodontic patients, aged 8 to 18, who applied a minimum of ten drops of carbamide peroxide liquid per application to the teeth along the gingiva in the maxillary and mandibular arches. Subjects were instructed to swish the resultant foam in the mouth for a minimum of 3 minutes then brush with the residue without rinsing. This regimen was conducted four times a day for 3 years. A significant decrease in caries incidence was noted. There was no evidence of black hairy tongue as a result of prolonged use of aqueous peroxides, nor were any other deleterious side effects observed.

Shipman et al[67] observed 25 hospital patients who used 2-minute direct applications of 10% carbamide peroxide solutions three times a day for 1 month. Urea peroxide (carbamide peroxide) significantly reduced plaque scores, although gingival inflammation scores were not significantly affected because of the debilitated nature of the patients involved in the study. No ill effects were reported. The solutions were subsequently recommended as an adjunct to personal oral hygiene care.

Tartakow et al[68] followed 60 orthodontic patients, aged 10 to 17 years, as they applied a 10% carbamide peroxide preparation to the gingiva above all the teeth. Subjects were to swish the resultant foam around in the mouth for a few minutes and expectorate the excess four times a day for 3 months. This regimen resulted in a reduction of the edema and redness of inflamed gingival tissues and improvement in gingival contours. No adverse effects were noted in the test group.

In a study by Williams,[69] 58 patients from 1 to 19 years of age were treated with carbamide peroxide solutions for infections of the mouth and throat for 3 to 7 days with positive results. The preparation administered was considered nontoxic and side effects were described as minimal and transitory.

Shapiro et al[70] tested 94 dental students, aged 19 to 25, as they applied the 10% carbamide peroxide solution to their teeth and gingiva for 2 minutes, without rinsing for 5 minutes afterward, twice daily, for 6 month's treatment time. A significant reduction in plaque scores was observed, and there was no evidence of untoward side effects on the gingiva, mucosa, tongue, cheeks, or the dentition. No observable systemic side effects in any of the subjects were reported in the course of the study.

Reddy and Salkin[71] studied 69 dental students from 20 to 30 years of age who used daily rinses of carbamide peroxide for 3 weeks but no other oral hygiene measures. A significant reduction in gingivitis was noted, and no adverse side effects were reported.

Animal studies recently conducted in collaboration between Austin College and the University of North Carolina have indicated the median lethal dose for 10% carbamide peroxide (Proxigel, Gly-Oxide) in mice to be from 87.18 to 143.83 mg/kg.[59] When extrapolated for a human 75 kg in weight, the median lethal dose for 10% carbamide peroxide solutions would be 6.5 to 8.0 L. Vital bleaching with the nightguard technique typically requires only 1 to 2 oz of solution over several weeks. Therefore, a wide margin of safety is afforded in this regard. These animal studies also have determined that there is no potential for mutagenicity of cells after ingestion of 10% carbamide peroxide.[59] This finding is in contrast to that for eugenol, which has been found to cause some cellular changes, but is still considered nonmutagenic.[73] The only systemic concern that has been noted by a manufacturer of one of the over-the-counter products (Gly-Oxide) in more than 40 years is that overuse can result in a mild laxative effect because of the glycerine base.

Summary

Recently, interest in vital tooth bleaching has experienced a resurgence. A recently introduced bleaching method referred to as nightguard vital bleaching involves the use of a soft, plastic, nightguard-styled

prosthesis filled with a commercially available 10% carbamide peroxide solution (Proxigel) to bleach vital teeth.

Although there is some concern for the potentiating effects of peroxide solutions in the presence of known carcinogens, the majority of current and past literature and research indicates that the current use of a 10% carbamide peroxide solution in the nightguard method advocated for bleaching vital teeth is as safe as most other esthetic treatment alternatives administered to patients on a routine basis.

Acknowledgments

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