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Carbamide Peroxide and Its Use in Oral Hygiene and Health

Abstract: Plaque accumulation, dental caries and periodontal disease are an increasing concern for elderly, special care and orthodontic patients as a result of numerous predisposing factors which make maintenance of adequate oral hygiene difficult, even with traditional oral hygiene practices. This article will propose a technique whereby the anti-bacterial properties of tray-applied carbamide peroxide are used to improve oral health for these patients.

CPD/Clinical Relevance: Traditional oral hygiene practices may be unsatisfactory for elderly, special care and orthodontic patients. This article proposes a technique whereby the anti-bacterial properties of tray-applied carbamide peroxide are used to improve the oral health for these patients.

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Whilst it is apparent that, for dental patients with low to moderate caries risk and low to moderate risk of periodontal disease, a low sugar diet, brushing with fluoridated toothpaste and interproximal cleaning should be adequate to maintain oral hygiene and plaque removal,[1] there is a group of higher risk patients where, due to predisposing factors, an additional member of the 'preventive toolkit' would be beneficial.

Who is a higher risk patient?

Elderly

Latest population data by the UK Parliament (2016)[2] shows that, by 2020, the number of individuals over 85 will rise by 18%. With more patients than ever retaining their teeth, it is evident that older patients will take up a greater proportion of dental clinicians' care. Many elderly patients suffer from oral health challenges. In particular, polypharmacy and side-effects from multiple medications, results in elderly patients suffering from a reduction in salivary flow and a dry mouth. In addition, degenerative and inflammatory changes result in many patients experiencing reduced manual dexterity. This results in difficulties in oral hygiene and plaque removal which may lead to dental caries, especially root surface caries (Figures 1, 2 and 3). This is especially pertinent for elderly patients with heavily restored dentitions and secondary decay adjacent to direct and indirect restorations.[3] These patients, who may have had excellent dental treatment and hygiene practices throughout their lives, would be at high risk for dental diseases in their later years.[4]

Special care patients

Special care patients are '*individuals and groups in society who have a physical, sensory, intellectual, mental, medical, emotional or social impairment or disability or, more often, a combination of a number of these factors*'.[5] These patients are at risk of oral disease for numerous reasons:

- Xerostomia;
- Medication side-effects;
- Compromised immune systems;
- Impaired manual dexterity and physical challenges: Parkinson's disease,[6] stroke[7] and advanced age;[8]
- Mental challenges: Alzheimer's disease;[9]
- Carers' attitude to oral healthcare;[10]
- Radiation-induced xerostomia

Orthodontic patients

Orthodontic patients are at risk of enamel demineralization, caries and periodontal disease. This may be due to:

- Increased difficulty in maintaining cleanliness of fixed appliances;[11]
- Increased plaque retention;
- Alteration in plaque composition becoming more anaerobic.[12]

It would seem that further chemotherapeutic agents would be

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Figure 1. Early root caries present on the UR1. This is a common presentation amongst elderly and special care patients.

Figure 2. Gingival recession and root caries on LR4, LR5 and LR6.

Figure 3. A root caries lesion on the LL4.

Figure 4. It is essential that, on delivery of the custom tray to the patient, the clinician demonstrates effectively the correct application of carbamide peroxide, to minimize side-effects associated with incorrect application.

beneficial for the described patients as mechanical means alone are insufficient. The chemotherapeutic agent would ideally demonstrate anti-cariogenic, antibacterial and antiplaque properties whilst being safe to use and demonstrating minimal side-effects. The use of carbamide peroxide (CP) as a chemotherapeutic agent may be useful for improving the oral health of the category of patients listed above.

Carbamide peroxide: a history of whitening?

Since its first publication by Van Haywood and Heymann in 1989,[13] tray-applied 10% carbamide peroxide (CP) has proven itself as a safe and effective way to whiten teeth. However, CP, also known as urea peroxide, was initially used as an oral antiseptic agent.[14] Several studies in the early 70s demonstrated its effect on plaque control and gingival inflammation,[15-19] whilst another study by Fogel and Magill, in 1971,[20] demonstrated carbamide peroxide's ability to prevent white spot lesions and reduce dental caries significantly. The oral antiseptic use of CP was what lead to the incidental discovery of tooth whitening by Dr Bill Klusmeier in 1968.[14]

The mechanism behind the prophylactic effect of carbamide peroxide

Dental caries

Ten percent carbamide peroxide applied in custom-fitted trays has been shown to increase plaque pH to a mean peak of 8.06 and remains significantly higher than baseline 2 hours after application. Furthermore, saliva flow and saliva pH was also shown to increase above baseline following the two hour wear of CP in custom trays.[21]

The critical pH value for demineralization of enamel and dentine to occur is 5.2–5.7 and 6.0–6.5, respectively.[22] The elevation of plaque and saliva pH above these values is what has presumably reduced demineralization and caries rates.

The carbamide peroxide effect on cariogenic bacteria may also affect dental caries. Deng *et al*[23] demonstrated that hydroxyl radicals released from both hydrogen and carbamide peroxide *in vitro* react with bacterial membrane lipids and DNA, thus causing bacterial cell death. Furthermore, an *in vivo* and *in vitro* study by Bentley *et al*,[24] investigating the effect of CP on cariogenic bacteria, found that *in vitro* 10% CP could inhibit *Streptococcus mutans* and *lactobacillus*. However, the *in vivo* study found that only reduction in salivary *lactobacillus* were demonstrated, with salivary levels of *Streptococcus mutans* not being affected. This was attributed to hydroxyl radicals released by carbamide peroxide having no effect on the aerobic *Streptococcus mutans.*

Gingival health

In 2003, an *in vivo* study by Almas *et al*[25] demonstrated that, following application of 10% CP in custom trays, a reduction in bleeding on probing, Plaque Index and Gingival Index scores was observed. However, no appropriate controls were used.

In 2004, a double blind, randomized, controlled, parallel group clinical trial by Brunton *et al*[26] demonstrated that self-application of CP (at a concentration of 16–18%) resulted in a statistically significant reduction in gingival scores ($P < 0.001$).

Zinner *et al*[27] proposed that alterations in plaque microflora, the debridement properties of peroxides and the ability of the CP to increase availability of oxygen thus promoting tissue healing, resulted in a reduction in gingivitis.

Chlorhexidine gluconate vs carbamide peroxide

One of the most common antimicrobials prescribed for patients unable to maintain adequate oral hygiene and plaque control is chlorhexidine digluconate (CHX). This stems from its excellent substantivity resulting in activity for several hours.[28] However, the recent incidents of chlorhexidine hypersensitivities,[29] coupled with the well-known side-effect of extrinsic staining following prolonged use, have brought into question its validity as a prolonged antimicrobial agent.[30]

Carbamide peroxide may

have properties similar or even superior to that of CHX. An *in vitro* study in 2013, by Yao *et al*,[31] showed that 10% CP bleaching agent demonstrated a superior bactericidal and dislodging effect on oral biofilm cultured within an *in vitro* anaerobic model compared to a control and 1% chlorhexidine solution. However, further additional research, such as *in vivo* split mouth studies, are required to demonstrate the comparison between CP and chlorhexidine solution further.

Additionally, 10% CP in a custom-fitted tray worn overnight, especially in carbopol-containing products, has substantivity of over 10 hours, which is similar to the 12 hours of substantivity associated with chlorhexidine mouthwashes.[32,33]

Van Haywood[4] described a protocol whereby the combination of both therapeutic agents could be utilized. This involved a 30 second wash of chlorhexidine prior to bedtime followed by the overnight tray application of 10% CP. The obvious benefit of this protocol is the reduction of extrinsic staining associated with chlorhexidine. However, an additional improved antimicrobial efficacy would also be observed, resulting from CP effectiveness at reducing *lactobacillus* propagation and chlorhexidine's effectiveness at reducing *S. mutans* propagation.

Clinical protocol

The following protocol is based on that suggested by Lazarchik and Van Haywood.[34]

History

A thorough history must be taken prior to treatment. All past, present and future medication and treatments must be inquired about. This will help provide insight into clinical observances (xerostomia, gingivitis) and prediction for clinical outcomes. Medical history will be of special importance with regards to bisphosphonate patients (especially IV) or cancer patients, as past treatment can have clinical effects even after treatment has stopped.[35] Such patients are still at risk of osteonecrosis of the jaw (ONJ) even post-treatment and, as such, special importance must be placed on reducing potential invasive procedures by ensuring optimum oral hygiene.

Previous oral hygiene behaviours must be inquired about. This is essential as standard oral hygiene practice should be demonstrated or attempted prior to commencing additional prevention.

Dental examination

An initial, thorough dental examination must be carried out prior to commencing treatment. This must include all soft, hard tissue, temporomandibular joints and occlusion. Vitality testing and radiographs of any suspect teeth should be carried out prior to commencing treatment to assess for any pathology. This is essential as teeth with existing periapical pathoses have been known to be exacerbated during 10% CP custom tray treatment.[36]

It is also essential that any restorations in the aesthetic area are identified prior to treatment. It should be explained to the patient that, post-treatment, the restorations shade may no longer match and therefore require replacing.

Initial treatment

If possible, existing carious lesions, periodontal disease and periapical pathoses should be treated prior to commencing treatment. An initial dental prophylaxis is also recommended prior to impression-taking.

Impressions

Alginate impressions of the areas to be treated must be taken. Accurate record of the teeth and several millimetres of adjacent tissue is required.

Pouring impressions and tray design

Impressions can be poured in the traditional manner. A non-scalloped, straight line tray with no reservoirs, which extends to cover 1 mm beyond the gingival margin, is suggested for caries prevention, oral hygiene improvement and plaque reduction.

The 0.035" soft, thin, flexible vacuum-formed thick material is used in most cases. Patients suffering from mild bruxism can use 0.060" and 0.080" trays. However, if the bruxism is more severe, day time use may be beneficial to reduce possible pumping of the CP out of the tray during parafunction. It is essential that the tray doesn't extend onto the incisive papilla, frenal attachments and into undercuts. Undercuts can be blocked out with light-activated resin before tray fabrication. The tray should be trimmed using sharp tissue scissors (ultra trim scissors, Optident, UK).

Delivery

It is essential that the fit of the customized tray is examined intra-orally and adjusted as required. There should be no blanching of the soft tissues and the patient should identify any uncomfortable areas. This will minimize mucosal trauma, which will be of extreme importance in high risk bisphosphonate patients to minimize ONJ risks,[37] and in patients with thin gingival biotype which may be damaged by ill-fitting margins.

Delivery of the tray should be provided with adequate detailed oral and written instructions to either the caregiver or the patient (Figure 4). It has been reported that, in 20% of patients, wearing the custom tray alone can result in sensitivity.[38] Therefore, it may be beneficial for the patient to try the tray in empty for one or two nights to adjust to any sensations and improve patient tolerance. Tray-applied CP can be used overnight or during day time for a minimum of two hours.

It is essential that the correct placement and amount of 10% carbamide peroxide is demonstrated or explained to the patient. The correct amount will only cover the tooth surfaces without excessive leakage and will vary for each custom tray and each patient. However, in the author's experience, this will roughly be one fifth of a 1.2 ml syringe of 10% CP gel. The 30 second use of chlorhexidine prior to the overnight tray application of 10% CP, as described previously, should also be described to the patient.

Boil and form tray: orthodontic patients only?

For orthodontic patients undergoing treatment, traditional vacuum custom trays are not practical. Owing to the movement of teeth, a new tray would be required every few months. Furthermore, accurate alginate impression of orthodontic

patients are difficult due to brackets and wires, especially in the gingival margin area. A possible solution to this is the boil and form tray. This involves using a thermoplastic preformed tray, bringing it to the boil and adapting it to the mouth using finger pressure. The tray is then trimmed and polished to fit.[39] As no impressions are required, this type of tray is also ideal for those patients who can't tolerate impressions.

Side-effects and safety

The long-term safety profile of prolonged 10% CP use is well known, with 10 year follow-up studies demonstrating no noticeable side-effects up to 10 years following a six week treatment.[40]

Sensitivity is the main side-effect resulting from 10% CP in custom trays. Unlike other forms of tooth sensitivity, whereby the mechanism of action is explained by Brännström and Åström's hydrodynamic theory,[41] CP-associated sensitivity results from easy passage of CP breakdown products (hydrogen peroxide and urea)[42] through the dentine, enamel and pulp. The sensation of the sensitivity often occurs during the early stages of treatment, usually persists for two to three days, is usually mild to moderate in severity and transient in nature.[36]

A detailed sensitivity history on initial patient examination is the best way to predict future sensitivity. Patients should be asked if their teeth are sensitive to cold stimuli. Existing sensitivity can be examined by gently blowing air on teeth or contacting teeth with the dental probe. All other predisposing factors, such as pulp size, exposed dentine, cracks, gingival recession, caries, sex or age of the patient, or other physical characteristics are not predictive of who would have sensitivity.[43]

Those with a history of sensitivity should brush with a desensitizing toothpaste containing potassium nitrate (such as *Pronamel Daily Protection*, GlaxoSmithKline Consumer Healthcare) for 2 weeks prior to commencing treatment and should continue brushing with the toothpaste during the treatment.[44] As mentioned previously, wearing an empty tray for one or two nights prior to treatment will also be beneficial.[45]

If sensitivity occurs during treatment, a passive approach could be taken, whereby the frequency of application of CP or wearing time is reduced. An active approach, involving placement of a desensitizing toothpaste in the custom tray for 10–30 minutes, is also another possible option. If the active approach is chosen, a toothpaste without sodium lauryl sulphate should be used to minimize gingival irritation. Modern CP formulations contain potassium nitrate and fluoride to reduce sensitivity.[43]

Gingival irritation is also a commonly observed clinical side-effect in tooth bleaching. It may or may not occur with tooth sensitivity. For most patients, gingival irritation is tolerable and is not a barrier to completing the treatment. An ill-fitted tray is usually the primary cause for the irritation and the problem is usually resolved by properly trimming the tray. Higher concentrations (greater than 10% CP) and extrusion of CP out of the tray can also cause gingival irritation.[36] This can be prevented by ensuring that the patient uses the correct amount (as mentioned earlier) of CP in the tray and ensuring that excess CP is wiped away after tray placement intra-orally. This should be mentioned to the patient at the delivery stage of treatment.

Another 'side-effect' of using CP is the bleaching of the teeth. This may be beneficial to the patient but, as mentioned earlier, may result in restorations in the aesthetic zone no longer being a matching shade and thus requiring replacement. The patient must be informed about this prior to obtaining full consent.

An increase in calculus build-up may also result from custom tray-applied CP. This is because calculus is more likely to form in a basic environment.[46] Although calculus doesn't directly cause periodontal disease, it is a plaque-retentive factor and therefore should be removed.[47]

Cost effectiveness

The cost of the proposed treatment may be more expensive than traditional oral hygiene methods. There are several CP-containing mouthwashes available, such as Gly-Oxide® (GlaxoSmithKline), which are more affordable than CP in syringe form. However, these products do not contain carbopol and, as a result, do not remain in the tray as long as CP in syringe form. Therefore, the substantivity is much less than CP available in syringes. If a more viscous, bulk CP product could be developed, the treatment would be more economical.

The costs and benefits of the treatment (Table 1) must be discussed on an individual basis with the patient. A better informed, more demanding elderly population is less likely to accept poor aesthetics associated with extrinsic staining and traditional treatment philosophies based around extractions and replacement of teeth with complete dentures.[48] Furthermore, complex restorative work of a failing dentition is biologically, psychologically and financially costly. Poor plaque control in orthodontic patients may lead to white spot lesions, accelerated bone loss and eventual termination of treatment.[49] Therefore, the proposed treatment may be cost-effective amongst several patients.

Costs	Benefits
■ Purchase of CP ■ Fabrication of customized/ boil and form tray	■ Preservation of existing restorations ■ Preservation of teeth ■ Prevention of pain associated with oral disease ■ No extrinsic staining associated with traditional chlorhexidine mouthwashes ■ Prevention of white spots, bone loss and termination of treatment associated with poor oral hygiene and orthodontics

Table 1. A list of potential costs and benefits of tray-applied orthodontic treatment.

Conclusion

Oral hygiene and plaque control are essential to the prevention of oral

disease. However, traditional oral hygiene methods may not always be sufficient. The use of custom/boil and form applied CP may provide clinicians and patients with a simple, safe and effective method for improving patients' oral hygiene and oral health when traditional methods are unsatisfactory. The application method required little manual dexterity, which is beneficial for elderly and special care patients. Patient/carer compliance and traditional oral hygiene practice is still essential and must be emphasized to the patient.

Ultimately, further research is still required to prove the effectiveness of the treatment definitively and also to develop a more cost-effective product.

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